Rosacea: A Review

Brittney Culp, BA, and Noah Scheinfeld, MD

Educational Objectives

After reviewing this article, readers should be able to:

- Identify the common clinical presentations of rosacea.
- Review appropriate treatment options for rosacea, including topical, systemic, and other therapies.
- Differentiate between newer treatments for rosacea, both FDA-approved and non–FDA-approved.
- Determine the most appropriate treatment strategies for patients with rosacea.

Abstract

Rosacea is a chronic inflammatory condition of the facial skin affecting the blood vessels and pilosebaceous units. Rosacea is more common in persons of northern and western European descent with a fair complexion, but it can affect skin of any color. Although symptoms may wax and wane during the short term, rosacea can progress with time. Patients usually present with complaints of flushing and blushing and sensitive skin, and their skin may be especially irritated by topical preparations. Rosacea has a variety of triggers; however, they may be unnoticed by the patient.

Standard treatments approved by the FDA include azelaic acid, topical metronidazole, and oral tetracyclines, in particular minocycline and doxycycline. Other topical treatments include topical clindamycin, subantimicrobial-dose doxycycline, and sulfur products. Azithromycin and controlled-release minocycline are possible options for treating rosacea, but the FDA has not approved either agent for this indication.

Introduction

A common inflammatory condition, rosacea typically manifests in people with pale skin and light eyes, with a reported prevalence of between 0.5% and 10%.[1,2] It has many different clinical presentations as well as defined variants that help to dictate treatment.

Ms. Culp is a fourth-year medical student at Texas Tech University School of Medicine in Amarillo, Texas. Dr. Scheinfeld is Assistant Professor at Columbia University and a dermatologist in private practice. He can be reached at 30 Central Park South, Suite 2D, New York, NY 10019 (212-991-6490).

Epidemiology

Rosacea is more common in persons of northern and western European descent. As such, it is very common in the U.S. and in the European Union. Rosacea occurs less frequently in other ethnic groups. Some reports state that approximately 4% of rosacea patients are of African, Latino, or Asian descent.[3] It is estimated that from 10 to 20 million Americans have the condition. In a Swedish survey of people between 20 and 60 years of age, approximately 10% were thought to have rosacea, with a female-to-male ratio of 3:1. Rosacea is usually manifested as flushing in patients in their 20s, becomes troublesome to patients in their 30s, and may continue to progress thereafter.[4] Morbidity associated with rosacea typically occurs in the fourth and fifth decades of life.[5]

Pediatric rosacea is a poorly defined condition, and it is most likely underreported because of the tendency to characterize flushing and erythema as a "healthy glow." Pediatric patients are likely to have a family history of rosacea, and the condition may persist and progress in adulthood.[6]

Clinical Presentation and Diagnosis

Patients usually present with complaints of flushing, blushing, and sensitive skin. They may be unaware of these symptoms prior to diagnosis, but a variety of triggers, or factors that induce or exacerbate rosacea, exist (Table 1).[5,7,8,]

Rosacea is manifested as erythematous flushing, blushing, telangiectasias, papules, and pustules affecting the central third of the face. In areas of long-standing disease, yellow-orange plaques (phymas) can develop, resulting from sebaceous hyperplasia, most commonly on the nose (rhinophyma).[9] The red papules, pustules, and telangiectasias appear in the same distribution, albeit it with a lower frequency, in Asians and Hispanics; however, because of the pigmentation, they may not appear as erythematous.[3] African-Americans generally do not have red papules and erythema; instead, they have the granulomatous form of rosacea.

Many experts report that rosacea can occur in areas other than the face. In erythemato-telangiectatic rosacea (ETR), one may observe macular redness of the ears, the lateral facial contours, the neck, the upper portion of the chest, and the scalp. These extrafacial manifestations in ETR are uncommon and are usually seen only in areas affected by flushing and by chronic sun damage. Acneiform lesions have been observed on the central part of the chest and on the scalp, the neck, and, occasionally, the limbs.[10]

Table 1 Triggers of Rosacea

Ingested/Iatrogenic	Environmental
Foods and drinks	***Temperature***
Cheese (except cottage)	Sauna heat
Chocolate	Overheating
Spicy food	Sun lamp
Soy sauce	Humidity
Vanilla	Hot baths
Dairy products	***Weather***
Liver	Sun
Beverages	Heat
Red wine	Strong wind
Hot drinks	Cold
Alcohol (beer, bourbon, gin, vodka)	***Emotion***
Drugs	Anger
Niacin	Stress
Nitroglycerin	Rage
Tobacco	Embarrassment
Topical agents	***Activity***
Topical corticosteroids	Exercise
Retinoids	Menopause
Cosmetics (sometimes)	Caffeine withdrawal
Acetones	Chronic cough
Alcohol	Straining

Data from Rohrich RJ, Griffin JR, Adams WP Jr. *Plast Reconstr Surg* 2002;110(3):860-869; quiz, 870;[1] and Scheinfeld NS. Rosacea. *Skinmed* 2006;5:191–194.[2]

For a diagnosis of rosacea, one or more of the following primary features concentrated on the convex areas of the face is required: flushing (transient erythema), nontransient erythema, papules and pustules, and telangiectasia. Secondary features include burning or stinging, edema, plaques, a dry appearance, ocular manifestations, peripheral locations, and phymatous changes. The relative abundance of other associated findings often dictates the subtype of disease (Table 2) and treatment.

