Standard Management Options for Rosacea, Part 2: Options According to Subtype

Richard Odom, MD; Mark Dahl, MD; Jeffrey Dover, MD; Zoe Draelos, MD; Lynn Drake, MD; Marian Macsai, MD; Frank Powell, MD; Diane Thiboutot, MD; Guy F. Webster, MD, PhD; Jonathan Wilkin, MD; National Rosacea Society Expert Committee on the Classification and Staging of Rosacea

The standard management options were developed by a consensus committee and review panel of 26 experts to assist in providing optimal patient care based on the standard classification and grading systems for rosacea that were developed to perform research; analyze results and compare data from different sources; and provide a common terminology and reference for the diagnosis, treatment, and assessment of results in clinical practice. We discuss the standard management options for rosacea in 2 parts: (1) overview and broad spectrum of care, and (2) management options according to subtype. The menu of options is considered provisional and may be expanded and updated as appropriate.

Managing the various potential signs and symptoms of rosacea calls for consideration of a broad spectrum of care, and a more precise selection of therapeutic options may become increasingly possible as the mechanisms of action of therapies are more definitively established.

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Dr. Odom is from the Department of Dermatology, University of California, San Francisco. Dr. Dahl is from the Department of Dermatology, Mayo Clinic, Scottsdale, Arizona. Dr. Dover is from the Department of Dermatology, Yale University, New Haven, Connecticut. Dr. Draelos is from Dermatology Consulting Services, High Point, North Carolina. Dr. Drake is from the Department of Dermatology, Harvard University, Boston, Massachusetts. Dr. Macsai is from the Department of Ophthalmology, Northwestern University, Chicago, Illinois. Dr. Powell is from the Department of Dermatology, Mater Misericordiae University Hospital, Dublin, Ireland. Dr. Thiboutot is from the Department of Dermatology, The Pennsylvania State University College of Medicine, Hershey. Dr. Webster is from the Department of Dermatology, Thomas Jefferson University, Philadelphia, Pennsylvania. Dr. Wilkin is from the National Rosacea Society Medical Advisory Board, Barrington, Illinois.
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Correspondence: Richard Odom, MD, National Rosacea Society, 196 James St, Barrington, IL 60010 (nrosacea@aol.com).

Management of Rosacea by Subtype

The management of rosacea should be tailored to address the individual signs and symptoms of each patient and often may be keyed to subtypes and levels of severity while noting that patients often experience more than one subtype concurrently.[1] Using the standard grading system, primary features of each subtype are graded as mild, moderate, or severe (grades 1–3, respectively), and most secondary signs and symptoms are graded as simply present or absent (Tables 1–4). All patients should be advised of proper skin care procedures, including the use of sunscreen as well as avoidance of environmental and lifestyle factors that may affect their individual cases.

Subtype 1: Erythematotelangiectatic Rosacea

Erythematotelangiectatic rosacea is primarily characterized by flushing and persistent erythema of the central face. The appearance of telangiectases is common but not essential to the diagnosis, while burning and stinging sensations, edema, and roughness or scaling are common secondary features.

Table 1.

Management Options for Erythematotelangiectatic Rosacea (Subtype 1)

Clinical Features	Grade	Typical Features by Grade	Therapeutic Approach
Flushing and persistent erythema of the central face; possible telangiectases; easily irritated facial skin; burning and stinging may be reported; edema, roughness, or scaling may be present	1 (mild)	Occasional mild flushing, faint persistent erythema, rare telangiectases	Identification and avoidance of environmental and lifestyle triggers to minimize flushing and irritation may be especially important in addition to an appropriate skin care regimen; nonirritating cosmetics may conceal the appearance of erythema and telangiectases
	2 (moderate)	Frequent troublesome flushing, moderate persistent erythema, several distinct telangiectases	In addition to above: long-pulsed dye or KTP lasers or IPL devices can remove telangiectases and reduce vascular erythema, and may reduce flushing
	3 (severe)	Frequent severe flushing; pronounced persistent erythema; possible edema; many prominent telangiectases; possible burning, stinging, roughness, or scaling	In addition to above: flushing may be moderated by drugs specific to individual causes, such as NSAIDs for dry flushing, α-agonists or beta-blockers for neurally induced flushing, HRT for menopausal flushing; thermoregulatory flushing can be reduced by cooling the neck and mouth; emotionally induced flushing may benefit from psychological counseling or biofeedback

Abbreviations: KTP, potassium-titanyl-phosphate; IPL, intense pulsed light; NSAIDs, nonsteroidal anti-inflammatory drugs; HRT, hormone replacement therapy.

Patients with this subtype often have a history of flushing alone.

