Rosacea: Clinical Aspects and Treatments

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GENERAL PURPOSE: To review the clinical presentation and treatment of rosacea.

TARGET AUDIENCE: This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES: After participating in this educational activity, the participant will:

1. Distinguish the clinical manifestations of rosacea subtypes.
2. Identify pharmacologic and nonpharmacologic treatment options for patients who have rosacea.

ABSTRACT

Rosacea is a chronic inflammatory disease characterized by a diverse set of nonspecific clinical signs including erythema, flushing, papules and pustules, skin thickening (especially enlarged nose) and thread-like vessels in the central facial region, and potential ocular involvement. This review focuses on the epidemiology, clinical presentation, and treatment of rosacea. Other related topics discussed include the psychosocial impact and differential diagnoses.

KEYWORDS: anti-inflammatory therapies, erythema, flushing, inflammatory rosacea, laser intervention, ocular rosacea, phymatous rosacea, rosacea, surgery, telangiectasia

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INTRODUCTION

Rosacea is a chronic inflammatory skin condition affecting the central facial region (forehead, cheeks, chin) that can involve erythema, thread-like vessels (telangiectasia), papules and pustules, and ocular manifestations; it is usually observed in patients older than 30 years. Global population studies on the prevalence of rosacea reveal a wide range, with studies conducted in the Faroe Islands reporting a low of 0.09% and Estonia reporting a high of 22%. However, most studies report a prevalence of between 1% and 3%.[1] There is a higher prevalence among fair-skinned individuals and women.[2]

The symptoms and signs of rosacea occur in the facial region and can have a substantial impact on an individual's physical appearance. Patients with rosacea often experience psychological comorbidities including depression, anxiety, social phobias, and lowered self-esteem. They are often victims of social stigmas, with excessive alcohol ingestion being associated with the enlarged red nose (rhinophyma, a form of localized lymphedema). Given the pervasive effect of these psychosocial factors on the lives of patients with rosacea, these clinical signs should be addressed as part of the treatment options.

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Clinical Features

Because of the lack of diagnostic tests specific to rosacea, diagnosis relies primarily on clinical observations. The standard for rosacea classification was originally set by the National Rosacea Society Expert Committee in 2002, but has since been updated by a Canadian rosacea expert panel in 2016 and the Global Rosacea Consensus panel in 2017.[3–5]

Although persistent central facial erythema and phymatous changes are individually sufficient for a diagnosis of rosacea, other major features include papules and pustules, flushing, and telangiectasia. Less common symptoms include burning, stinging, and dryness.[4] However, burning and stinging are clinical symptoms usually resulting from local inflammation. A summary of the clinical features of rosacea is provided in Table 1.

Healthcare professionals must be aware that these features are also observed in other conditions affecting the facial skin resulting in misdiagnoses, especially in patients of color. For example, acne vulgaris also exhibits papules and pustules, but often presents with comedones, which are not typically observed in rosacea. The importance of making an accurate diagnosis of rosacea is illustrated by the common misdiagnosis of rosacea as seborrheic dermatitis or contact irritant/allergic dermatitis around the eyes. This can lead to treatment with topical steroids, which can result in hypopigmentation, atrophy, telangiectasia, and monomorphous papular-pustular steroid acne, with stronger topical steroids and longer-term use increasing the risk.[6] A summary of differential diagnoses of rosacea is provided in Table 2. However, rosacea may also coexist with these other skin conditions.

Investigations in Selected Patients

Rosacea needs to be distinguished from systemic lupus. Patients with subacute cutaneous lupus often have other systemic symptoms and signs such as photosensitivity on photo-exposed areas; Raynaud phenomena with cold sensitivity and color changes of the fingers and toes (blue, white, and then erythema during the recovery period); arthralgias or sore joints, often first thing in the morning; and oral ulcers (aphthae are relatively common). Patients should have laboratory screens performed for antinuclear antigen, extractable nuclear antigen, rheumatoid factor, complement (decreased C4 and/or C3), and anti-DNA antibodies along with a complete blood count to look for low white blood cell count and kidney function, which is often decreased with anti-DNA antibodies. Patients often have a positive rheumatoid factor before the antinuclear antigen becomes positive and a positive extractable nuclear antigen is often associated with subpositive tests for Ro (SS-A) and La (SS-B) antigens.