Some clinicians still use staging for determining appropriate treatment of rosacea. Stages range from frequent flushing in pre-rosacea to rhinophyma, hyperplasia, and other inflammatory changes seen in Stage 3 (Table 3).

Variants of Rosacea and Differential Diagnosis

Two variants of rosacea are not captured in the four major subtypes presented in Table 2.

Rosacea fulminans, which manifests with multiple erythematous papules, pustules, nodules, and purulent discharging cysts, is a severe manifestation of rosacea. On rare occasions, this form can be associated with Crohn's disease, ulcerative colitis, colon cancer recurrence, and pregnancy.[11] It can be treated with prednisone 0.5 to 1 mg/kg, followed by oral isotretinoin (Accutane, Roche).

Histologically, granulomatous rosacea can resemble sarcoid or cutaneous tuberculosis. Particularly in people of color, granulomatous rosacea is manifested as firm, skin-colored papules. This type of rosacea is more prevalent in African-Americans and in Afro-Caribbeans than in persons of lighter skin. This form of rosacea usually presents as yellowish-brown nodules and papules in the malar, perioral, and periocular regions. FACE syndrome (*f*acial *A*fro-Caribbean *c*hildhood *e*ruption) is now considered a variant of granulomatous rosacea and is characterized by grouped papules in perinasal and perioral locations. The histological picture is similar to that of granulomatous rosacea.[3]

Several skin conditions resemble rosacea and should be

Table 2 Major Subtypes of Rosacea

Subtype	Characteristics
Erythemato-telangiectatic	• Flushing lasts more than 10 minutes • Burning or stinging associated with flushing • Persistent erythema of the central aspects of the face • Telangiectasias
Papulopustular	• Small, dome-shaped erythematous papules • Tiny surmounting pustules on the central aspects of the face • Solid facial erythema and edema • Phymatous changes
Phymatous	• Thickening of skin with irregular surface contours • Affects nose, chin, forehead, eyes, or eyelids
Ocular[45,46]	• Burning, stinging, and itching of eyes • Sensitivity to light • Foreign body sensations • Blepharitis • Conjunctivitis

Data from references 10, 13, 31, 45, and 46.

Table 3 Stages of Rosacea

Stage	Symptoms and Signs
Pre-rosacea	Frequent flushing Irritation caused by topical preparations
Stage 1	Transient facial erythema that becomes more persistent Slight telangiectasias Increased skin sensitivity
Stage 2	Persistent, spreading erythema Edema, papules, pustules Enlarged pores Ocular changes
Stage 3	Large inflammatory nodules and furuncles Tissue hyperplasia, fibroplasias Rhinophyma

Data from 5, 9, 10, 35, and 40.

considered in the clinical differential diagnosis. The most common conditions seen in clinical practice are listed in Table 4.

Treatment

As a result of the development and release of newer topical formulations, the diagnosis and treatment of rosacea have received renewed attention over the past several years.[12] However, the cure for rosacea remains elusive, and all currently used medications are for symptomatic control only. No precise treatment algorithm has become the standard of care; treatment remains empirical.[13,14]

According to a Cochrane Database Review, the quality of studies evaluating rosacea treatments has generally been poor. It is possible that topical metronidazole (e.g., MetroGel, MetroCream, Galderma) and azelaic acid (Azelex, Allergan) as well as oral metronidazole (Flagyl, Pfizer) and tetracycline (Sumycin, Par) might be effective, but there is insufficient evidence for the effectiveness of other treatments. Well-designed, double-blind, randomized clinical trials are needed to evaluate current treatments.[15]

The existing evidence for the treatment of rosacea in patients of color is also meager.[16] To treat darker skin successfully, clinicians must pay special attention to the presence or potential development of pigmentary alteration or keloids. Clinicians can provide effective care to these patients with the judicious use of widely available over-the-counter (OTC) and prescription products.

