Rosacea: Diagnosis and Treatment

LINDA K. OGE', MD, *Louisiana State University Department of Family Medicine, University Hospital and Clinics, Lafayette, Louisiana*
HERBERT L. MUNCIE, MD, *Louisiana State University Department of Family Medicine, New Orleans, Louisiana*
AMANDA R. PHILLIPS-SAVOY, MD, MPH, *Louisiana State University Department of Family Medicine, University Hospital and Clinics, Lafayette, Louisiana*

Rosacea is a chronic facial skin condition of unknown cause. It is characterized by marked involvement of the central face with transient or persistent erythema, telangiectasia, inflammatory papules and pustules, or hyperplasia of the connective tissue. Transient erythema, or flushing, is often accompanied by a feeling of warmth. It usually lasts for less than five minutes and may spread to the neck and chest. Less common findings include erythematous plaques, scaling, edema, phymatous changes (thickening of skin due to hyperplasia of sebaceous glands), and ocular symptoms. The National Rosacea Society Expert Committee defines four subtypes of rosacea (erythematotelangiectatic, papulopustular, phymatous, and ocular) and one variant (granulomatous). Treatment starts with avoidance of triggers and use of mild cleansing agents and moisturizing regimens, as well as photoprotection with wide-brimmed hats and broad-spectrum sunscreens (minimum sun protection factor of 30). For inflammatory lesions and erythema, the recommended initial treatments are topical metronidazole or azelaic acid. Once-daily brimonidine, a topical alpha-adrenergic receptor agonist, is effective in reducing erythema. Papulopustular rosacea can be treated with systemic therapy including tetracyclines, most commonly subantimicrobial-dose doxycycline. Phymatous rosacea is treated primarily with laser or light-based therapies. Ocular rosacea is managed with lid hygiene, topical cyclosporine, and topical or systemic antibiotics. (*Am Fam Physician*. 2015;92(3):187-196. Copyright © 2015 American Academy of Family Physicians.)

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CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 180.

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▶ **Patient information**: A handout on this topic is available at http://www.aafp.org/afp/2015/0801/p187-s1.html.

Rosacea is a chronic facial skin condition characterized by marked involvement of the central face with transient or persistent erythema, inflammatory papules or pustules, telangiectasia, or hyperplasia of the connective tissue.[1,2] Transient erythema, or flushing, usually lasts less than five minutes and may spread to the neck and chest, often accompanied by a feeling of warmth. Less common findings include erythematous plaques, scaling, edema, phymatous changes (thickening of skin due to hyperplasia of sebaceous glands), and ocular symptoms. Rosacea can be associated with low self-esteem, embarrassment, and diminished quality of life. In a national survey, 65% of patients with rosacea reported symptoms of depression.[3]

The exact prevalence of rosacea in the United States is unknown[4,5]; however, it is probably between 1.3% and 2.1%, and may be as high as 5%.[6] Women are affected more often than men, but men are more likely to have phymatous changes, especially rhinophyma.[7]

Subtypes

The National Rosacea Society Expert Committee defined four subtypes *(Table 1)* and one variant.[8] Granulomatous rosacea is the sole variant with firm, indurated papules or nodules. Many dermatologists consider rosacea fulminans and perioral dermatitis as rosacea variants. Patients may experience fluctuation in symptoms and overlapping of symptoms between subtypes.[9]

Pathophysiology

The etiology of rosacea is unknown but is likely multifactorial. Factors involved in the pathophysiology include the dense presence of sebaceous glands on the face, the physiology of the nerve innervation, and the vascular composition of the skin.[10] Numerous triggers initiate or aggravate the clinical manifestations of rosacea, including ultraviolet light, heat, spicy foods, and alcohol *(Table 2)*.[4,11]

A predilection for fair-skinned individuals of Celtic or northern European descent suggests a genetic component to rosacea.[10] However, no specific gene has been

Table 1. Subtypes and Variants of Rosacea and Their Characteristics

Classification	*Characteristics*
Subtype	
Erythemato-telangiectatic	Flushing and persistent central facial erythema with or without telangiectasia
Papulopustular	Persistent central facial erythema with transient, central facial papules or pustules or both
Phymatous	Thickening skin, irregular surface nodularities and enlargement; may occur on the nose, chin, forehead, cheeks, or ears
Ocular	Foreign body sensation in the eye, burning or stinging, dryness, itching, ocular photosensitivity, blurred vision, telangiectasia of the sclera or other parts of the eye, or periorbital edema
Variant	
Granulomatous	Noninflammatory; hard; brown, yellow, or red cutaneous papules; or nodules of uniform size

NOTE: *Photos of these subtypes of acne rosacea are available at http://www.aafp.org/afp/2009/0901/p461.html.*

Reprinted with permission from Wilkin J, Dahl M, Detmar M, et al. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. J Am Acad Dermatol. *2002;46(4):586. http://www.sciencedirect.com/science/journal/01909622/.*

Table 2. Triggers Associated with Worsening Rosacea Symptoms

Trigger	*Patients with rosacea who report trigger (%)*
Sun exposure	81
Emotional stress	79
Hot weather	75
Wind	57
Strenuous exercise	56
Alcohol consumption	52
Cold weather	46
Spicy foods	45
Certain skin care products	41
Heated beverages	36
Certain cosmetics (comedogenic)	27
Medications (topical steroids, niacin, beta blockers)	15
Dairy products	8
Other factors	24

Information from references 4 and 11.