Systemic lupus is much less common than rosacea and often involves women at a younger age (15-35 years), whereas rosacea onset is more common at age 30 to 50 years. In the presence of gastrointestinal symptoms (usually cramps and diarrhea) and a darker red erythema associated with the facial flushing, carcinoid and related symptoms may be involved, although rare. Providers should collect 24-hour urine samples for 5-hydroxyindoleacetic acid and stool samples for vasoactive intestinal peptide; a plasma serotonin level may also be helpful.

Table 1. CLINICAL FEATURES OF ROSACEA

Diagnostic Features	Major Features	Minor Features
Centrofacial erythema (persistent)	Flushing (often transient)	Burning
	Ocular manifestations	Stinging
Phymatous changes	Papules and pustules	Edema
	Telangiectasia	Dryness

ROSACEA SUBTYPES

Common groupings of clinical features have been designated as rosacea subtypes. The four main subtypes are flushing and erythema (erythrotelangiectatic), inflammatory papules and pustules, phymatous (enlarged tissue with the nose being most common), and ocular rosacea. However, patients often exhibit characteristics of multiple rosacea subtypes concurrently, and some clinicians consider the four subtypes to be part of one continuum.[7] Presentations of rosacea are provided in the Figure.

Erythrotelangiectatic Subtype

Flushing and erythematic rosacea are characterized by flushing and persistent erythema in the central facial region, excluding the periocular skin. Less commonly, the erythema can extend beyond the central facial region, including the neck and upper trunk. Although facial erythema may be experienced in response to hot temperatures, alcohol, or emotional stress, patients with rosacea experience erythema that is slower in onset but more prolonged.[8] Patients with flushing and erythematic rosacea tend to lack the sebaceous skin quality observed in other rosacea subtypes and often have no history of acne.[9,10] Telangiectasia is also commonly observed, but not required for the diagnosis of this subtype.[3] These thread-like vessels result from persistent erythema leading to reactive telangiectasia, as first described by Wilkin et al.[11] This is distinct from sun-induced telangiectasia, which is most commonly observed in light-skinned individuals (Fitzpatrick types I and II).