In view of the clinical and histological variation found in rosacea patients, it is no surprise that ETR and the papulopustular, phymatous, and glandular types respond to different therapies. From a practical standpoint, subtyping can guide therapeutic decisions. Certain modalities are useful in all patients, stemming from overlap among the subtypes; however, the timing of their use may vary.[16]

The current gold standard of oral medical treatment is tetracycline-type antibiotics. Newer light treatments, with intense pulsed light and long-pulsed dye lasers, seem to be effective at decreasing erythema and eliminating telangiectasias, but these modalities are expensive and usually do not permanently eliminate erythema or telangiectasias.[17] Flushing can be treated with medications that have provided some success in other studies, including beta-blockers, clonidine (Catapres, Boehringer Ingelheim), naloxone (Narcan, Endo), ondansetron (Zofran, GlaxoSmithKline), and selective serotonin reuptake inhibitors (SSRIs). However, evidence supporting many of these therapies is limited.[16]

FDA-approved topical and oral therapies are presented in Table 5; non–FDA-approved oral treatments are listed in Table 6, and non–FDA-approved topical treatments are outlined in Table 7.

Topical Therapy

FDA-Approved Topical Agents

The efficacy of topical therapy for rosacea relates primarily to the reduction in inflammatory lesions (papules, pustules), a decreased intensity of erythema, a decrease in the number and intensity of flares, and amelioration of symptoms, which may include stinging, pruritus, and burning. The list of standard topical agents used to treat rosacea includes topical

Table 4 Differential Diagnosis of Rosacea

Disease	Similarities	Differences
Acne vulgaris[9,12]	• Papules, pustules, erythema	• Comedones • Earlier onset • Not limited to central third of face • No telangiectasias or flushing
Steroid rosacea[41,47]	• Erythema, papules, pustules, telangiectasias • Central third of face	• Related to topical application of corticosteroids, tacrolimus (Protopic, Astellas/Fujisawa), and pimecrolimus (Elidel, Novartis)
Seborrheic dermatitis	• Blepharitis • Erythema	• Scaling, eczematous changes • Paranasal, nasolabial, extrafacial distribution
Perioral dermatitis[7,48]	• Erythema, papules	• Perioral distribution • Smaller lesions • No telangiectasia, flushing, or blushing
Contact dermatitis	• Erythema, papules, pustules • Burning, stinging	• Follows size and shape of causal agent • Scaling • Spongiosis and parakeratosis on histology
Photodermatitis	• Erythema, papules, plaques	• Seasonal • Usually extrafacial
Lupus	• Erythema	• Malar distribution • Photosensitivity

Data from references 7, 9, 12, 41, 47, and 48.

Table 5 FDA-Approved Topical and Oral Therapies for Rosacea

Topical Antibiotics	Non-antibiotics	Oral Antibiotics
Metronidazole 0.25%, 0.75%, 1% cream, gel, lotion (e.g., MetroCream, MetroGel)	Azelaic acid 15% gel (Azelex)	Doxycycline, USP (Oracea Capsules) 40 mg once daily (30-mg immediate-release and 10-mg delayed-release beads)
	Sodium sulfacetamide 10% and sulfur 5% combination, lotion, cream, pledgets, short-contact preparation, cleanser (Sulfacet)	
	Sodium sulfacetamide 10% lotion	
	Sodium sulfacetamide 10%, sulfur 5%, sunblock lotion combination	

antibiotics, such as clindamycin (Cleocin, Pfizer), erythromycin (Akne-Mycin, DTP Laboratories/Healthpoint Ltd.) and metronidazole, sulfacetamide–sulfur (Sulfacet, Sanofi-Aventis), and azelaic acid (Azelex).[12]

Some studies have indicated efficacy for a number of treatments. Topical metronidazole is more effective than placebo in clinical studies. Between-patient and within-patient trials showed clear improvement in those using azelaic acid when compared with placebo.[15] In a randomized trial comparing 15% azelaic acid and 0.75% metronidazole gel (MetroGel), azelaic acid was clinically superior in improving the inflammatory lesions and erythema associated with rosacea.[18] However, studies show a greater potential for irritation from azelaic acid 15% than from metronidazole gel 0.75%, which had significantly greater potential risk of irritation when compared with metronidazole 1% gel.[19] However, three cases of allergic contact dermatitis resulting from topical metronidazole have been reported.[20]

Other topical treatments include sulfur products, such as sodium sulfacetamide 10%/sulfur 5% combinations with or without a sun-blocking agent. These are available in lotions, creams, pledgets, short-contact preparations, and cleansers.

