

# Consensus Recommendations From the American Acne & Rosacea Society on the Management of Rosacea, Part 1: A Status Report on the Disease State, General Measures, and Adjunctive Skin Care

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*Rosacea is a common clinical diagnosis that encompasses a variety of presentations, predominantly involving the centrofacial skin. Reported to present most commonly in adults of Northern European heritage with fair skin, rosacea can affect males and females of all ethnicities and skin types. Pathophysiologic mechanisms that appear to correlate with the manifestation of rosacea have been the focus of multiple research studies, with outcomes providing a better understanding of why some individuals are affected and how their visible signs and symptoms develop. A better appreciation of the pathophysiologic mechanisms and inflammatory pathways of rosacea*

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This article is the first of a 5-part series. The second part will appear next month.

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has allowed therapeutic strategies to be optimally incorporated. Part 1 of this 5-part series discusses the rosacea disease state with an emphasis on clinical correlation, reviews adjunctive skin care for cutaneous rosacea, and provides management caveats.

*Cutis*. 2013;92:234-240.

**G**uidelines on the management of rosacea have been previously published by the American Acne & Rosacea Society; however, these guidelines were limited to medical management and were developed prior to the emergence and/or consolidation of more recent data on pathophysiologic mechanisms associated with rosacea.<sup>1</sup> In March 2013, an update on the pathophysiologic mechanisms, clinical manifestations, and overall management of rosacea was published in a supplement from the American Acne & Rosacea Society.<sup>2</sup> This publication reviewed the most current and clinically applicable information on pathophysiologic mechanisms that appear to be operative in rosacea, with emphasis on the major clinical presentations of central facial erythema without inflammatory lesions (erythematotelangiectatic rosacea [ETR][subtype 1]) and central facial erythema with inflammatory lesions (papulopustular rosacea [PPR][subtype 2]).<sup>3</sup> Of course, new information and data gleaned from research on pathophysiologic mechanisms of the disease are a moving target, and we must remain open-minded regarding new concepts that are brought forward, especially when careful analysis suggests potential scientific validity.

An important concept to recognize is that the term *rosacea* does not define one specific clinical presentation. Rosacea is a diagnosis that is made clinically and is comprised of a variety of potential clinical manifestations that vary in presentation and magnitude among different patients.<sup>1,3-11</sup> Individual clinical features of rosacea, especially those that become persistent between flares, also vary in the timing of their emergence over the course of the disease.<sup>1,3-8,10-13</sup> Ultimately, the pathophysiologic mechanisms that are believed to be associated with rosacea may or may not be operative, or they may vary in the degree of their contribution to the clinical presentation of rosacea in an individual patient at any given point.<sup>7,8,10-14</sup>

## DIAGNOSIS AND CLINICAL ASSESSMENT OF ROSACEA

The diagnosis of rosacea is based on clinical evaluation of the patient's medical history, physical examination, and reasonable exclusion of other disorders that may be included in the differential diagnosis on a case-by-case basis.<sup>1,3-8</sup> The introduction of rosacea

subtypes in 2002 helped to better define individual clinical presentations of rosacea based on specific signs and symptoms.<sup>3</sup> The use of subtypes to better define the clinical diagnosis of rosacea was a major advance for dermatologists, and clinicians now share the common ground for diagnosis based on a peer-reviewed publication authored by dermatologists who are recognized for their strong research and/or clinical interest in rosacea. This landmark publication provided a foundation for discussion about rosacea, with a greater likelihood that dermatologists would be on the same page regarding its clinical manifestations in any given patient. Subtype classification also facilitated the evaluation of rosacea therapies to better select treatments that may be more or less beneficial for treating specific clinical features.<sup>3,5,7,8</sup>