Table 2. DIFFERENTIAL DIAGNOSES OF ROSACEA

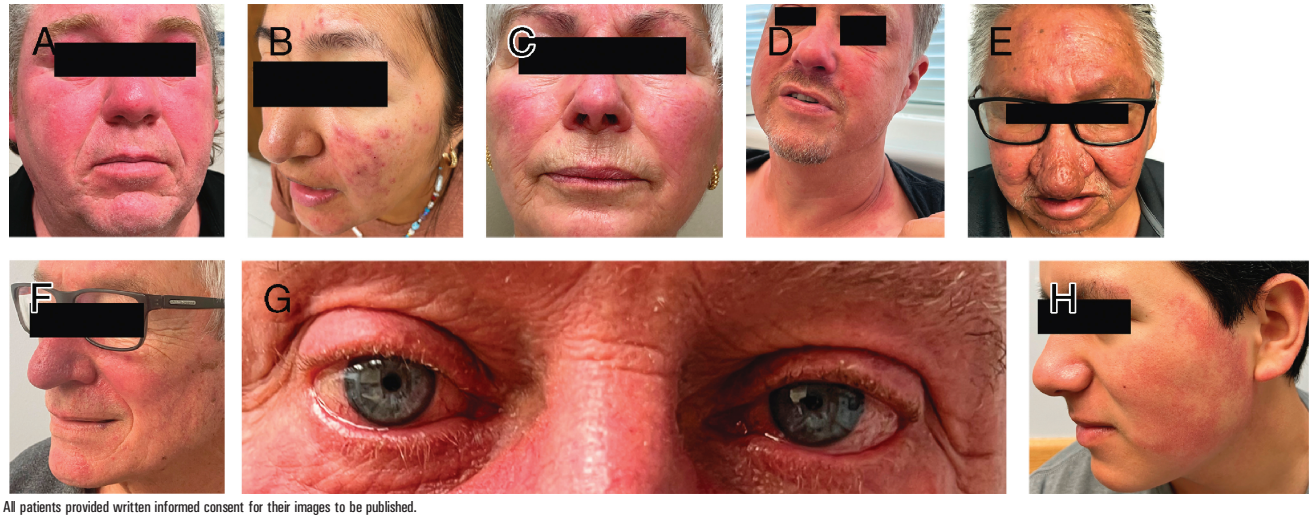
Differential Diagnoses	Differences with Rosacea	Symptoms Common to Rosacea
Acne vulgaris	No flushing, erythema concentrated around pimples, presence of comedones. Frequent involvement in upper chest and back	Papules, pustules predominately on the face, but uncommonly can occur in extrafacial locations
Contact dermatitis (80% irritant, 20% allergic)	Very itchy rash. Symptoms disappear after triggering substance is removed (allergy has discrete margins; irritant is often more diffuse and less prominent)	May include erythema, skin thickening (phyma), itch, burning, and stinging
Keratosis pilaris	Many patients are asymptomatic. Affected areas may be itchy; typically, only affects cheeks—no ocular involvement. Affects extrafacial regions (upper and outer arms, anterior thighs). Erythema around blocked hair follicles that is uniformly red or pink	Erythema, follicular papules/pustules, without comedones
Subacute cutaneous lupus	Red, ring-shaped, scaly, nonscarring rashes appearing on sun-exposed areas; can evolve into discoid lesions	Fixed dermal erythema and can be photoaggravated
Perioral/periocular dermatitis	Rash, erythema, and pustules concentrated around mouth, nose, and eyes; younger individuals/no other rosacea features	Papules, pustules—perioral or periocular dermatitis can exist as a subtype of rosacea
Seborrheic dermatitis	Greasy, yellowish scale with dandruff. Affects ears, eyebrows, and scalp; no pustules	Erythema
Steroid acne	Uniform pustules and chest involvement. Symptoms gradually disappear after triggering steroid substance is removed	Papules, pustules (pustules may be present without papules—check that no topical steroids are being used)

Inflammatory Subtype: Papulopustular

Inflammatory rosacea is characterized by persistent erythema in the central facial region and erythematous papules and pustules.[3] This subtype appears similar to acne vulgaris but lacks comedones.[12] Similar to the flushing and erythematic subtype, the erythema excludes the periocular skin; some patients also report burning or stinging sensations. Although thread-like vessels may be present, they are often obscured by the dermal erythema.[3,8] Mild edema may be present during flare-ups, but repeated episodes can result in phymatous thickening of the skin that is more common in men.[13]

Figure. CLINICAL PRESENTATIONS OF ROSACEA

A, Persistent erythema with thickening of the cheeks and nose. B, Diffuse erythema concentrated around erythematous papules and pustules. C, Persistent erythema with thread-like vessels. D, Persistent erythema with extension beyond centrofacial region involving the neck and upper central chest and enlargement of the nose. E, Severe thickening and enlargement of the nose and cheeks (rhinophyma). F, Persistent erythema with thread-like vessels and thickening of the cheeks and nose. G, Ocular involvement consisting of blepharitis and conjunctival hyperemia. H, Persistent erythema of the centrofacial region with involvement of the earlobes.



All patients provided written informed consent for their images to be published.