Table 3. Guidelines for the Diagnosis of Rosacea

Presence of one or more of the following primary features:	**May include one or more of the following secondary features:**
Flushing (transient erythema)	Burning or stinging
Nontransient erythema	Plaque
Papules and pustules	Dry appearance
Telangiectasia	Edema
	Ocular manifestations
	Peripheral location
	Phymatous changes

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identified.[4] Patients with the genetic predisposition have a receptor that mediates neovascular regulation. When exposed to triggers, neuropeptide release (flushing, edema) occurs, resulting in recruitment of proinflammatory cells to the skin.[10]

Diagnosis

Rosacea is diagnosed based on a compatible history and physical examination[12] *(Table 3[8])*. One of the following centrofacial features is required: flushing, nontransient erythema *(Figures 1A and 1B)*, telangiectasia *(Figure 1C)*, or papules/pustules[8] *(Figures 2A and 2B)*. Laboratory testing is not useful.

Patients may receive a misdiagnosis of skin conditions that share similar features. Rosacea is commonly misdiagnosed as adult acne vulgaris, photodermatitis, seborrheic dermatitis, or contact dermatitis. *Table 4* lists features that distinguish these conditions from rosacea. Less common mimicking conditions include systemic lupus erythematosus, atopic dermatitis, folliculitis, bromoderma, and mastocytosis.

Treatment

GENERAL MEASURES

Although rosacea findings may change over time, no proven natural progression exists.[13] Treatment decisions are based on the patient's current clinical manifestations *(Table 5)*.

Because rosacea can be triggered by a variety of stimuli, avoidance of known triggers is recommended. To

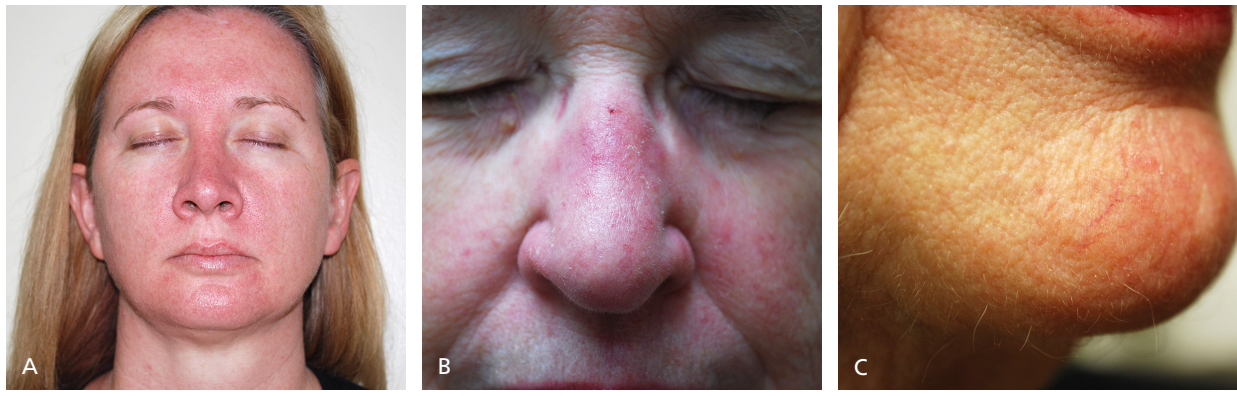

Figure 1. Facial erythema with telangiectasia. *(A)* Frontal view of centrofacial erythema. *(B)* Close-up view of centrofacial erythema with scaling. *(C)* Close-up view of telangiectasias on lateral chin.