The subtype designations are buckets that assist in categorizing rosacea presentations; however, these subtypes do not take into account the chronicity of the disease or the evolution of individual clinical features over time. Based on more recent research that was not available when the subtype classification was written, the clinical features of rosacea appear to correlate with different pathophysiologic mechanisms, with differences in expression of specific features noted among rosacea patients.<sup>2,5,7,8,13,14</sup> Rosacea management is best approached via assessment of the spectrum of clinical manifestations present in each individual patient at the time of his/her presentation. Categorization by subtype may lead some clinicians to use an algorithmic approach to therapy based on which diagnostic bucket applies to the patient. With patients classified by subtype, selection of therapy may be limited by preconceived concepts of therapies that are reported to be effective for that subtype designation rather than individual therapies that are correlated with the specific clinical manifestations present at the office visit. A rational approach when evaluating a patient with rosacea is to take into account the broad range of interpatient variability in specific clinical features that cross lines which tend to separate subtypes; the relative contribution of each feature to the overall clinical picture; and the appreciation of the chronicity of rosacea.<sup>2,7,8</sup> From this standpoint, therapeutic options can then be considered based on our current understanding of how effectively they address both the specific manifestations of rosacea and their degree of contribution to the overall clinical picture. Multiple therapies often are warranted, either in combination or staggered in their sequence of use.

## MAJOR CLINICAL PRESENTATIONS OF ROSACEA

A description of the natural course of rosacea was originally described in 1975 and appeared in publication

in a more recent textbook edition in 2000,<sup>4</sup> revealing that over time rosacea progresses in the following stages: prerosacea (intermittent flushing only); persistent facial erythema with intermittent bouts of facial flushing; facial erythema with flares that also exhibit inflammatory lesions; and ultimately a more severe state of facial erythema and inflammatory lesions, with or without phyma development. This description of rosacea progression was based on the clinical impressions of the authors, primarily due to the absence of any published or independently performed longitudinal studies on the natural course of rosacea.<sup>4</sup> However, although patients may exhibit changes in clinical manifestations over time, there is no definitive evidence or consensus that rosacea progresses in these stages. The use of the term *subtype* was suggested in a 2002 publication on rosacea diagnosis and classification by a panel of dermatologists working with the National Rosacea Society.<sup>3</sup> The subtype classification improved the clinical differentiation of the major patterns of rosacea based on signs and symptoms.

It is currently believed that many rosacea patients indefinitely present with the same overall clinical patterns, though some features such as intensity of persistent facial erythema and visible telangiectases may worsen over time.<sup>2,3,5,7,8</sup> It also is recognized that some patients can exhibit additional features at a later point in time such as phymatous changes or inflammatory lesions that did not occur in the past.<sup>3,5,7,8</sup> The latter observation further supports the importance of approaching the management of rosacea based on the clinical manifestations noted in the individual patient at that point in time.

The central diagnostic feature that is almost universally present in rosacea is diffuse centrofacial erythema (DCE), which increases in intensity during a flare. This reaction often is referred to as flushing and is due to acute or subacute vasodilation of superficial cutaneous vasculature.<sup>2,3,5,7,8,13,14</sup> Telangiectases commonly are present. Inflammatory lesions may or may not be present. When they are present, inflammatory lesions define the group with papulopustular rosacea (papulopustular lesions and facial erythema during a flare).

Diffuse centrofacial erythema intensifies in magnitude during a flare and persists between flares at a lesser degree of intensity as persistent DCE (vascular erythema). The flared state is induced by triggering certain neurovascular and acute inflammatory pathways in rosacea-prone skin.<sup>5,9</sup> There are multiple potential sources that collectively contribute to overall facial erythema in rosacea. It is important to differentiate these factors from a clinical perspective, as each is responsive to certain therapeutic approaches but may not be as responsive to others.<sup>7,8</sup>