Phymatous Subtype: Rhinophyma and Other Facial Locations

Phymatous rosacea is characterized by localized skin thickening (lymphedema-like) and surface nodularity that seldom develops before the age of 40 years. It commonly occurs with the other rosacea subtypes.[3] However, unlike the other subtypes, phymatous rosacea is more common in men than in women, by a ratio of between 5:1 and 30:1.[14] The most common region affected is the nose (rhinophyma), but other facial regions can also be affected, including the forehead (metophyma), eyelids (blepharophyma), ears (otophyma), and chin (gnathophyma). There are four subtypes of rhinophyma: glandular, fibrous, fibroangiomatous, and actinic.[8]

In the glandular form of rhinophyma, the nose takes on a pitted, enlarged appearance due to hyperplasia of sebaceous glands. The enlargement is often asymmetric, with humps and grooves. The skin either takes on a normal or red color, with increased secretion of sebum. External extraction results in the secretion of a white substance composed of a mixture of sebum, bacteria, corneocytes, and, occasionally, *Demodex folliculorum* mites.

In the fibrous form of rhinophyma, the enlargement of the nose is predominately due to hyperplasia of the connective tissue. Through histologic studies, accumulation of actinically damaged elastotic material and vascular enlargement can also be observed.

In fibroangiomatous rhinophyma, the nose takes on an enlarged, red appearance, often with pustules and telangiectasia. However, unlike the other forms of rhinophyma, hyperplasia of sebaceous glands is less prominent.

In actinic rhinophyma, nasal distortion is caused by the accumulation of nodular masses of elastic tissue typical of severe actinic damage.[15] Prominent thread-like vessels are present. Severe hyperplasia of sebaceous glands is observed, with widely dilated ducts congested with horny material in thickened sebum. Dense amounts of *D folliculorum* mites, *Cutibacterium acnes* bacteria, and *Pityrosporum* yeast are often present within the sebaceous follicles.[16]

Ocular Subtype

Most cases of ocular rosacea are characterized by blepharitis, conjunctivitis, and/or chalazion formation (inflammation of a blocked oil gland). However, ocular telangiectasia, photophobia, burning, stinging, dryness, itching, blurred vision, and periocular erythema can also occur. Similar to the phymatous subtype, ocular rosacea commonly appears with the other rosacea subtypes.[3] In patients with rosacea, the prevalence of ocular manifestations ranges from 10% to greater than 50%.[17] Although ocular rosacea can precede the cutaneous forms of rosacea, it most often occurs concurrently with or after cutaneous manisfestations.[3] In severe cases, corneal scarring and vascularization can result in blindness.[18] Unfortunately, treatments targeting the cutaneous symptoms of rosacea may be insufficient in reducing the risk of vision loss from ocular rosacea. As a result, other ophthalmologic interventions may be required in some patients.[3]

TREATMENT

The choice of therapy is guided by the signs and symptoms present. Patient education should focus on the avoidance of triggers (Table 3), proper use of sun protection, and gentle skin care. Although there is no current cure for rosacea, there are several pharmaceutical and nonpharmaceutical interventions available that focus on symptom and sign reduction. Treatments are summarized in Table 4.

Pharmaceutical Topical Treatments

Azelaic acid. Azelaic acid is an FDA-approved dicarboxylic acid available in a 15% gel or 20% cream for the treatment of papules and pustules in rosacea. Azelaic acid is believed to reduce rosacea symptoms and signs because of its anti-inflammatory properties.[20] Azelaic acid may also help improve postinflammatory hyperpigmentation.

A double-blind study demonstrated that azelaic acid significantly reduced the number of inflammatory lesions by 58% compared with 40% for vehicle ($P = .0001$). Further, a significantly higher proportion of patients treated with azelaic acid experienced improvement in erythema (44% vs 29% for vehicle; $P = .0017$).[21] Initial improvement from azelaic acid may be noted within

Table 3. ROSACEA TRIGGER FACTORS

Trigger Factors	Examples
Food	Meat: liver Dairy products: yogurt, sour cream, cheeses (excluding cottage cheese) Vegetables: eggplant, tomatoes, spinach, lima and navy beans, peas Fruits: avocados, bananas, red plums, raisins, figs, citrus fruits Condiments/flavoring: chocolate and vanilla, soy sauce, vinegars Other: hot and spicy foods, yeast extract
Beverage	Alcohol, hot beverages
Psychological	Stress, anxiety
Environmental	Sun, wind, hot/cold temperatures, humidity
Cosmetic	Products containing alcohol, witch hazel, fragrances, acetone
Medical	Menopause, caffeine withdrawal syndrome, chronic cough, vasodilators, topical steroids
Physical	Exercise, heavy lifting

Adapted with permission from Gupta and Chaudhry,[19] 2005.

