

# BEST PRACTICES IN:

## Treating Rosacea: Current Insights

### Is It Rosacea?

Individuals who experience erythema, papules and pustules, and visible blood vessels on their face often assume that these symptoms are the result of adult acne, sunburn or windburn, or normal effects of aging.<sup>1</sup> The culprit may actually be rosacea, a chronic skin disorder that, if not treated early, can continue to flare and worsen.

The differential diagnosis of rosacea is challenging because rosacea may resemble a number of other skin disorders, such as acne vulgaris, seborrheic dermatitis, perioral dermatitis, sarcoidosis, and lupus erythematosus.<sup>1</sup> Rosacea is sometimes misleadingly referred to as “acne rosacea,” but it is actually a very different disease from acne vulgaris. Unlike acne, rosacea is not a disorder of the pilosebaceous unit—there is no increase in sebum and there are no comedones.<sup>2</sup>

The precise etiology and pathophysiology of rosacea is unknown, but it is thought to involve atrophy of the papillary dermis, causing easier visualization of the dermal capillaries.<sup>1</sup> Increased blood flow in the superficial vasculature may result in edema, which might contribute to fibroplasias and rhinophyma associated with late-stage rosacea. The role of *Helicobacter pylori* and *Demodex* mites in the development of rosacea is speculative, but remains unknown.<sup>3</sup>

The onset of rosacea is usually between the ages of 25 and 50 years, most commonly in women with fair complexions.<sup>4</sup> According to estimates from the National Rosacea Society, most of the 14 million Americans who have rosacea do not know that they have the disease.<sup>5</sup>

Unlike acne, which affects sebaceous hair-bearing areas, rosacea is found predominantly on the convex areas of the central face—the nose, chin, central forehead, and cheeks,<sup>2</sup> and can also affect the scalp and neck.<sup>6</sup> In addition to skin manifestations of rosacea, about half of patients also have ocular rosacea, which can cause serious eye irritation.<sup>7</sup> The most common cutaneous signs of ocular rosacea are telangiectasia, irregularity of lid margins, and meibomian gland dysfunction.<sup>6</sup>

### Managing Rosacea: Target Potential Triggers

Rosacea can be treated and controlled, but there is currently no cure. Since the pathophysiology of rosacea is unknown, therapeutic options empirically target the symptoms of the disease.

Before initiating therapy, any trigger factors should be identified. Triggers, which are specific for individual patients, can cause a flare-up of the symptoms of rosacea.<sup>8</sup> Triggers include hot or cold temperature, sun, wind, hot beverages, exercise, spicy food, alcohol, stress, menopause, medications such as vasodilators and topical corticosteroids, and skin-care products that contain alcohol, witch hazel, or fragrances.<sup>6</sup> Trigger factors that induce flushing should be avoided.

### Treatment Options for Rosacea

Topical treatment options, such as metronidazole and azelaic acid, can decrease the number of inflammatory lesions (papules and pustules).<sup>6</sup> Another topical treatment approved for rosacea is sodium sulfacetamide 10%/sulfur 5%, which appears to confer anti-inflammatory benefits.<sup>9</sup> It is currently available in a number of different formulations, including cleansers, lotions, creams, water-based gels, and leave-on suspensions. These formulations are generally well tolerated, with facial dryness as the most frequently reported reaction.<sup>10</sup> Application-site reactions are usually transient and mild.

Oral antibiotics, such as tetracycline, doxycycline, and minocycline, have long been accepted as safe and effective treatments for rosacea. The most common side effects of tetracyclines include gastrointestinal disturbances (nausea, vomiting, and diarrhea).<sup>11</sup> Additionally, all tetracyclines carry warnings of phototoxicity reactions.<sup>11</sup> In 2006, a 40-mg (delayed-release) capsule formulation of doxycycline was approved for once-daily administration in the treatment of inflammatory lesions of adult rosacea. This form of doxycycline reduces inflammation with a low incidence of side effects and reduced risk of development of bacterial resistance.<sup>11</sup> The most common adverse events reported in phase III clinical trials were nasopharyngitis, diarrhea, and headache.<sup>12</sup>

### Newer Topical Formulations

The most prescribed topical treatment for rosacea is metronidazole, which was the first topical therapy approved for rosacea.<sup>6,13</sup> The most recent formulation of metronidazole is a water-based 1% aqueous gel applied once daily. Older metronidazole formulations had limited solubility, could not deliver high concentrations to the skin, and required twice-daily use.<sup>14</sup> The metronidazole 1% gel contains a higher concentration of active ingredient in a novel vehicle, which allows greater solubilization of metronidazole and improves drug delivery.<sup>4</sup> The vehicle is a 92% water-based gel derived from a unique combination of hydrosolubilizing agents known as HSA-3-niacinamide, betacyclodextrin, and a low concentration of propylene glycol.<sup>15</sup> Side effects associated with the use of topical metronidazole include scaling, stinging, burning, skin irritation, dryness, itching, transient redness, metallic taste, tingling, numbness of extremities, and nausea.<sup>13,16</sup>