### Facial Erythema Only

Erythematotelangiectatic rosacea (subtype 1) is the most common presentation of rosacea<sup>3,5,6</sup> and is clinically defined as DCE secondary to sustained vasodilation without inflammatory lesions and often with symptoms of skin sensitivity (eg, stinging, burning).<sup>3</sup> The increased facial erythema that occurs during an ETR flare represents acute vasodilation and innate inflammation, which exacerbate the intensity of DCE and associated symptoms (Figure 1).<sup>3,5,7,8,13,14</sup> The DCE that persists between ETR flares is due to the presence of enlarged and chronically dilated superficial cutaneous vasculature and telangiectases (fixed vascular changes) that have developed over time.<sup>1-8,13,14,15</sup> Concurrent with the increase in facial erythema during a flare, soft centrofacial edema of varying severity also may be present, occurring secondary to extravascular fluid leakage with associated perivascular inflammation and lymphedema caused by engorgement of lymphatic vessels.<sup>3,5,7,13,14</sup> Persistent erythema and telangiectasia formation can be seen in association with both chronic photodamage and rosacea, especially in individuals with fair skin (ie, Fitzpatrick skin types I and II).

At times, the clinical differentiation of rosacea from chronic photodamage may be challenging for clinicians. In cases of chronic photodamage, cutaneous involvement tends to be more diffuse, affecting the lateral face and neck, sometimes with



**Figure 1.** A woman with a rosacea flare who presented with diffuse centrofacial erythema with increased intensity of symptoms of burning and stinging. Multiple telangiectases were present and papulopustular lesions were absent.

poikilodermatous changes (eg, poikiloderma of Civatte). In males with chronic photodamage, the helices of the ears often exhibit persistent erythema. Facial erythema associated with rosacea tends to exhibit centrafacial predominance. Unlike chronic photodamage, intermittent flares of DCE occur in rosacea. Of course, many patients with rosacea also may have concurrent skin changes resulting from chronic photodamage, as facial skin is frequently exposed to sunlight over time.

### Facial Erythema With Inflammatory Lesions

The second most common clinical presentation of rosacea is PPR (subtype 2), which is clinically defined by the presence of inflammatory lesions, predominantly in a centrafacial distribution and usually with DCE (Figure 2).<sup>3</sup> Facial erythema associated with PPR is almost always multifactorial with relative contribution from at least 4 distinct sources: (1) erythema directly associated with the inflammatory lesions themselves (lesional erythema); (2) focal concentric flaring of erythema that surrounds individual inflammatory lesions (perilesional erythema); (3) erythema secondary to inflammatory cascades that are augmented during a PPR flare; and (4) erythema associated with acute vasodilation and chronic vasodilation, the latter being secondary to fixed vascular changes that persist between flares.<sup>1-8,10,13-18</sup> In some cases, PPR presents with inflammatory lesions and a predominance of focal perilesional erythema with little to no diffuse facial erythema (Figure 3). It is likely that the underlying pathophysiologic pathways that collectively translate to visible manifestations of PPR differ among patients in their presence and/or relative intensity, thus accounting for the interpatient variability that often is observed in clinical practice.<sup>3,5,7,8</sup> Presenting in rosacea patients with facial erythema only, centrafacial edema also may occur in patients with rosacea who exhibit facial erythema with papulopustular lesions.

### Phymas

Phymatous rosacea (subtype 3) is characterized primarily by sebaceous and fibrous coalescent tissue proliferation that most commonly affects the distal nose but also can affect other facial skin sites such as the chin or forehead.<sup>3-5</sup> Phymatous rosacea often coexists with other signs and symptoms of rosacea, including the PPR and ETR subtypes. In some cases, phymas occur alone, with or without visible skin inflammation.<sup>3-6,12-14</sup>

### Ocular Disease

Ocular rosacea (subtype 4) is reported to present in 50% or more of patients with cutaneous rosacea.



**Figure 2.** A man with a papulopustular rosacea flare associated with diffuse centrafacial erythema that was composed of both lesional/perilesional erythema and vascular erythema (background erythema). Diffuse fine flaking of facial skin was characteristic of rosacea dermatitis.



**Figure 3.** A woman with a rosacea flare characterized by multiple inflammatory lesions (papules and pustules) that predominantly involved the central face with lesional/perilesional erythema and minimal vascular erythema.