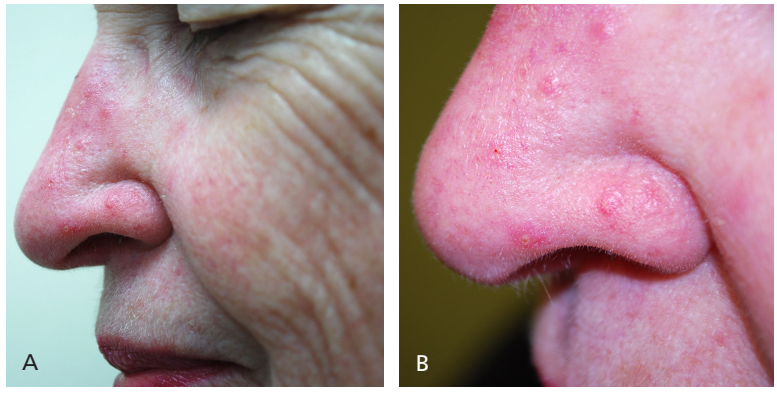

Figure 2. Inflammatory lesions (papules and pustules). *(A)* Papulopustular lesions and scaling on the lateral nose. *(B)* Close-up view of papulopustular rosacea.

identify potential triggers, patients should be encouraged to keep a journal documenting exposures, diet, and activities that cause flare-ups.[14]

Properly selected skin care products improve and maintain the integrity of the stratum corneum permeability barrier and reduce skin sensitivity.[15] Mild cleansing and moisturizing regimens improve patient satisfaction. Cleansers should be fragrance- and abrasive-free with a mildly acidic to neutral pH. Recommended skin cleansers include lipid-free, nonalkaline cleansers (e.g., Cetaphil) and sensitive skin synthetic detergent bars (e.g., Dove Sensitive Skin Bar).[16] Patients should cleanse gently with their fingertips, avoid use of abrasive materials, and pat dry for better absorption of moisturizers. Moisturizers should contain emollients and occlusives.[14]

Although no individual skin care product has been well studied, some products found to improve dryness include polyhydroxy acid (Neostrata), lipid-free nonalkaline (Cetaphil), and ceramide-based formulas (Cerave).[16] Patients should avoid astringents, toners, sensory stimulants, and potentially irritating ingredients.[16] Photoprotection is universally recommended, including the use of wide-brimmed hats and broad-spectrum sunscreens (minimum sun protection factor [SPF] of 30).[13] Dimethicone- and simethicone-based products containing titanium dioxide and zinc oxide may be better tolerated.[2] Cosmetics with green or yellow tint applied to the central facial erythema may conceal redness.[14]

FDA-APPROVED TOPICAL THERAPIES

Topical agents are first-line therapy in the treatment of mild to moderate rosacea *(Table 6)*.[17,18] Medication therapy is based on the presence or absence of persistent central facial erythema or inflammation (e.g., papules, pustules, lesional and perilesional erythema), the severity of symptoms, and the patient's response to previous therapeutic interventions.

Five topical agents are approved by the U.S. Food and Drug Administration (FDA) for the treatment of rosacea: metronidazole 0.75% lotion (Metrolotion), 0.75% cream (Metrocream), and 1% gel (Metrogel); azelaic acid 15% gel (Finacea); sulfacetamide 10%/sulfur 5% cream, foam, lotion, or suspension; brimonidine 0.33%

Table 4. Skin Conditions That Share Similar Features with Rosacea

Condition	*Distinguishing features*
Acne vulgaris	Comedone formation No ocular symptoms
Contact dermatitis	Associated with itching and often improves over time when causative agent is removed
Photodermatitis	Rash appears on multiple body parts with sunlight exposure
Seborrheic dermatitis	Has distinct distribution pattern involving the scalp, eyebrows, and nasolabial folds
Systemic lupus erythematosus	Rarely has pustules

gel (Mirvaso); and most recently, topical ivermectin 1% cream (Soolantra).

Metronidazole. Metronidazole is hypothesized to reduce oxidative stress, and has proven effective in reducing erythema and inflammation.[19] No significant difference in clinical benefit was found using different vehicles (gel, cream, or lotion) or strengths (0.75% or 1%). Adverse effects were mild, including pruritus, irritation, and dryness.[14]

Azelaic Acid. Azelaic acid is effective against erythema and inflammatory lesions via inhibiting production of reactive oxygen species in neutrophils.[19] No difference in effectiveness was found between once- or twice-daily dosing.[20] Adverse events include mild and transient burning, stinging, and irritation.[19]

Metronidazole vs. Azelaic Acid. Three studies assessed the effectiveness of metronidazole vs. azelaic acid. Although physician-assessed outcomes suggested that azelaic acid may be more effective than metronidazole, patient evaluations found no statistically significant differences. Azelaic acid had a higher incidence of adverse events, including dryness, stinging, scaling, itching, and burning. Symptoms were mild to moderate, and transient in both groups. Neither agent was found to be effective against telangiectasia.[19]

Sulfacetamide/Sulfur. FDA approval of sulfacetamide/sulfur was granted primarily based on historical use before the implementation of more rigorous standards. Studies demonstrated effectiveness, but were also characterized by high or uncertain risk of bias.[17,19]