Table 6 Non–FDA-Approved Oral Treatment of Rosacea

Standard but Non-approved Oral Antibiotics	Useful but Less Commonly Used Oral Antibiotics	Oral Antibiotics Reported but Not in Common Clinical Use	Oral Treatment of Flushing	Non-antibiotic Oral Treatment
Tetracycline 500 mg b.i.d.	Azithromycin 250 mg t.i.w. (Zithromax)	Penicillin 2.4 million units q.d.	Oral contraceptives (Ovosiston)	Ivermectin 250 µ/kg q.w. (Stromectol)
Doxycycline 50–100 mg b.i.d.	Clarithromycin 250–500 mg b.i.d.–q.d. (Biaxin)	Erythromycin 250–500 mg b.i.d.–q.i.d. (Akne-Mycin)	Psychiatric medications • Amitriptyline 25 mg q.d. (Elavil) • Clonidine 0.1 mg q.d. (Catapres) • Pimozide (Orap)	Isotretinoin 0.15–2 mg/kg q.d. (Accutane)
Minocycline 50–100 mg b.i.d.	Doxycycline, subantimicrobial dose, 20 mg b.i.d. (Periostat)	Amoxicillin or ampicillin 100–500 mg q.d.–b.i.d.	Aspirin	Acitretin 25–50 mg q.d. (Soriatane)
Minocycline time-released 45, 90, 135 mg (Solodyn)		Metronidazole 250 mg b.i.d.–t.i.d. (MetroCream, MetroGel)	Beta blockers	Ketoconazole 400 mg q.d. x 1–4 weeks (Nizoral)
		Dapsone 50–200 mg q.d.	Ondansetron (Zofran)	Spirolactone 50 mg q.d. x 4 weeks (Aldactone)
			COX-2 inhibitors	Prednisone 1 mg/kg (for rosacea fulminans only)

b.i.d. = twice daily; COX-2 = cyclooxygenase-2; mg = milligram; q.d. = once daily; q.i.d. = four times daily; q.w. = weekly; t.i.w. = three times weekly.

Table 7 **Non–FDA-Approved Topical Treatment of Rosacea**

Topical Antibiotics	Topical Treatment Reportedly Used Effectively	Topical Treatments Theoretically Useful But Not Used Clinically
Clindamycin 1% lotion, gel, solution, pledget (Cleocin)	Azelaic acid 20% cream (Azelex)	Crotamiton 10% q.d.–t.i.d. (Eurax)
Erythromycin 2% solution, ointment, pledget (Akne-Mycin)	Permethrin cream 5% q.d.–q.w. (Nix)	Lindane 1% cream q.d.
Benzoyl peroxide 5%/ clindamycin 1% (BenzaClin, Benzamycin)	Adapalene cream, gel (Differin)	Benzoyl peroxide, gel, wash q.d.–b.i.d. (Benzac, Benzagel)
Sunscreen with dimethicone or cyclomethicone	Tacrolimus ointment q.d.–b.i.d. (Protopic)	Retinaldehyde 0.05% cream
Benzoyl peroxide 5% and erythromycin 1% combination cream, pledget	Pimecrolimus 1% Cream q.d.–b.i.d. (Elidel)	Tretinoin cream, gel (Retin-A)
	Oxymetazoline q.d. (Afrin)	Tazarotene cream, gel (Tazorac, Avage)

b.i.d. = twice daily; mg = milligram; q.d. = once daily; q.i.d. = four times daily; q.w. = weekly (every week).
Data from Arcangelo VP, ed. *Pharmacotherapeutics for Advanced Practice: A Practical Approach*. Lippincott Williams & Wilkins, 2005.

Sodium sulfacetamide 10% alone may also be used.

Non–FDA-Approved Topical Agents

When used for four to eight weeks, pimecrolimus 1% cream (Elidel, Novartis), a topical calcineurin inhibitor, was no more efficacious than the vehicle creams.[21] However, in an open-label, six-week pilot study in which patients used pimecrolimus 1% cream twice daily, nearly 50% of patients had clear skin and most showed at least modest improvement. Cutaneous adverse events, consisting of local burning, stinging, and itching occurred in fewer than 20% of patients.[22]

Symptomatic treatment with alpha-blockers has also been noteworthy. Patient using a topically administered selective alpha$_1$-agonist showed a positive clinical response in treatment-resistant ETR rosacea.[23] This was demonstrated as a durable improvement in the erythema, a marked decrease of erythematous flares, relief from stinging and burning, and an absence of adverse effects. It seems plausible that the erythema and flushing of ETR might result, at least in part, from an abnormal expression, function, distribution, or responsiveness of alpha-adrenergic receptors, probably of an alpha$_1$-receptor subtype and that the topical application of agonists selective for alpha$_1$-adrenergic receptors, such as oxymetazoline (Afrin, Schering-Plough) may be successful in treating these clinical manifestations.[23]

1-Methylnicotinamide 0.25% (MNA+) as a chloride salt might be a useful agent for treating rosacea.[24] Applied twice daily for four weeks, improvement rated as moderate to good was observed in 26 of 34 cases; however, seven patients showed no clinical response.