Because this subtype of rosacea may be difficult to treat, identification and avoidance of environmental and lifestyle triggers to minimize flushing and irritation of the skin may be especially important.[1]

Although no drugs to reduce flushing have been approved by the US Food and Drug Administration (FDA), off-label use of certain medications may potentially have a moderating effect for grades 2 and 3 flushing. It should be noted, however, that there are no broad-spectrum

antiflushing medications, and those specific to the cause of the flushing should be chosen.

Flushing is a phenomenon of vasodilation that can be considered an abnormality of cutaneous vascular smooth muscle control. Vascular smooth muscle is controlled by circulating vasoactive agents or by autonomic nerves.

Circulating vasoactive agents are associated with dry flushing and may be exogenous (eg, alcohol, calcium channel-blocking agents, and nicotinic acid [niacin]) or endogenous (eg, histamine and prostaglandins). Management options to mediate flushing caused by endogenous agents may include aspirin, indomethacin, or other nonsteroidal anti-inflammatory drugs that also may reduce erythema. Antihistamines may be prescribed to reduce flushing related to histamines produced endogenously or exogenously by certain foods.[2]

When vasodilation is controlled by autonomic nerves, it is accompanied by sweating.[2] This flushing usually results from heat in the ambient surroundings or from exercise or hot drinks, for example. In this case, flushing may be reduced by cooling the neck and face with a cold wet towel or a fan. Ice chips held in the mouth and ingestion of ice water may be effective.[2] Flushing also may be diminished, of course, by avoidance of other potential environmental and lifestyle factors.[1]

In severe cases, the alpha 2 agonist clonidine or a beta-blocker such as nadolol may sometimes reduce neurally mediated flushing.[2] For women with menopausal flushing, hormone replacement therapy prescribed by a gynecologist or primary care physician could be considered but should be used with caution.

Flushing also may have emotional origins for some patients, and these individuals may additionally benefit from psychological counseling or biofeedback.

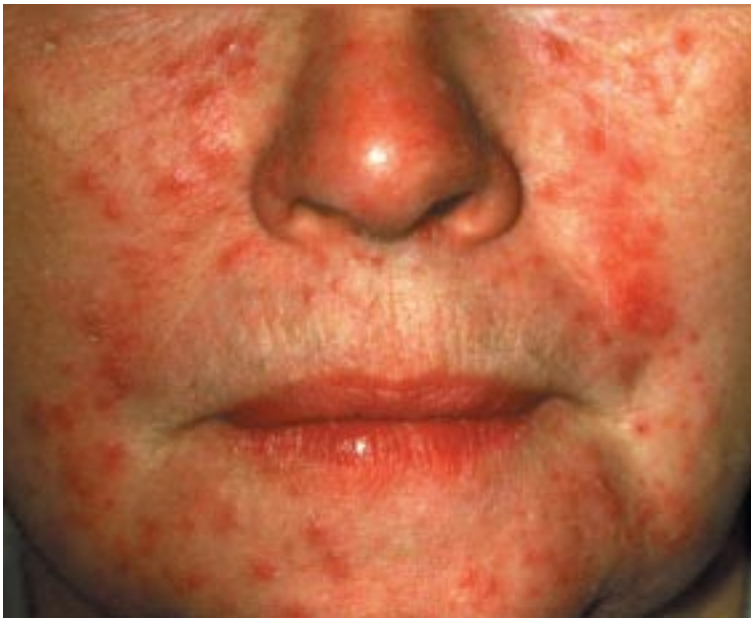
Telangiectases and background erythema are commonly treated with laser therapy,[3-8] including long-pulsed dye, potassium-titanyl-phosphate, and diode lasers, which have been associated with little or no purpura.[4] They also may be reduced by intense pulsed light therapy,[7,9] and electrocautery is an additional option for telangiectasia. Although published clinical data are limited, lasers and intense pulsed light also may be used to reduce flushing.[6]

The appearance of flushing, erythema, and telangiectases also may be concealed with cosmetics.[1] In addition, burning, stinging, roughness, and/or scaling may be minimized by selecting appropriate over-the-counter products, including nonirritating cosmetics, nonsoap cleansers, moisturizers, and appropriate cleansing techniques. Sunblocks or sunscreens may be particularly important.

Subtype 2: Papulopustular Rosacea

This subtype is characterized by persistent central facial erythema with transient central facial papules or pustules, or both (Figure). In these patients, topical therapies and oral antibiotics are prescribed, though the modes of action have not been definitively established.

Topical therapies FDA approved for the treatment of rosacea including metronidazole and azelaic



Subtype 2 (papulopustular) rosacea is characterized by persistent central facial erythema with transient central facial papules or pustules, or both.

Table 2.