Table 5. Management of Rosacea

	Central facial erythema	
	Without papulopustular lesions	*With papulopustular lesions*
		Mild to moderate
General measures	Evaluate severity of erythema, inflammation, telangiectasia, and associated symptoms Begin mild nonalkaline skin cleansing and moisturizing regimen Avoid astringents, toners, abrasives, fragrances, and sensory stimulants (e.g., camphor, menthol, alcohol, acetone) Use broad-spectrum sunscreen; sun protection factor (SPF) 30 or greater (zinc oxide or titanium dioxide) Educate on trigger avoidance Consider use of yellow- or green-tinted cosmetics to conceal redness	
First-line therapy	Topical metronidazole (Metrogel, Metrocream, Metrolotion); azelaic acid (Finacea), or brimonidine (Mirvaso) for erythema Vascular laser therapy (pulsed dye laser, intense pulsed light, Nd:YAG laser) for erythema and telangiectasia	Topical metronidazole or azelaic acid for inflammation and erythema Topical brimonidine for erythema if needed as adjunctive therapy; may be used in combination with metronidazole or azelaic acid for erythema Topical ivermectin for inflammation; may be used in combination with azelaic acid or metronidazole Vascular laser therapy (pulsed dye laser, intense pulsed light, Nd:YAG laser) for telangiectasia
Second-line therapy	—	Alternate topical therapies (sulfacetamide/sulfur, benzoyl peroxide, erythromycin, clindamycin) *or* Subantimicrobial (anti-inflammatory) dose doxycycline, 40 mg once per day or 20 mg twice per day, alone or in combination with topical agents
Third-line therapy	—	If limited or no response at 8 to 12 weeks, consider antimicrobial (antibiotic) dose of doxycycline (100 to 200 mg once per day) Topical retinoids
Refractory	—	Consider treatment in the moderate to severe category

Nd:YAG = neodymium:yttrium-aluminum-garnet.

Transient application site reactions occur, and some patients comment about the odor. Use of this second-line agent should be avoided in persons with sulfa allergy.

Brimonidine. Topical metronidazole, topical azelaic acid, and oral doxycycline reduce erythema related to vascular inflammation; however, they have negligible effects on background erythema caused by permanently dilated superficial vessels. Conversely, alpha-adrenergic receptor agonists promote vasoconstriction but have no effect on papulopustular rosacea. Once-daily brimonidine, a topical alpha-adrenergic receptor agonist, is effective in reducing erythema. No tachyphylaxis, rebound erythema, or aggravation of inflammatory lesions was noted. Adverse events were mild, including irritation, burning, dry skin, pruritus, and erythema.[21] Oxymetazoline 0.05% nasal solution (Afrin), also an alpha-adrenergic receptor agonist, applied once daily reduces diffuse central erythema based on case reports.[22]

Ivermectin. Topical ivermectin was approved by the FDA in 2014 for the treatment of papulopustular rosacea.[23] Two studies demonstrated effectiveness vs. placebo, and a third found that ivermectin was slightly more effective than topical metronidazole in patient- and physician-assessed outcomes and quality of life.[18,23]

NON–FDA-APPROVED TOPICAL THERAPIES

One study of permethrin (Elimite) vs. azelaic acid vs. metronidazole demonstrated similar effectiveness in reducing erythema and lesion counts. Two additional

	Phymatous	*Ocular*
Moderate to severe		
Same as for mild to moderate	Same as for central facial erythema	Lid hygiene (warm compresses and cleansing of lashes and lids with baby shampoo scrubs)
Topical metronidazole or azelaic acid for inflammation plus subantimicrobial (anti-inflammatory) dose of doxycycline (Oracea), 40 mg once per day or 20 mg twice per day Topical brimonidine for erythema if needed as adjunctive therapy Vascular laser therapy (pulsed dye laser, intense pulsed light, Nd:YAG laser) for telangiectasia	Isotretinoin, 0.3 to 1 mg per kg per day for 12 to 28 weeks Microdose therapy for maintenance	Topical antibiotics (metronidazole or erythromycin)
If limited or no response at 8 to 12 weeks, consider antimicrobial (antibiotic) dose of doxycycline (100 to 200 mg once per day)	Vascular laser therapy (pulsed dye laser, intense pulsed light, Nd:YAG laser, and carbon dioxide laser) Dermabrasion, electroscalpel, electrosurgery, loop cautery	Oral tetracyclines (preferred), or metronidazole or azithromycin (Zithromax) Cyclosporine ophthalmic emulsion (Restasis) Ophthalmologic referral
If limited or no response at reassessment, consider alternative oral antibiotic (tetracycline, minocycline [Minocin], metronidazole [Flagyl], azithromycin) and/or topical treatment (sulfacetamide/sulfur, benzoyl peroxide, erythromycin, clindamycin, permethrin [Elimite])	—	—
If refractory to treatment, consider oral isotretinoin (requires participation in online risk reduction program, iPledge: https://www.ipledgeprogram.com)	—	—

studies of permethrin vs. metronidazole demonstrated comparable effectiveness in reducing erythema and papules but not pustules.[19]