The presence of *Demodex folliculorum* may be important in the inflammatory reaction of rosacea. Crotamiton 10% cream (Eurax, Novartis in U.K.) or permethrin 5% cream (Nix, Warner-Lambert) may be useful, but these medications are rarely successful in eradicating the organism. Oral or topical ivermectin (Stromectol, Merck) may also be useful in such cases.[25]

Other experimental therapies include other topical antibiotics such as clindamycin and erythromycin as well as antibiotics combined with benzoyl peroxide (e.g., BenzaClin, Benzamycin, Dermik/Sanofi-Aventis). Increased strengths of azelaic acid have been used effectively, but are not yet approved by the FDA. Adapalene cream or gel (Differin, Galderma) has been used with some effectiveness as well. Treatments that should be theoretically useful based on pathogenesis of rosacea include lindane 1% cream, retinaldehyde 0.05% cream, tretinoin cream or gel (Retin-A, Ortho-Neutrogena), and tazarotene cream (Tazorac, Avage, Allergan). However, these agents have not yet been reported as useful in clinical practice for treating rosacea (Table 7).[14]

Oral Therapy

FDA-Approved Oral Agents

The cornerstone of the oral treatment of rosacea involves the use of tetracyclines. Tetracycline (Sumycin) 500 mg twice a day is an effective treatment, but when it is taken with food, its absorption may be decreased. Doxycycline (Vibramycin, Pfizer) and minocycline (Minocin, Triax/Wyeth) 50–100 mg once daily to twice daily are the most currently used oral antibiotics by dermatologists for the treatment of rosacea. A new time-released form of minocycline (Solodyn, Medicis) at doses of 45, 90, and 135 mg is indicated to treat only inflammatory lesions of non-nodular, moderate-to-severe acne vulgaris in patients 12 years of age and older, but it can be used if other treatment has failed. It is the first weight-based antibiotic oral therapy for rosacea.[26]

Controlled-release doxycycline 40 mg (Oracea, Galderma) is effective in treating inflammatory papules and pustules, but not erythema that is associated with rosacea.[27] Other reports have found this agent and dose to be a useful alternative to higher microbial doses of doxycycline.[26,28]

Non–FDA-Approved Oral Agents

Azithromycin (Zithromax, Pfizer), perhaps acting as an antioxidant, appears to be useful for treating rosacea in doses of 250 mg three times per week.[29,30] If azithromycin, which is now available as a generic brand, is competitively priced with minocycline and doxycycline, its minimal side effects, lack of drug interactions, and three-times-weekly dosing could make it a good alternative for rosacea patients.

The systemic treatment of *Helicobacter pylori* infection has been advocated as a possible therapy for rosacea. In some studies, the two conditions have been found to be associated. Eradication of *H. pylori* can be achieved using a triple-therapy regimen lasting one to two weeks consisting of omeprazole (Prilosec, AstraZeneca) and a combination of two of the following: clarithromycin (Biaxin, Abbott), metronidazole, or amoxicillin (Amoxil, GlaxoSmithKline).[31]

Although not commonly used clinically, other oral antibiotics with reported efficacy include penicillin 2.4 million units daily, erythromycin 250–500 mg two to four times daily, amoxicillin or ampicillin (Principen, Apothecon) 100–500 mg daily or twice daily, metronidazole at doses of 250 mg two to three times daily, and dapsone 50 to 200 mg once daily.

Non-antibacterial regimens can also be used. Isotretinoin has proved effective for rosacea.[16] Although effects may be delayed with isotretinoin, when compared with standard therapies, a reduction in the number of papules is evident within two weeks. The most significant results have been noted in younger patients with less severe manifestations of disease; however, isotretinoin has also been useful for treating and reducing phymatous changes.[16] Acitretin (Soriatane, Roche), ketoconazole (Nizoral, Janssen), spironolactone (Aldactone, Pfizer), and prednisone are also reported to be effective.

Oral agents reported to treat flushing include oral contraceptives, some psychoactive drugs, aspirin, beta-blockers, ondansetron, and cyclooxygenase-2 (COX-2) inhibitors. The oral contraceptives chlormadinon acetate/mestranol (Ovosiston) and the antiandrogen agent cyproterone have been suggested as being effective hormonal treatments for rosacea.

Combination Therapies

Effective treatments, including topical metronidazole and systemic antibiotics, have anti-inflammatory activity, which may actually be more important than their antimicrobial activity. For mild-to-moderate rosacea, an anti-inflammatory dose of doxycycline in combination with topical metronidazole gel 1% appears to be effective in reducing inflammatory lesion counts, and it is well tolerated.[32]

Phototherapy

Several reports have found light-based treatments to be effective for the erythema of rosacea. Multiplexed laser appears to help in reducing erythema and telangiectasia.[33] Intense pulsed light (IPL) at a wavelength of 550 to 670 nm may be effective for rosacea and solar lentigines, and it is particularly useful for ETR.[34] Both the flash lamp-pumped, long-pulse dye laser and the potassium-titanyl-phosphate laser may be used to treat facial telangiectasias.[25]