Table 4. ROSACEA TREATMENTS BY SUBTYPE AND SEVERITY

Subtype	Severity	Topical	Systemic	Nonpharmaceutical
Flushing and erythema	All	Azelaic acid[a] Brimonidine[a] Oxymetazoline[a]	Clonidine Doxycycline Macrolide antibiotics[a]	Vascular laser; intense pulsed light
Inflammatory	Mild	Azelaic acid[a] Clindamycin Erythromycin Ivermectin[a] Metronidazole[a]	Doxycycline[a] Macrolide antibiotics[a] Tetracycline[a]	None
	Moderate/severe	Azelaic acid[a] Benzoyl peroxide Ivermectin[a] Metronidazole[a]	Doxycycline[a] Isotretinoin Macrolide antibiotics[a] Tetracycline[a]	None
Rhinophyma	Mild/moderate	Topical retinoids[a]	Doxycycline[a] Isotretinoin Tetracycline[a]	Laser
	Severe	None	Isotretinoin	Surgery[a]
Ocular	All	Cyclosporine[a] Pimecrolimus Tacrolimus	Doxycycline[a] Macrolide antibiotics Tetracycline[a]	None

[a]First-line treatments.

the first few weeks of use. However, substantial improvement may take as long as 12 to 15 weeks of therapy. Adverse reactions include stinging, burning, itching, and dryness.

Benzoyl peroxide. Benzoyl peroxide is an antibacterial agent typically used for treating acne vulgaris. Its use in treating rosacea has been limited due to risks of causing irritation and erythema. However, the FDA recently approved an encapsulated benzoyl peroxide 5% cream for the treatment of papules and pustules in rosacea. Encapsulation of benzoyl peroxide allows for slow release, reducing the risk of irritation. The effectiveness of benzoyl peroxide can likely be attributed to its anti-inflammatory properties. Benzoyl peroxide is antibacterial and, unlike clindamycin, is less likely to have resistant bacteria.

A double-blind clinical trial demonstrated the effectiveness of encapsulated benzoyl peroxide in reducing inflammatory lesions by 68% after 12 weeks compared with 38% reduction for vehicle. Initial improvements were observable after 4 weeks of treatment.[22] Adverse reactions include application site erythema (contact irritation, but less commonly contact allergy) and pain and nasopharyngitis. Benzoyl peroxide is contraindicated for individuals who are pregnant or lactating.

Brimonidine and oxymetazoline. Brimonidine 0.33% gel and oxymetazoline 1.0% cream are α2 and α1 adrenergic receptor agonists, respectively, that have been FDA approved for the treatment of rosacea-related flushing-related erythema. As α-adrenergic receptor agonists, both brimonidine and oxymetazoline exert their effects through vasoconstriction.

In a double-blind study, among the patients who showed a two-point improvement on the clinical erythema assessment scale, 12% to 14% received oxymetazoline compared with 6% to 7% for vehicle, and 25% to 31% received brimonidine compared with 9% to 11% for vehicle.[23] Brimonidine has also been recommended for maintenance therapy of erythema with minimal adverse reactions and possible tachyphylaxis. However, brimonidine may lose its therapeutic effect with continued use in clinical practice. Adverse reactions for brimonidine include rebound erythema, burning, and headaches. For oxymetazoline, application site dermatitis and worsening of erythema have been reported.