Benzoyl peroxide alone or in combination with clindamycin has proven effective; however, adverse events included burning, stinging, and itching.[19] Erythromycin 2% gel had no statistically significant effectiveness in physician- or patient-assessed outcomes.[17,19]

Table 6. Topical Therapies for Rosacea

Therapy	*Formulation and dosage*	*Effectiveness*	*Adverse effects*
Metronidazole† (Metrogel, Metrocream, Metrolotion)	0.75% gel, cream, or lotion: twice per day 1% gel: once per day	Papules, pustules, erythema	Pruritus, stinging, irritation, dryness
Azelaic acid† (Finacea)	15% gel once or twice per day	Papules, pustules, erythema	Stinging, irritation, burning
Sulfacetamide/sulfur† (several brands)	10%/5% cream and other formulations; once or twice per day	Papules, pustules, erythema	Irritation, malodorous, avoid in persons with sulfa allergy
Brimonidine† (Mirvaso)	0.33% gel once per day	Erythema	Pruritus, burning, irritation, dryness, erythema; use with caution in patients with CAD or CVD
Ivermectin† (Soolantra)	1% cream once per day	Papules, pustules	Burning, skin irritation
Permethrin (Elimite)	5% cream once per day	Papules, erythema	Irritation, burning
Benzoyl peroxide	5% gel once or twice per day	Papules, pustules, erythema	Erythema, burning
Clindamycin	1% gel twice per day	Papules, pustules	Pruritus, burning, irritation, dryness
Erythromycin	2% gel twice per day	Papules, pustules	Pruritus, erythema, irritation, dryness
Pimecrolimus (Elidel)	1% cream twice per day	Erythema	Burning
Tretinoin	Cream: 0.025%, 0.05%, 0.1% Gel: 0.01%, 0.025% Once per night at bedtime	Papules, pustules, erythema, possibly telangiectasia	Peeling, erythema, pruritus, dryness, irritation, may exacerbate rosacea photosensitivity
Oxymetazoline (Afrin)	0.05% nasal solution every six hours	Erythema	Irritation, burning
Cyclosporine (Restasis)	0.5% ophthalmic emulsion every 12 hours	Ocular	Hyperemia, burning, blurred vision, tearing

CAD = coronary artery disease; CVD = cardiovascular disease; KLK5 = kallikrein-related peptidase 5; NA = not available; OTC = over the counter; RCTs = randomized controlled trials.

**—Estimated retail price based on information obtained from http://www.goodrx.com (accessed April 3, 2015). Discounts available from multiple retailers. Generic price listed first; brand price listed in parentheses. Cost: $ = less than $50; $$ = $50 to $100; $$$ = $100 to $250; $$$$ = more than $250.*

†—U.S. Food and Drug Administration–approved therapies.

Information from references 17 and 18.

Pimecrolimus 1% cream (Elidel), when compared with placebo, did not improve participant-assessed outcomes. Experts recommend considering use in patients with erythema that does not respond to other treatments.[17,19]

Mechanism of action	*Evidence*	*Cost**
Antioxidant, anti-inflammatory	RCTs	$$$ ($$$$) 45- to 60-g tubes of cream or gel; 59-mL bottle of lotion
Antioxidant; decreases KLK5 and cathelicidin	RCTs	NA ($$$$) 50-g tube
Antibacterial	Small studies and historical precedent	$$ to $$$$ 28- to 57-g tube
Vasoconstriction	RCTs	NA ($$$$) 30-g tube
Antiparastic/anti-inflammatory	RCTs	NA ($$$$) 30-g tube
Antiparasitic	Limited studies	$$ ($$) 60-g tube
Antibacterial	Limited studies	$ ($$) 90-g tube Available OTC
Antibiotic	Limited studies	$$ ($$$) 60-g tube
Antibiotic	Limited studies	$ (NA) 60-g tube
Anti-inflammatory	Limited studies	NA ($$$$) 60-g tube
Stimulates epithelial cell turnover	Limited studies	$ ($$$) 20-g tube of cream 15-g tube of gel
Vasoconstriction	Case studies	$ ($) Available OTC
Immunomodulation	RCTs	NA ($$$) 30 vials of 0.4 mL

Topical retinoids have limited data to support their use. One small study suggested a reduction in papulopustular lesions. A randomized, double-blind, placebo-controlled study of combination clindamycin 1.2%/tretinoin 0.025% gel (Veltin; Ziana) suggested benefit in the reduction of telangiectasia and erythema.[17,24]