Nonmedical Therapies

Patients should be instructed about the regular use of sunscreens, the appropriate use of concealing makeup, and the need for careful follow-up of any ocular symptoms.[35] Basic skin-care regimens, including the daily use of a sunscreen, offer significant benefits (Table 8). Clinical assessments, confirmed by biophysical measurements (electrical capacitance, transepidermal water loss, and lactic acid stinging test), indicated that moisturizers contributed to the restoration of the skin barrier. Skin dryness, roughness, and desquamation were much improved, and skin sensitivity was significantly reduced. Skin properties were enhanced, and skin discomfort was relieved.[36]

Kinetin (N6-furfuryladenine) is a plant cytokinin that reportedly helps restore skin barrier function and may be beneficial for improving the signs and symptoms of rosacea. A twice-daily application of kinetin 0.1% lotion was found to be a well-tolerated moisturizing lotion choice for patients with mild-to-moderate inflammatory rosacea.[37,38]

In one trial, treatment with oral minocycline, spironolactone, and Chibixiao, a Chinese herb, was superior to minocycline and spironolactone alone.[39]

Beyond treating the symptoms of rosacea, physicians should address psychological problems and should provide patient education. Patients' concerns about their appearance and a lack of hope for effective therapy can cause psychological distress, which can be immediately alleviated when patients learn that rosacea is a recognized and controllable disorder. Patients are often concerned that others might believe that their symptoms are caused by overindulgence in alcohol or by poor personal hygiene.

Although alcohol consumption can exacerbate rosacea, symptoms also occur in people who abstain from alcohol. Patients should also be reassured that rosacea is often unrelated to poor hygiene. Education about triggers can help patients gain control over rosacea symptoms.[40]

Table 8 Guidelines for Sunscreen and Cosmetics in Rosacea Patients with Sensitive Skin and Skin Barrier Dysfunction

- Cleansers should be soap-free.
- Choose sunscreens that protect against ultraviolet A (UV-A) and UV-B light; titanium dioxide and zinc oxide are tolerated best.
- Cosmetics and sunscreens should contain protective silicones.
- Choose a light foundation that is easy to spread and can be set with powder; foundations that contain UV-A and UV-B sunscreen are encouraged.
- Avoid astringents, toners, menthols, camphor, and products that contain sodium lauryl sulfate.
- Avoid waterproof cosmetics and heavy foundations that are more difficult to apply and to remove without irritating solvents.

Data from Baxi S. *US Pharmacist* 2007;32(7):13–17;[42] and Pray JJ, Pray WS. *US Pharmacist* 2003;28(6).[43]

Duration of Therapy

Like acne, rosacea naturally waxes and wanes. However, because the damage from rosacea can be progressive (unlike acne), the continuous use of therapy has advantages. Many acne and rosacea patients can continue with an antibiotic for more than a year without adverse effects.[41] However, physicians should keep in mind the increased bacterial resistance caused by prolonged use of antibiotics. Long-term therapy with minocycline beyond six months also carries an increased risk of pigmentary deposition.[41]

Role of the Pharmacist

Patients with any form of facial eruption are often acutely embarrassed or highly apprehensive about consulting a pharmacist. Rosacea is a disfiguring condition, constantly visible to anyone with whom the individual has face-to-face interaction, and it can produce a great deal of stress, embarrassment, frustration, anger, and depression. Patients cannot often predict the duration of the condition, the degree of severity, or the likelihood of a favorable treatment outcome.

Pharmacists play a vital role in evaluating the patient. This includes obtaining a medication history, observing the number and types of lesions, referring patients to a physician if needed, helping to choose the appropriate therapeutic regimen, and counseling patients. Pharmacists should discuss the goals of treatment, realistic expectations, length of therapy, appropriate use of products, and the importance of adhering to the regimen.[42] Pharmacists can help physicians in educating patients about the causes of acne and rosacea by dispelling myths that these conditions are related to poor hygiene or eating poorly and by helping patients to identify triggers for worsening rosacea. The range of treatments for rosacea can be overwhelming to patients and physicians. Pharmacists can help patients choose appropriate products and advise them on when to consult a dermatologist.[43]

To decrease the risks of drug interactions, pharmacists maintain updated patient medication profiles, including use of herbal products, OTC medications, and natural supplements, and they monitor for "red-flag" drugs or drugs with a narrow therapeutic index. Pharmacists have a responsibility to warn patients and prescribers about drug interactions.[44]

Conclusion

When patients present with rosacea, appropriate therapeutic strategies should address the clinical features, the subtype of rosacea, and the staging or severity of lesions.[45–48] Patients with typical features of pre-rosacea and only transient symptoms may respond to OTC agents. However, the increasing abundance of primary rosacea features (e.g., flushing, nontransient erythema, papules, pustules, telangiectasias) and secondary features (e.g., burning, stinging, edema, ocular manifestations, extrafacial lesions, phymatous changes) should lead physicians and pharmacists to consider prescription therapy instead of OTC treatments.