Cyclosporine. Cyclosporine is a calcineurin inhibitor available as a 0.05% ophthalmic emulsion that is effective in reducing ocular rosacea symptoms and signs. The effectiveness of cyclosporine has been linked to reducing inflammation within the conjunctiva.

In one study, patients using cyclosporine emulsion twice daily for 3 months had a 75% mean decrease in ocular symptoms and features including blepharitis, conjunctival hyperemia, and erythema, among others ($P < .01$).[24] Cyclosporine is generally well tolerated, but stinging and local irritation have been reported.

Ivermectin. Ivermectin is an FDA-approved parasiticide available as a 1% cream for the treatment of inflammatory lesions in rosacea. The efficacy of topical ivermectin

is attributed to its anthelmintic effects on *D folliculorum* mites and its anti-inflammatory properties.

In a double-blind study, ivermectin significantly reduced the number of inflammatory lesions by 75% compared with 50% for vehicle ($P < .001$).[25] Adverse reactions including skin burning and irritation have been reported. Exercise caution when prescribing ivermectin cream to pregnant or nursing individuals because of the risk of harm to the fetus or nursing infant.

Macrolide class antibiotics (clindamycin and erythromycin). Clindamycin is a second-generation member of the macrolide class of antibiotics available orally or as a topical 1.0% lotion. Topically applied clindamycin has demonstrated effectiveness in treating papules and pustules in rosacea. The efficacy of clindamycin is believed to be due to its anti-inflammatory and antioxidative properties. In one study, patients who took 250 mg four times daily for 3 weeks, followed by 250 mg twice daily for 9 weeks, observed greater than 80% reduction in inflammatory lesion count.[26] Common adverse reactions include burning, itching, and dryness.

Erythromycin is a first-generation member of the macrolide class of antibiotics available orally or as a topical 2.0% gel. Topically applied erythromycin is effective in treating papules and pustules. In one study, most patients who applied erythromycin 2.0% twice daily for 8 weeks observed a 50% to 75% reduction in papules and pustules. Improvements were noticeable by week 4.[27] Common adverse reactions include stinging and dryness.

Metronidazole. Metronidazole is an FDA-approved antibiotic available in a 0.75%/1.0% cream, 0.75% lotion, or 1.0% gel indicated for the treatment of papules and pustules. A metronidazole 10% cream intended for use in treating bacterial vaginosis may be prescribed off-label if the weaker topical metronidazole formulations are not effective. The efficacy of metronidazole is attributed to its antioxidative and anti-inflammatory properties.

In a double-blind study, patients treated with metronidazole 1.0% gel once daily reduced their inflammatory lesion count by 58% compared with 30% for vehicle ($P < .015$).[28] Adverse reactions are mild, with local irritation and dryness being the most commonly reported.

Pimecrolimus and tacrolimus. Similar to cyclosporine, pimecrolimus and tacrolimus are both calcineurin inhibitors. Tacrolimus 0.03%/0.1% ointment and pimecrolimus 1.0% cream have been used to treat eyelids in patients with ocular rosacea. Their effectiveness is attributed to building up the eyelid epidermal barrier and controlling inflammation locally. Adverse reactions include stinging and burning on application, but cooling can minimize these effects (keep in refrigerator prior to use).

Topical retinoids. Topical retinoids such as adapalene and tretinoin can be used to treat clinically inflamed, mild to moderate rosacea-related tissue enlargements (phymas). The benefits of topical retinoids in rosacea may relate to their anti-inflammatory and extracellular matrix repair properties.

In a 12-week randomized trial that compared patients treated with a topical retinoid (adapalene 0.1% gel, third-generation retinoid) and metronidazole 0.75% gel, adapalene was associated with greater reductions in inflammatory lesions ($P < .05$).[29] Adverse reactions include irritation and photosensitization. Similar to topical ivermectin, there is evidence of potential risk to fetuses. Thus, it is not recommended for patients who are pregnant or lactating.