Cream containing 1% extract of a flavonoid-rich plant (*Chrysanthellum indicum*) demonstrated effectiveness based on patient and physician assessment of rosacea severity.[19]

THERAPIES FOR DIFFUSE CENTRAL ERYTHEMA AND TELANGIECTASIA

Pulsed dye laser, intense pulsed light, and near infrared lasers appear to be effective in treating facial erythema and telangiectasia, although not papulopustular lesions. The cost of these modalities is significant and may not be covered by insurance. Intermittent retreatment is necessary. Adverse events include blistering, purpura, loss of pigmentation, ulceration, and scarring. Near infrared lasers have a greater risk of complications and should be reserved for prominent telangiectasias.[25]

SYSTEMIC THERAPIES FOR FACIAL ERYTHEMA WITH PAPULOPUSTULAR ROSACEA

Tetracycline and its derivatives have historically been used for the treatment of papulopustular and ocular rosacea. However, the only FDA-approved oral agent is modified-release doxycycline capsule, 40 mg (Oracea). Subantimicrobial-dose doxycycline at 40 mg once daily or 20 mg twice daily is recommended as initial oral therapy[26] *(eTable A)*. Use of subantimicrobial-dose doxycycline avoids development of bacterial resistance while enhancing safety and tolerability.[19,27] Adverse reactions include photosensitivity, candidal vaginitis, pill esophagitis, diarrhea, and pseudotumor cerebri. Minocycline (Minocin) has limited data to support its use and uncommon but serious complications, including autoimmune hepatitis, cutaneous hyperpigmentation, vertigo, and drug-induced eosinophilia with systemic symptoms. Patients with symptoms that do not respond to initial therapy may be prescribed antimicrobial-dose doxycycline, tetracycline, minocycline, or other antibiotics.[19,26]

Ampicillin, erythromycin, and clarithromycin (Biaxin), although effective against papulopustular rosacea in a few studies, are not oral agents of choice because of drug interactions, gastrointestinal intolerance, and concerns about promoting antibiotic resistance. Azithromycin (Zithromax) has greater tolerability, but use has been supported only by case reports and small studies.[19,26]

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendations	*Evidence rating*	*References*
Mild cleansers and moisturizers, broad-spectrum sunscreens (sun protection factor [SPF] 30 or greater), and sun avoidance measures should be used to manage all cutaneous rosacea subtypes.	C	13, 15, 16
First-line therapy for mild to moderate inflammatory rosacea includes topical metronidazole (Metrolotion, Metrocream, Metrogel) or azelaic acid (Finacea).	A	19
Brimonidine (Mirvaso) can be used to treat persistent facial erythema associated with rosacea.	A	17, 21
Topical ivermectin (Soolantra) may be used for the treatment of papulopustular rosacea.	B	18
Subantimicrobial-dose doxycycline (Oracea) can be used to treat inflammatory lesions of papulopustular rosacea.	A	19, 27
Subantimicrobial-dose doxycycline in combination with topical azelaic acid or metronidazole can be used to treat moderate to severe inflammatory lesions or mild inflammatory lesions that have not responded to initial therapy.	C	17, 26, 29
Mild ocular rosacea should be treated with eyelid hygiene and topical antibiotic agents, such as metronidazole and erythromycin.	C	30, 31
Topical ophthalmic cyclosporine drops (Restasis) are more effective than artificial tears in the management of mild ocular rosacea.	B	19

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

Oral metronidazole (Flagyl) has demonstrated similar effectiveness when compared with tetracyclines in four studies,[18] but the risk of a disulfiram (Antabuse)-like reaction with alcohol (i.e., nausea, vomiting, diaphoresis, flushing of the skin, tachycardia, shortness of breath, headache, confusion, dizziness), and the rare risk of neuropathy and seizures, relegates its use to patients experiencing treatment failures or intolerance of other agents.[19,26]

Oral isotretinoin may have a role in the management of refractory papulopustular and phymatous rosacea.[19,28] One study found low-dose isotretinoin to be more effective than doxycycline in physician- and patient-assessed outcomes.[18]

For patients with moderate to severe papulopustular rosacea or those experiencing an inadequate response to topical therapy, limited studies support combination therapy (usually oral subantimicrobial-dose doxycycline and topical metronidazole or azelaic acid).[18,26,29]

Therapy for Phymatous Rosacea

Phymatous rosacea *(Figure 3)* can be disfiguring and difficult to treat. Best results are achieved when treatment is instituted early. Oral isotretinoin may be effective in reducing nasal volume in early disease *(Table 5)*; however, recurrence is likely after discontinuation, and mucinous and fibrotic changes are unresponsive.[26,28] Surgical techniques including laser- or light-based therapies (pulsed dye laser, intense pulsed light, carbon dioxide laser), electrosurgery, dermabrasion, tangential excision, electroscalpel, loop cautery, and scissor sculpting are effective in correcting or minimizing phymatous changes and may be life-changing.[25,26]