For patients with inflammatory papules or pustules and a significant erythematous component, topical therapy may be considered. The most effective topical therapies seem to be azelaic acid and metronidazole. Health care providers should also take into account each patient's sensitivity to irritation from topical agents.

Oral antibiotics, such as doxycycline 50 mg daily or twice daily, can be used for rosacea that is refractory to topical therapies. Oral therapy should be considered for patients who have mostly inflammatory papules and pustules without significant erythema. Younger patients with less severe manifestations of disease and patients with phymatous changes may have excellent responses to isotretinoin.

Combinations of topical and oral therapy may provide satisfactory results for individuals with mild-to-moderate rosacea or for those with both inflammatory and erythematous components. The best combination therapy appears to be doxycycline and metronidazole gel 1%.

Physicians and pharmacists should use FDA-approved therapies unless the patient's condition is refractory to typical treatment.

Pharmacists should be reminded to obtain medication histories, to assess the severity of symptoms, and to consider referring patients for appropriate treatment. Pharmacists can be helpful in educating patients about realistic treatment outcomes and in counseling them about compliance and the appropriate use of prescribed therapies.

References

1. Rohrich RJ, Griffin JR, Adams WP Jr. Rhinophyma: Review and update. *Plast Reconstr Surg* 2002;110(3):860–869; quiz, 870.
2. Scheinfeld NS. Rosacea. *Skinmed* 2006;5:191–194.
3. Halder RM, Brooks HL, Callendar VD. Acne in ethnic skin. *Dermatol Clin* 2003;21(4).
4. Berg M, Liden S. An epidemiological study of rosacea. *Acta Dermatol Venereol* 1989;69:419–423.
5. Pray WS, Pray JJ. Differentiating between rosacea and acne. *US Pharmacist* 2004;29(4).
6. Kroshinsky D, Glick SA. Pediatric rosacea. *Dermatol Ther* 2006; 19(4):196–201.
7. Shelley WB, Shelley ED. *Advanced Dermatologic Therapy II*, 2nd ed. Philadelphia: WB Saunders; 2001.
8. Berth-Jones J, Clark SM, Henderson CA. Rosacea and perioral dermatitis. *In:* Lebwohl M, Heymann WR, Berth-Jones J, et al., eds. *Treatment of Skin Disease*. London: Mosby; 2002.
9. Rosacea. *In:* Marks JG, Miller JJ (eds.). *Principles of Dermatology,* 4th ed. Philadelphia: Elsevier/Saunders; 2006.
10. Crawford GH, Pelle MT, James WD. Rosacea: I. Etiology, pathogenesis, and subtype classification. *J Am Acad Dermatol* 2004; 51(3);327–341.
11. Helm KF, Menz J, Gibson LE, Dicken CH. A clinical and histopathologic study of granulomatous rosacea. *J Am Acad Dermatol* 1991;25:1038–1043.
12. Del Rosso JQ. Medical treatment of rosacea with emphasis on topical therapies. *Exp Opin Pharmacother* 2004;1:5–13.
13. Norwood R, Norwood D. Treating rosacea. *US Pharmacist* 2007; 32(9):45–53.
14. Dressler-Carre M. Acne vulgaris and rosacea. *In:* Arcangelo VP, ed. *Pharmacotherapeutics for Advanced Practice: A Practical Approach*. Philadelphia: Lippincott Williams & Wilkins, 2005.
15. Van Zurren EJ, Graber MA, Hollis S, et al. Interventions for rosacea. *Cochrane Database Syst Rev* 2005(3).
16. Pelle MT, Crawford GH, James WD. Rosacea II: Therapy. *J Am Acad Dermatol* 2004;51(4):499–512.
17. Nally JB, Berson DS. Topical therapies for rosacea. *J Drugs Dermatol* 2006;5:23–26.
18. Elewski BE, Flesicher AB, Pariser DM. A comparison of 15% azelaic acid gel and 0.75% metronidzole gel in the topical treatment