Management Options for Papulopustular Rosacea (Subtype 2)

Clinical Features	Grade	Typical Features by Grade	Therapeutic Approach
Persistent erythema with transient papules and/or pustules of the central face, burning and stinging may be reported	1 (mild)	Few to several papules or pustules without plaques, mild persistent erythema	Topical therapy, possibly with an initial course of oral antibiotic, to bring symptoms under control, and use topical medication alone to maintain remission; a controlled-release anti-inflammatory dose of oral antibiotic may be used
	2 (moderate)	Several to many papules or pustules without plaques, moderate persistent erythema	In addition to above: possibly an oral antibiotic in divided doses or an anti-inflammatory dose until remission is achieved, with or followed by long-term topical therapy
	3 (severe)	Numerous and/or extensive papules or pustules with or without plaques, severe persistent erythema, possible burning and stinging	In addition to above: in refractory cases, alternative oral and topical therapies may be used; skin care regimen may address burning and stinging

acid as well as topical sodium sulfacetamide–sulfur may be used alone or in conjunction with oral therapy administered initially or at any point during treatment. A controlled-release formulation of oral doxycycline is FDA approved for rosacea with low plasma levels that do not exert antimicrobial effects while retaining anti-inflammatory activity.[10] Topical therapy and/or a controlled-release oral therapy for rosacea may be used for grades 1 and 2 disease. For grade 3, an oral antibiotic may be used initially with a topical therapy to bring the disorder under immediate control. Once remission has been achieved, it often may be maintained on a long-term basis with a topical or controlled-release agent alone for an indefinite period.[11]

In some cases, oral drug therapy for grades 2 and 3 and/or in patients with ocular involvement may consist of off-label systemic tetracycline (or other members of the tetracycline family) administered as 1 g/d in divided doses for 2 to 3 weeks, followed by 0.5 g/d for 2 to 3 weeks.[12] Some physicians may prescribe higher doses, longer courses, or other tetracyclines such as doxycycline or minocycline.

In refractory cases, off label oral trimethoprim-sulfamethoxazole, trimethoprim alone, metronidazole, erythromycin, ampicillin, clindamycin, or dapsone may be prescribed. Off-label isotretinoin reportedly may be effective, especially in otherwise refractory cases or when the patulous follicles of incipient rhinophyma are present. Use of isotretinoin requires careful monitoring, and long-lasting remission is not common.

Additional off-label alternatives for refractory rosacea may include other antibacterial agents, mild

Table 3.

Management Options for Phymatous Rosacea (Subtype 3)

Clinical Features	Grade	Typical Features by Grade	Therapeutic Approach
Skin thickening, irregular surface nodularities, and enlargement; rhinophyma is most common, but other affected locations may include the chin, forehead, cheeks, and ears; patulous follicles and telangiectases may occur	1 (mild)	Patulous follicles with no contour changes	Topical and systemic therapy as described for subtype 2 (papulopustular) rosacea if inflammatory lesions are present; carefully monitored isotretinoin may reduce incipient rhinophyma
	2 (moderate)	Change in contour without nodular component	In addition to above: may require surgical therapy, including cryosurgery, radiofrequency ablation, electrosurgery, heated scalpel, electrocautery, tangential excision combined with scissor sculpturing, skin grafting, and dermabrasion; CO_2 or erbium:YAG lasers may be used as a bloodless scalpel to remove excess tissue and recontour the nose
	3 (severe)	Change in contour with nodular component	See above

topical retinoids, or adapalene.[13,14] It also has been suggested in isolated reports that drugs eradicating *Demodex folliculorum* may play a role in treating certain cases of papulopustular rosacea, including topical permethrin; systemic ivermectin; and topical crotamiton, sulfur, and lindane.[15] Use on the face for patients with rosacea is off label, and if prescribed, patients should be cautioned about the irritation potential of these agents.

While there was historical speculation on the treatment of *Helicobacter pylori* to manage rosacea, studies found no substantial difference in the abatement of rosacea following *H pylori* treatment compared with patients in placebo control groups.[16,17]

In certain exceptional cases, short-term use of a low-strength topical steroid may be considered for rapid resolution of inflammation. However, long-term use of these agents often produces rosacealike manifestations, commonly called steroid-induced rosacea, and therefore should be avoided. Topical calcineurin inhibitors such as tacrolimus and pimecrolimus also may be of value in treating erythema from active inflammation,[12] though they have been reported to induce a rosacealike eruption.[18-21] Topical retinoids have been recommended by some to repair the dermis by decreasing abnormal elastin, increasing collagen, increasing glycosaminoglycan, and decreasing telangiectases.[22]

Possible burning and stinging sensations may be dealt with as described for erythematotelangiectatic rosacea.

Subtype 3: Phymatous Rosacea

In addition to a primary feature of rosacea (flushing, erythema, telangiectases, papules or pustules),

Table 4.