Ocular rosacea can exist alone and most often affects the eyelids; it also can involve the conjunctivae, sclerae, and/or corneas. Flares generally are independent of the activity or severity of concurrent cutaneous rosacea, if present (Figure 4).<sup>3,19-21</sup> Signs



**Figure 4.** A flare of ocular rosacea with blepharitis, conjunctivitis, and scleritis in an adult male with minimal cutaneous rosacea (papulopustular type). Eyelid swelling and erythema with conjunctival and scleral injection were noted. The patient reported grittiness and foreign body sensation in the eyes, with absence of visual changes or symptoms. No corneal abnormalities were found on ophthalmologic examination. The patient responded to use of sulfacetamide eyedrops and oral doxycycline.

and symptoms of cutaneous rosacea precede ocular involvement in approximately 50% of cases that exhibit concurrent involvement of both the facial skin and eyes; in approximately 20% of cases, signs and symptoms of ocular rosacea precede cutaneous rosacea.<sup>19-21</sup> Although the management of ocular rosacea is not emphasized in our discussion, clinicians are encouraged to inquire about symptoms suggestive of ocular rosacea (ie, sensitivity to light; stye; gritty, scratchy, itchy, red, or bloodshot eyes; blurred vision; eye allergies; foreign body sensation) and to examine the eyes for visible signs of ocular rosacea (eg, blepharitis, conjunctivitis, scleritis, stye formation).

## DIFFERENTIAL DIAGNOSIS

Clinicians are encouraged to consider other facial disorders that may simulate rosacea in the differential diagnosis,<sup>3</sup> including disorders that are associated with facial erythema, with or without inflammatory lesions, and some that also wax and wane in intensity with bouts of dilation of facial vasculature (flushing), with or without presence of facial edema. Facial disorders that may simulate individual presentations of rosacea include chronic photodamage; contact dermatitis; seborrheic dermatitis; early chronic cutaneous lupus erythematosus; systemic lupus erythematosus; carcinoid syndrome; and other underlying disorders associated with intermittent flushing, altered metabolism of ingested alcohol due to genetic enzyme mutations (ie, Asian red face syndrome), and niacin ingestion.<sup>3</sup>

## RECOMMENDATIONS ON ADJUNCTIVE SKIN CARE: AN INTEGRAL COMPONENT OF ROSACEA MANAGEMENT

After a diagnosis of rosacea is made, management should be directed at clearing and/or reducing signs and symptoms, with multiple therapies often required to optimize therapeutic outcomes. A few general recommendations on adjunctive skin care are suggested that may augment therapeutic response and reduce the risk for skin tolerability reactions.

### General Skin Care

Skin care designated by the dermatologist or his/her assigned staff is suggested as a component of rosacea management. The stratum corneum (SC) permeability barrier is impaired in patients with rosacea and is characterized by increased centofacial transepidermal water loss.<sup>5,7,8,22</sup> The impairment of the SC permeability barrier is known to jump-start the release of cytokines tumor necrosis factor  $\alpha$ , IL-1, and IL-6, and associated cutaneous inflammation as the compromised epidermis initiates self-repair; these changes sometimes progress to rosacea dermatitis, with visible signs such as fine scaling and peeling (Figure 2) and associated symptoms of heightened skin sensitivity (ie, stinging, burning).<sup>22-24</sup> Heightened skin sensitivity may occur with exposure to many commonly used skin care and personal hygiene products.<sup>25</sup> Symptoms of sensitive skin tend to be more common and more severe in patients with DCE only (classic ETR), though exceptions exist with many untreated patients with PPR reporting facial skin symptoms such as stinging and burning.<sup>2,5,6,26-28</sup>

*Management Caveats*—Clinician-designated skin care, including a gentle, well-formulated facial cleanser and moisturizer/barrier repair product, is an important component of the overall management of rosacea, with some data demonstrating the ability to adjunctively improve therapeutic outcomes and reduce skin irritation in patients undergoing medical therapy.<sup>1,6,24,26,29-34</sup>