In 2002, azelaic acid 15% gel was approved for the topical treatment of inflammatory stages of rosacea. The 15% gel formulation was formulated for improved drug delivery and bioavailability, and has been shown to be superior to metronidazole 0.75% gel in reduction of mean lesion count and in reduction of inflammatory lesions and severity of erythema.<sup>17</sup> A relatively recent study that compared the safety and efficacy of once-daily metronidazole 1% gel with twice-daily azelaic acid 15% gel in the management of rosacea found that metronidazole 1% gel was as effective as twice-daily treatment with azelaic acid 15% gel in reducing inflammatory lesions and improvement in investigator global severity scores.<sup>13</sup> Erythema was also reduced in association with inflammatory lesion reductions. In addition, stinging and burning was statistically worse for the patients treated with azelaic acid 15% gel twice daily compared with metronidazole 1% gel once daily after 15 weeks of treatment. However, a worst score of moderate scaling was seen in significantly more patients treated with metronidazole 1% gel than in those treated with azelaic acid 15% gel.<sup>13</sup>

### Surgical Therapies

Treatment for rosacea is usually performed solely to improve the appearance of the skin. Intense pulsed light therapy can be effective in treating the vascular symptoms of rosacea, such as telangiectasia and persistent erythema, which are not responsive to topical and oral therapies.<sup>7</sup>

Individuals with advanced cases of rosacea may develop rhinophyma, which is hyperplasia of the sebaceous glands, connective tissue, and blood vessels of the nose.<sup>6</sup> This condition occurs more frequently in men than in women. Excess tissue can be surgically removed by cryosurgery, dermabrasion, electrosurgery, sharp blade excision, shaving with a razor, and laser surgery.

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### Summary

Rosacea is often mistaken for other skin disorders such as acne vulgaris. The distinguishing features of rosacea include redness on the nose, chin, forehead, or cheeks; visible blood vessels, erythema, papules, and pustules; and the absence of comedones. Rosacea cannot be prevented or cured, but it can be treated and controlled with lifestyle modifications and medical therapy. Metronidazole was the first topical therapy approved for the treatment of inflammatory lesions of rosacea and remains part of the therapeutic foundation. A newer formulation of metronidazole—the 1% gel—incorporates a higher concentration of metronidazole with a vehicle that helps skin penetration of metronidazole. Other topical agents that reduce symptoms associated with rosacea include azelaic acid and sodium sulfacetamide/sulfur. Depending on the severity at initial presentation, systemic antibiotic and surgical therapies may be combined with topical therapy.

### References

1. Cohen AF, Tiemstra JD. Diagnosis and treatment of rosacea. *J Am Board Fam Pract.* 2002;15:214-217.
2. Kendall C. Five things...you may not know about rosacea. *Pulse.* 2006;60-62.
3. Webster G. New developments in rosacea. *Skin & Aging.* 2006;15:10-13.
4. Dow G, Basu S. A novel aqueous metronidazole 1% gel with hydrosolubilizing agents (HSA-3™). *Cutis.* 2006;77:18-26.
5. National Rosacea Society. What is rosacea? Available at: <http://www.rosacea.org/index.php>. Accessed March 11, 2008.
6. Gupta AK, Chaudhry MM. Rosacea and its management: An overview. *J Eur Acad Dermatol Venerol.* 2005;19:273-285.
7. Bikowski JB, Goldman MP. Rosacea: Where are we now? *J Drugs Dermatol.* 2004;3:251-261.
8. Fretzin M. A review of rosacea treatments. *Cosmetic Derm.* 2004;17:293-300.
9. Del Rosso JQ. A status report on the medical management of rosacea: Focus on topical therapies. *Cutis.* 2002;70:271-275.
10. Del Rosso JQ. Feature: cheek to cheek. *Skin & Aging.* 2004;12:56-58.
11. Bikowski JB. Subantimicrobial dose doxycycline for acne and rosacea. *SKINmed.* 2003;2:234-245.
12. Del Rosso JQ, Webster GF, Jackson M, et al. Two randomized phase III clinical trials evaluating anti-inflammatory dose doxycycline (40-mg doxycycline, USP capsules) administered once daily for treatment of rosacea. *J Am Acad Dermatol.* 2007;56:791-802.
13. Wolf JE, Jr, Kerrouche N, Arsonnaud S. Efficacy and safety of once-daily metronidazole 1% gel compared with twice-daily azelaic acid 15% gel in the treatment of rosacea. *Cutis.* 2006;77:3-11.
14. Wolf JE, Jr. The role of topical metronidazole in the treatment of rosacea. *Cutis.* 2004;73:19-28.
15. Draelos Z. Assessment of skin barrier function in rosacea patients with a novel 1% metronidazole gel. *J Drugs Dermatol.* 2005;4:557-562.
16. Thiboutot D. Advances in rosacea therapy. A review of available therapies. *Skin & Aging.* 2007;5(suppl):7-9.
17. Elewski BE, Fleischer AB, Jr, Pariser DM. A comparison of 15% azelaic acid gel and 0.75% metronidazole gel in the topical treatment of papulopustular rosacea: Results of a randomized trial. *Arch Dermatol.* 2003;139:1444-1450.

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