Pharmaceutical Systemic Treatments

Tetracycline class antibiotics (doxycycline and tetracycline). Doxycycline is a second-generation member of the tetracycline family of antibiotics approved by the FDA at an anti-inflammatory controlled-release 40-mg dose for the treatment of papules and pustules in rosacea. The effectiveness of doxycycline is attributed to its anti-inflammatory properties rather than its antimicrobial effect.

In a two-parallel-group double-blind study, del Rosso et al[30] administered 40-mg controlled-release doxycycline to patients once daily for 16 weeks. Inflammatory lesion counts were significantly reduced by 48% and 59% in the treatment groups compared with 22% and 30% for placebo ($P < .001$).[30] Although also available in antimicrobial doses (100–200 mg daily), the efficacy of a 40-mg dose appears to be equivalent to a 100-mg dose, but with fewer adverse reactions.[31]

Doxycycline has long been used in the treatment of ocular rosacea. Although placebo-controlled studies are lacking, several studies have demonstrated its effectiveness in alleviating ocular rosacea symptoms and signs such as blepharitis, dermal erythema, and telangiectasia.[32]

Anti-inflammatory doses of doxycycline are well tolerated, with common adverse reactions including photosensitivity, nasopharyngitis, diarrhea, and headaches. If doxycycline is taken with meals or dairy products, the absorption is decreased by approximately 20%. To avoid photosensitivity, it should be taken later in the day. If doxycycline is taken in the evening (eg, 1 hour before bed), patients should drink a full glass of water with the dose to avoid esophageal irritation. Doxycycline is contraindicated in pregnancy due to risk of harm to the fetus.

Tetracycline is the first-generation member of the tetracycline family of antibiotics. The mechanism of action of tetracycline is similar to that of doxycycline, and subantimicrobial dosages of tetracycline are often recommended (500 mg or less daily) to alleviate risk of antibiotic resistance. Second-generation tetracyclines such as doxycycline are often preferred because of improved bioavailability and elimination half-lives and reduced

risk of gastrointestinal adverse effects. Approximately 1,000 mg of tetracycline is equivalent to 100 mg of doxycycline.

In a double-blind study, patients who took tetracycline for 6 weeks exhibited a significant reduction in inflammatory lesions (78% compared with 10% for placebo; $P = .05$).[33] Similarly, in a study on ocular rosacea, patients taking tetracycline exhibited a significant reduction in total ocular symptoms by 6 weeks ($P = .012$).[34] Adverse reactions are typically gastrointestinal in nature and include nausea, diarrhea, and constipation. As with other tetracycline-class drugs, tetracycline is contraindicated during pregnancy.

Macrolide class antibiotics. Macrolides are a class of antibiotics including erythromycin and its second-generation derivatives, azithromycin and clarithromycin. Macrolides, in topical or oral forms, may be recommended as a rosacea treatment in patients who are hypersensitive to tetracycline class antibiotics or pregnant. The efficacy of macrolides is believed to stem from their anti-inflammatory and antioxidative properties.

In an uncontrolled study, 10 patients were treated with 250 mg azithromycin three times per week (Monday, Wednesday, Friday). After 4 weeks, most patients exhibited only residual erythema with complete disappearance of inflammatory lesions.[35] Adverse reactions are gastrointestinal in nature; however, the use of second-generation macrolides greatly reduces the risk.

Clonidine. Clonidine is an α2 adrenergic receptor agonist available as 0.025-, 0.1-, 0.2-, and 0.3-mg tablets. Clonidine is typically used for treating hypertension but has been used off-label to suppress the flushing observed in rosacea. Its effectiveness is attributed to its vasoconstrictive properties.

In a crossover trial involving 17 patients, researchers compared the effects of 0.05 mg clonidine twice daily versus placebo.[36] Five patients reported improvements in the frequency and severity of flushing.[36] Adverse reactions are mild and diminish with continued usage; they include hypotension, dry mouth, drowsiness, and dizziness.