Therapy for Ocular Rosacea

More than 50% of patients with cutaneous rosacea have ocular symptoms that may include tearing, foreign body sensation, itching, photophobia, and blurred vision. Ophthalmology consultation is recommended

Figure 3. Phymatous changes on tip of nose, inflammatory lesions (papules and pustules) visible laterally, and telangiectasia.

because complications (e.g., corneal ulcerations, scleritis, episcleritis, iritis, persistent hordeola and chalazia) may occur.[30] Blepharitis, recurrent hordeola, chalazia, and telangiectasias can affect the lid margin *(Figure 4)*. Mild symptoms can be managed with artificial tears, warm compresses, and cleansing the eyelashes with baby shampoo.[30] Long-term consumption of omega-3 fatty acids may improve meibomian-gland dysfunction.[31] Topical ophthalmic cyclosporine drops (Restasis) demonstrate statistically significant improvement in common signs and symptoms compared with artificial tears.[19] Topical metronidazole and erythromycin may be useful for eyelid symptoms. Patients may be treated with systemic therapy using tetracyclines or azithromycin.

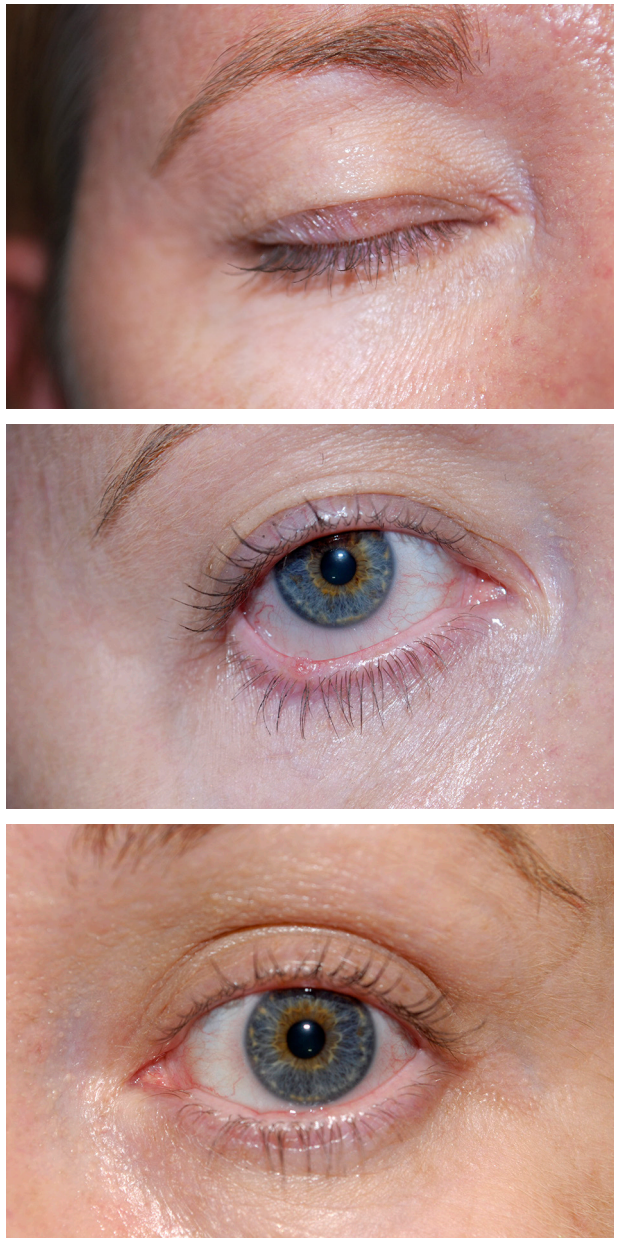

Figure 4. Ocular rosacea. *(top)* Telangiectasia of the upper lid. *(middle)* Lower-lid granuloma secondary to meibomian gland dysfunction; inflammation and scarring; mild conjunctivitis is also present. *(bottom)* Scarring of the lower lid margin secondary to recurrent bouts of inflammation.

Data Sources: We searched the Cochrane Database of Systematic Reviews, PubMed, Medline, and Essential Evidence Plus using keywords rosacea, rosacea and pathophysiology, rosacea and treatment outcome, rosacea and evidence-based medicine, rosacea and drug therapy, and rosacea and dermatological agents. The search included reviews, meta-analyses, randomized controlled trials, consensus guidelines, and clinical trials. Search dates: June 2014 and April 30, 2015.

EDITOR'S NOTE: Additional photos of various subtypes of acne rosacea are available at http://www.aafp.org/afp/2009/0901/p461.html.