To our knowledge, no large-scale comparative studies of rosacea patients are available to definitively recommend any individual skin care products; however, facial cleansers and moisturizers should be selected based on their ability to repair and maintain SC permeability barrier function, enhance skin hydration, and reduce the likelihood of skin irritation potentially associated with exogenous insults such as topical medications. Products also should not contain additives that are likely to induce irritant or allergic contact dermatitis and should ultimately be cosmetically pleasing to the patient.<sup>24,26,29-33</sup>

Although some skin care products containing various cosmeceuticals are promoted for the treatment of rosacea and/or reduction of facial redness, scientific

evidence in this area is limited and data from studies specifically for rosacea are sparse.

### Photoprotection

Although there is controversy regarding the role of chronic photodamage in the pathogenesis of rosacea, it is apparent that many of the clinical features of photodamage and persistent nontransient facial erythema in patients with rosacea are clinically similar (eg, fixed erythema, telangiectasia).<sup>5,7,8,14,35-37</sup> A recent study demonstrated molecular distinctions between 2 diagnostic groups: rosacea patients presenting with facial erythema only (classic ETR subtype) and nonrosacea patients with chronic photodamage presenting with facial erythema.<sup>38</sup> Participants in each group were differentiated by clinical assessment following protocol-based criteria before undergoing facial skin biopsy. The biopsy specimens were tested using multiple recognized methods that evaluated biologic markers and patterns of inflammation. This study showed different patterns and/or magnitudes of increased expression of several specific skin cytokines, enzymes, neuropeptides, cellular receptors, and mast cells in the study group with rosacea-affected skin compared to the nonrosacea group with chronic facial photodamage.<sup>38</sup> In addition, acute UV light exposure serves as a trigger for flaring of rosacea by stimulating innate inflammation, and UV exposure is a possible source of depletion of antioxidant reserve that has been noted in rosacea-affected skin, with the magnitude of depletion shown to correlate with rosacea severity.<sup>7,8,14,16,36,39</sup>

**Management Caveats**—Regular photoprotection through use of sun exposure avoidance techniques and proper sunscreen/sunblock use should be integrated into rosacea management.<sup>1,6-8,32,33</sup> As an integral part of rosacea management, regular photoprotection serves to reduce the likelihood that acute UV exposure will reach the threshold to trigger a flare of rosacea, though ambient heat can still induce a flare of rosacea independent of the level of UV exposure. Secondly, regular photoprotection also reduces skin changes that develop over time with chronic photodamage such as fixed erythema and telangiectases that stack onto the similar fixed vascular changes produced by rosacea over time.<sup>5-8</sup>

Although there is no particular sunscreen product that has been scientifically shown to be consistently superior in patients with rosacea, a product with a sun protection factor of 30 or greater should be considered to protect against incidental sun exposure. With assistance from clinicians and their staff, patients are encouraged to choose facial products that contain sunblock/sunscreen to provide adequate photoprotection, do not cause signs or symptoms of skin irritation

or allergy, and are cosmetically pleasing. In situations where the skin is exposed to water (eg, swimming) or profuse sweating, use of a water-resistant sunscreen can be beneficial, but it does not preclude the need for reapplication with prolonged sun exposure or after water exposure.

### CONCLUSION

Rosacea is a chronic inflammatory facial skin disorder seen predominantly in adults that exhibits a variety of clinical features and is associated with intermittent flares. Diffuse centrofacial erythema is a major feature of rosacea. Impairment of the SC permeability barrier appears to contribute to cutaneous inflammation and symptoms of skin sensitivity such as stinging and burning. Proper skin care and photoprotection both serve important roles in the management of rosacea and should be integrated into the treatment plan to assist in optimizing the therapeutic outcome. Part 2 of this series will discuss medical therapies in the management of rosacea, including topical therapies approved by the US Food and Drug Administration and other alternative topical therapies as well as newly emerging therapies.

**Acknowledgment**—The recommendations published here are primarily based on thorough literature review and observations from clinical experience and research when supported by reasonable consensus among the authors.

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