of papulopustular rosacea: Results of a randomized trial. *Arch Dermatol* 2003;139(11):1444–1450.
19. Colon LE, Johnson LA, Gottschalk RW. Cumulative irritation potential among metronidazole gel 1%, metronidazole gel 0.75%, and azelaic acid gel 15%. *Cutis* 2007;79:317–321.
20. Madsen JT, Thormann J, Kerre S, et al. Allergic contact dermatitis to topical metronidazole: Three cases. *Contact Dermatitis* 2007;56:364–366.
21. Weissenbacher S, Merkl J, Hildebrandt B, et al. Pimecrolimus cream 1% for papulopustular rosacea: A randomized vehicle-controlled double-blind trial. *Br J Dermatol* 2007;156:728–732.
22. Chu CY. An open-label pilot study to evaluate the safety and efficacy of topically applied pimecrolimus cream for the treatment of steroid-induced rosacea-like eruption. *J Eur Acad Dermatol Venereol* 2007;21:484–490.
23. Shanler SD, Ondo AL. Successful treatment of the erythema and flushing of rosacea using a topically applied selective alpha$_1$-adrenergic receptor agonist, oxymetazoline. *Arch Dermatol* 2007; 143(11):1369–1371.
24. Wozniacka A, Wierczorkowska M, Gebicki J, Sysa-Jedrzejowska A. Topical application of 1-methylnicotinamide in the treatment of rosacea: A pilot study. *Clin Exp Dermatol* 2005;30(6): 632–635.
25. Callender VD. Acne in ethnic skin: Special considerations for therapy. *Dermatol Ther* 2004;17(2):184–195.
26. Theobald K, Bradshaw M, Leyden J. Anti-inflammatory dose doxycycline (40 mg controlled-release) confers maximum anti-inflammatory efficacy in rosacea. *Skinmed* 2007;6:221–226.
27. Low-dose doxycycline (Oracea) for rosacea. *Med Lett Drugs Ther* 2007;49(1252):5–6.
28. Berman B, Perez OA, Zell D. Update on rosacea and anti-inflammatory-dose doxycycline. *Drugs Today (Barc)* 2007;43:27–34.
29. Fernandez-Obregon A, Patton DL. The role of *Chlamydia pneumoniae* in the etiology of acne rosacea: Response to the use of oral azithromycin. *Cutis* 2007;79:163–167.
30. Bakar O, Demircay Z, Yuksel M, et al. The effect of azithromycin on reactive oxygen species in rosacea. *Clin Exp Dermatol* 2007; 32:197–200.
31. Rebora A. The management of rosacea. *Am J Clin Dermatol* 2002;3:489–496.
32. Fowler JF. Combined effect of anti-inflammatory dose doxycycline (40-mg doxycycline, USP monohydrate controlled-release capsules) and metronidazole topical gel 1% in the treatment of rosacea. *J Drugs Dermatol* 2007;6(6);641–645.
33. Larson AA, Goldman MP. Recalcitrant rosacea successfully treated with multiplexed pulsed dye laser. *J Drugs Dermatol* 2007; 6:843–845.
34. Kawana S, Ochiai H, Tachihara R. Objective evaluation of the effect of intense pulsed light on rosacea and solar lentigines by spectrophotometric analysis of skin color. *Dermatol Surg* 2007; 33:449–454.
35. Blount BW, Pelletier AL. Rosacea: A common, yet commonly overlooked, condition. *Am Fam Physician* 2002;66(3):435–440.
36. Laqueize S, Czernieleski J, Baltas E. Beneficial use of Cetaphil moisturizing cream as part of a daily skin care regimen for individuals with rosacea. *J Dermatol Treat* 2007;18(3):158–162.
37. Wu JJ, Weistein GD, Kricorian GJ, et al. Topical kinetin 0.1% lotion for improving the signs and symptoms of rosacea. *Clin Exp Dermatol* 2007;32(6):693–695.
38. Wu J. Treatment of rosacea with herbal ingredients. *J Drugs Dermatol* 2006;5(1):29–32.
39. Yu TG, Zheng YZ, Zhu JT, Guo W. Effect of treatment of rosacea in females by Chibixiao recipe in combination with minocycline and spironolactone. *Chin J Integr Med* 2006;12:277–280.
40. Millikan L. Recognizing rosacea: Could you be misdiagnosing this common skin disorder? *Postgrad Med* 1999;105(2).
41. Smith K, Leyden JJ. Safety of doxycycline and minocycline: A systematic review. *Clin Ther* 2005;27(9):1329–1342.
42. Baxi S. OTC products for the treatment of acne. *US Pharmacist* 2007;32(7):13–17.
43. Pray JJ, Pray WS. Teenagers and acne: The role of the pharmacist. *US Pharmacist* 2003;28(6).
44. Rochester CD. Drug interactions in dermatology: Are they just skin deep? *US Pharmacist* 2007;32(4):HS29–HS39.
45. Stone DU, Chodosh J. Ocular rosacea: An update on pathogenesis and therapy. *Curr Opin Ophthalmol* 2004;15:499–502.
46. Kheirkhah A, Casas V, Li W, et al. Corneal manifestations of ocular *Demodex* infestation. *Am J Ophthalmol* 2007;143:743–749.
47. Bormann G, Gaber G, Fischer M, Marsch WC. Dapsone in rosacea fulminans. *J Eur Acad Dermatol Venereol* 2001;15:465–467.
48. Aroni K, Tsagroni E, Lazaris AC, et al. Rosacea: A clinicopathological approach. *Dermatology* 2004;209:177–182. ■

Conflict of Interest (COI) Statement

The authors have no relationships to disclose. The article contains discussion of off-label use. The content of this article has been reviewed under Jefferson's Continuing Medical Education COI policy.