The Authors

LINDA K. OGE', MD, is an assistant clinical professor and chief of family medicine at Louisiana State University Family Medicine Residency at University Hospital and Clinics in Lafayette.

HERBERT L. MUNCIE, MD, is a professor of family medicine and director of predoctoral education at Louisiana State University School of Medicine in New Orleans.

AMANDA R. PHILLIPS-SAVOY, MD, MPH, is an assistant clinical professor in the Department of Family Medicine at Louisiana State University Family Medicine Residency at University Hospital and Clinics.

Address correspondence to Linda K. Oge', MD, LSU Health UHC, 2390 West Congress St., Lafayette, LA 70506 (e-mail: loge@lsuhsc.edu). Reprints are not available from the authors.

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eTable A. Systemic Therapy for Rosacea

Therapy	*Dosage*	*Adverse effects*
Doxycycline (Oracea; anti-inflammatory/ subantimicrobial dose)†	40 mg once per day (30 mg per 10-mg modified-release capsule) 20 mg twice per day	Dose-related phototoxicity, GI adverse effects, pill esophagitis, pseudotumor cerebri, cutaneous hyperpigmentation (bluish/ brownish discoloration of skin, mucous membranes)
Doxycycline (antimicrobial dose)	100 mg once or twice per day	Tetracycline-related adverse effects as above Candidiasis
Tetracycline	250 to 500 mg twice per day	Tetracycline-related adverse effects as above Candidiasis
Minocycline (Minocin)	50 to 100 mg twice per day or once per day for long-acting	Tetracycline-related adverse effects as above Vertigo/dizziness, autoimmune hepatitis, drug-induced lupus-like syndrome Drug rash with eosinophilia and systemic symptoms
Metronidazole (Flagyl)	250 mg once per day	Disulfiram (Antabuse) reaction with alcohol, seizures, neuropathy Candidiasis
Azithromycin (Zithromax)	500 mg once per day for three consecutive days per week 250 mg once per day for three days per week	GI adverse effects, prolonged QT interval, hepatotoxicity, cholestasis Candidiasis
Erythromycin	250 mg twice per day	High incidence of GI adverse effects, prolonged QT interval
Clarithromycin (Biaxin)	250 to 500 mg twice per day	High incidence of GI adverse effects, prolonged QT interval
Isotretinoin	0.3 mg per kg per day or 10 to 20 mg per day initially for 4 to 6 months, followed by microdose therapy (0.03 to 0.17 mg per kg per day)	Teratogenicity, hyperlipidemia, hepatotoxicity, depression, dry skin, photosensitivity, impaired night vision

NOTE: *Therapies are listed in order of preference.*

GI = gastrointestinal; NA = not available; RCTs = randomized controlled trials.

**—Estimated retail price for one month's treatment based on information obtained at http://www.goodrx.com (accessed April 3, 2015). Discounts are available for multiple retailers. Generic price listed first; brand price listed in parentheses. Cost: $ = less than $50; $$ = $50 to $100; $$$ = $100 to $250; $$$$ = $250 to $500; $$$$$ = more than $500.*

†—*Only U.S. Food and Drug Administration–approved systemic therapy for the treatment of rosacea.*

Information from: Del Rosso JQ, Thiboutot D, Gallo R, et al. Consensus recommendations from the American Acne & Rosacea Society on the management of rosacea, part 3: a status report on systemic therapies. Cutis. *2014;93(1):18-28.*

Caveats	*Evidence*	*Cost**
Decreased absorption with vitamins, antacids, metal ions Contraindicated in pregnancy and lactation No generation of antibiotic resistance demonstrated	RCTs and open-label studies (large, high-quality studies)	NA ($$$$$) for 40 mg $$ for 20 mg
Decreased absorption with vitamins, antacids, metal ions Contraindicated in pregnancy and lactation	RCTs (few) and historical use	$ for 60 capsules $$ for 60 tablets
Decreased absorption with vitamins, antacids, metal ions Contraindicated in pregnancy and lactation Must be taken at least one hour before or two hours after meal	RCTs (few) and historical use	$
Contraindicated in pregnancy and lactation	Historical use	$ ($$$$$)
Drug interaction with lithium, anticoagulants, phenytoin (Dilantin)	Small studies	$ ($$$)
Caution in older patients	Small studies, case reports	$ ($$$) for 500 mg $ ($$) for 250 mg
High incidence of drug interactions Caution in older patients	Small studies	$$$$
High incidence of drug interactions Caution in older patients	Small studies	$$$ ($$$$$) for 250 mg $$$ ($$$$$) for 500 mg
Patients must enroll in National iPledge Program; physicians require special training to prescribe Refractory papulopustular and phymatous subtypes	RCTs (few)	$$$$ to $$$$$, depending on which generic is used and the dosage