Isotretinoin. Oral isotretinoin is a retinoid derivative of vitamin A that has not been approved by the FDA for treatment of rosacea but has nevertheless demonstrated effectiveness in treating severe, recalcitrant inflammatory rosacea. Patients who fail to respond to topical therapies and oral antibiotics are candidates for oral isotretinoin. Isotretinoin appears to downregulate the inflammatory pathway implicated in the pathogenesis of rosacea.

In one study, 22 patients with refractory inflammatory rosacea treated with 10 mg isotretinoin daily over 4 months showed substantial improvements.[37] Isotretinoin is not a first-line medication, with typical dosing approximately 0.2 mg/kg per day (usually a total of 10–20 mg per day). A course of treatment may take 5 to 6 months. If successful, maintenance therapy may involve topical metronidazole, azelaic acid, or other standard therapies for inflammatory rosacea.

Isotretinoin has also demonstrated effectiveness in the treatment of phymatous rosacea. Clinical and laboratory findings showed decreases in nasal volume and size of sebaceous glands.[38] Common adverse reactions include dry skin, dry mouth, and photosensitivity. Isotretinoin is contraindicated for patients who are pregnant or lactating because of reports of major fetal abnormalities.

Nonpharmaceutical Treatments

Vascular lasers. Pulsed-dye lasers, long pulsed-dye lasers, potassium-titanyl-phosphate lasers, and diode-pumped frequency-doubled lasers can be used to reduce facial erythema and telangiectasia in patients with rosacea. These lasers emit short-wavelength light that destroys vascular tissue without damaging the surrounding structures. In one study, most of the patients who received one to three pulsed-dye laser treatments spaced 6 to 12 weeks apart showed substantial reductions in erythema and telangiectasia.[39] Posttreatment pain, scarring, erythema, and hyperpigmentation have been reported. Most laser therapies require postlaser care, including avoiding direct sunlight.

Intense pulsed light. Intense pulsed light (IPL) consists of multiple wavelengths of light that can penetrate deeper into the skin than vascular lasers. Similar to vascular lasers, IPL also functions by targeting vascular tissue without damaging surrounding tissue. In a study of patients with rosacea who were treated with IPL, more than 90% of patients saw 75% to 100% clearance in vascular lesions including thread-like vessels after two or more sessions.[40] Adverse reactions are transient in nature and include edema and hypopigmentation.

Surgery. In severe cases of rhinophyma, surgical intervention is required to restore the cosmetic appearance of the nose. Currently, there is no consensus on the surgical technique. However, surgical sculpting with steel and electro-scalpels has produced favorable outcomes.

Recently, Chang et al[41] described an effective five-step procedure:

1. Dermabrasion with a motorized fine diamond burr to create a rough surface;
2. Dermaplaning with a no. 10 scalpel for controlled tissue removal;
3. Debulking with scissors to remove residual areas of thickened skin;
4. Electrocautery for coagulation; and
5. Resurfacing with an erbium-YAG (erbium-doped yttrium aluminum garnet) laser to soften treatment borders and seal wounds.

As with any surgical intervention, the risks and the potential recurrence of rosacea should be discussed with

the patient prior to the procedure. Hyperpigmentation, scarring, and further skin irritation are common outcomes following surgeries, and providers should discuss proper skin care and sun protection with the patient.

CONCLUSIONS

Rosacea is a chronic inflammatory condition that can be controlled but not cured. More evidence is emerging on the benefits of combining treatments for rosacea. These benefits include optimizing topical and systemic treatments for quicker results and longer remission periods that help minimize the burden of disease. ●

PRACTICE PEARLS

- Rosacea consists of several subtypes including flushing and erythematic, inflammatory, phymatous, and ocular.
- Different rosacea subtypes may and often do co-occur.
- The avoidance of triggers is important for the management of all rosacea forms and severities.
- Patients with mild to moderate rosacea are typically treated with topical and systemic treatments with anti-inflammatory properties.
- For patients with severe phymatous changes, laser and surgical interventions may be considered.

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