Management Options for Ocular Rosacea (Subtype 4)

Clinical Features	Grade	Typical Features by Grade	Therapeutic Approach
Watery or bloodshot appearance; foreign body sensation, burning or stinging, dryness, itching, light sensitivity, blurred vision, telangiectases of lid margins; lid and periocular erythema; blepharitis, recurrent conjunctivitis, styes (chalazion, hordeolum); episcleritis, iritis, and decreased visual acuity due to corneal complications (keratitis or ulcers) may occur	1 (mild)	Signs and symptoms affecting the eyelid margin and meibomian glands	Artificial tears and cleansing of eyelashes
	2 (moderate)	Signs and symptoms affecting the inner eyelid, tear secretion, and/or ocular surface	In addition to above: ophthalmic antibiotic ointment may be applied to eyelashes; an oral antibiotic also may be effective; if severity increases, consultation with an ophthalmologist may be needed
	3 (severe)	Advanced or nonresponsive disease of the eyelid margin or ocular surface; episcleritis, iritis, or keratitis in addition to corneal damage and potential vision loss	Care by an ophthalmologist is required and may include a topical steroid, alternative oral medications, and potential surgery

phymatous rosacea may include skin thickening, irregular surface nodularities, and patulous follicles. Enlargement commonly occurs on the nose (rhinophyma), though other affected locations may include the chin, forehead, cheeks, and ears.

Management options for grade 1 phymatous rosacea, with patulous follicles but no contour changes, include topical and systemic antibiotics if inflammatory lesions are present. Isotretinoin has been demonstrated to decrease nasal volume in rhinophyma, especially in younger patients with less advanced disease, though volume may increase again after therapy is stopped.[22,23] During isotretinoin therapy, numerous large sebaceous glands were reported to be diminished in size and number.[22] There also is evidence that topical retinoids may decrease fibrosis, elastosis, and sebaceous gland hypertrophy.[24-26]

Grades 2—change in contour without a nodular component—and 3—change in contour with a nodular component—phymatous rosacea may require surgical therapy, such as cryosurgery, radiofrequency ablation, electrosurgery, heated scalpel, electrocautery, tangential excision combined with scissor sculpturing, skin grafting, and dermabrasion. CO_2 or erbium:YAG lasers may be used as a bloodless scalpel to remove excess tissue and recontour the nose. Fractional resurfacing can be of value in mild cases.

Subtype 4: Ocular Rosacea

The common presentations of ocular rosacea are a watery or bloodshot appearance, foreign body sensation, burning or stinging, dryness, itching, light sensitivity, and blurred vision. A history of styes (chalazion, hordeolum) is a strong indication, as well as dry eye, recurrent conjunctivitis, or blepharitis. Telangiectases of the eyelid margins or lid and periocular erythema also may be present.

The meibomian glands typically are obstructed and often may be blocked. The formation of collarettes, narrow rims of loosened keratin around the base of the eyelashes, is common. A gritty granular symptom indicates damage to the ocular surface. Undiagnosed ocular rosacea may present with recurring inflammation such as episcleritis, iritis, and keratitis.

Ocular rosacea may appear in advance of the cutaneous form, and more than 60% of patients with cutaneous rosacea also may have ocular involvement. Treatment of cutaneous rosacea alone may be inadequate in lessening the risk for vision loss resulting from ocular rosacea, and referral to an ophthalmologist may be needed.

Treatment of grades 1 and 2 ocular rosacea may initially include artificial tears, and on a long-term basis, the patient should apply a warm compress and cleanse the eyelashes twice daily with baby shampoo on a wet washcloth rubbed onto the upper and lower eyelashes of the closed eyes. Antibiotic ointment may be appropriate to decrease the presence of *Propionibacterium acnes*, *Staphylococcus epidermidis*, and *Staphylococcus aureus*, and to soften any collarettes, allowing easy removal by the patient during eyelash hygiene. An oral tetracycline such as low-dose doxycycline may be necessary, and for grade 3 ocular rosacea, a topical steroid, cyclosporine ophthalmic emulsion, or alternative oral medications may be prescribed by the ophthalmologist. Any corneal ulceration requires immediate attention by an ophthalmologist, as it may involve loss of visual acuity.

Conclusion

Managing the various potential signs and symptoms of rosacea calls for consideration of a broad spectrum of care, and a more precise selection of therapeutic options may become increasingly possible as their mechanisms of action are more definitively known and the etiology and pathogenesis of rosacea are more completely understood. Meanwhile, however, the classification of rosacea by its morphologic features and grading by severity may serve as an appropriate guide for its effective management.

As with the standard classification and grading systems, the options described here are provisional and subject to modification with the development of new therapies, increase in scientific knowledge, and testing of their relevance and applicability by investigators and clinicians. Also, as with any consensus document, these options do not necessarily reflect the views of any single individual and not all comments were incorporated.

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