REVIEW

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Rosacea: An update

ABSTRACT

Rosacea is a common inflammatory skin disease affecting the central face of adults. Its etiology is unknown. Early diagnosis and appropriate treatment, usually with topical or systemic antibiotics or both, minimizes symptoms and helps to prevent complications.

KEY POINTS

Rosacea has a spectrum of cutaneous clinical findings: facial erythema, papules, pustules, telangiectasia, and rhinophyma.

Common triggers are sunlight, stress, exposure to extreme heat or cold, alcohol, hot beverages, and spicy foods.

Rosacea can resemble other diseases, including acne, seborrheic dermatitis, systemic lupus erythematosus, and sarcoidosis.

Ocular involvement occurs in more than 50% of patients with rosacea.

Oral tetracycline and topical metronidazole are the mainstays of therapy for rosacea.

ROSACEA is a chronic and recurrent inflammatory skin disease characterized by erythema, papules, pustules, telangiectasia, and occasionally sebaceous hyperplasia, which primarily affects the central face. The disease evolves in stages and affects middle-aged adults. Early diagnosis and thoughtful management help to control the disease and to minimize the patient's discomfort and emotional distress. Historically, rosacea has been a misunderstood disorder, often attributed to alcoholism and acne.[1]

INCIDENCE

Rosacea is a common and chronic disease that affects approximately 13 million Americans, or about 1 in 20 people. Because rosacea frequently affects people of northern European heritage, it is often called the "curse of the Celts."[2] In contrast, it is rarely seen in dark-skinned individuals.[3] In most patients, the onset occurs between the ages of 30 and 50. The early stages affect women more often than men at a ratio of 3 to 1, but men more often develop disfiguring rhinophyma.

PATHOGENESIS

The exact pathogenesis of rosacea is unknown, but it is probably multifactorial.

Gastrointestinal disease. A link with gastrointestinal disease (eg, dyspepsia with gastric hypochlorhydria and *Helicobacter pylori* infection) is inconclusive with regard to incidence and treatment.[4,5] An Italian study[4] suggested a causative association between *H pylori* and rosacea; histologic examination of the stomach mucosa revealed that 26 (84%) of 31 patients with rosacea had *H pylori* infection, compared with 50% in the general population. Serologic testing in another study[5] revealed anti-*H pylori* antibodies in 12 (27%) of 45 patients with

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rosacea compared with 15 (35%) of 43 healthy controls; the difference was not statistically significant. When Bamford et al[6] gave patients with rosacea and *H pylori* clarithromycin (500 mg orally three times daily) and omeprazole (40 mg daily) or placebo for 14 days in a third study, both groups improved, with no statistical difference between the groups.

H pylori produces urease, which catalyzes the hydrolysis of urea to CO_2 and ammonia. The theory is that the ammonia stimulates the release of various gastric hormones, including gastrin, which in turn induces flushing, a cardinal symptom of rosacea.[1]

Hypersensitivity to the mite *Demodex folliculorum* or its products may instigate rosacea, but the evidence is inconclusive.[7] The mites inhabit human follicles and sebaceous glands and induce lymphocytic infiltration that may lead to papule or pustule formation. In an early study,[8] patients treated with 3% sulfur ointment improved, but the treatment did not affect the *Demodex* population.

Vascular and hormonal factors may be important. Specifically, migraine headaches (which are common in patients with rosacea) and menopause (with its vasomotor instability) both support a vascular pathogenesis for rosacea.

Patients experience periods of remission and relapse

STAGES

Patients with rosacea experience periods of remission and relapse. In some, the disease progresses sequentially through stages; in others, it does not.

Episodic erythema may precede the first stage in susceptible persons. Such individuals are predisposed to blushing and flushing that is provoked by nonspecific triggers such as ultraviolet radiation, heat, cold, chemical irritation, strong emotions, alcoholic beverages, hot drinks, and spices.[9] Iodine injections (used during x-ray studies) and the use of topical corticosteroids can induce a rosacea flare. Eventually, flushing and blushing lead to permanent erythema on the central part of the face cheeks, nose, chin, and forehead and, occasionally, on the V-area of the chest. Proposed mediators of this erythema are substance P, histamine, serotonin, and prostaglandins.[10]

Stage 1 is characterized by persistent erythema and telangiectasia on the nose, cheeks, and glabella, usually coupled with sensitivity after applying facial cleansers, cosmetics, and sun screens. Ocular inflammation may develop.

Stage 2. Progression to stage 2 may occur within a year. This stage is characterized by persistent inflammatory papules, pustules, edema, erythema, telangiectasia, and, occasionally, by prominent facial pores that signify fibroplasia.

Stage 3. Only a small proportion of patients progress to stage 3, characterized by persistent deep erythema, telangiectasia, papules, pustules, large inflammatory nodules or granulomas, and tissue hyperplasia. Facial contours become coarse and irregular, and the thickened, edematous skin has a *peau d'orange* texture. Hypertrophy of connective tissue and sebaceous glands with increased collagen deposition leads to disfiguring rhinophyma, more often in men than women, although three times as many women as men have early-stage rosacea.

OCULAR ROSACEA

Ocular involvement occurs in more than 50% of patients with rosacea. Symptoms are nonspecific but include burning, stinging, tearing, and a foreign-body sensation.[11] Some patients experience contact-lens intolerance, photophobia, eye pain, conjunctival injection, and scaly, inflamed eyelids.

Suggested causative factors include a cell-mediated immune response to *Demodex folliculorum* and meibomian gland dysfunction.[12] Ophthalmic disease develops independently of facial rosacea and may precede it. Flushing tends to occur with ocular disease. Rosacea keratitis has a poor prognosis and can lead to corneal opacity, scarring, and blindness.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of rosacea includes acne vulgaris, seborrheic dermatitis, systemic and discoid lupus erythematosus, sarcoidosis, and systemic flushing disorders.

Acne vulgaris affects teenagers and young adults. Comedones and cysts are common in

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acne but not in rosacea. Telangiectasia and persistent erythema are uncommon in acne vulgaris.

Seborrheic dermatitis affects the face, typically the T-zone (eyebrows and nasal labial folds), and may affect the ears, scalp, and the middle of the chest. The dermatitis produces erythema and yellow, greasy scales, often with pruritus. Seborrheic dermatitis may coexist with rosacea.

Lupus erythematosus. The malar or "butterfly" rash of lupus erythematosus can mimic the background erythema of rosacea, but papules and pustules are rare with lupus. If the distinction is unclear, an antinuclear antibody test and a skin biopsy for histology and direct immunofluorescence are warranted.

Facial sarcoidosis may resemble granulomatous rosacea. A skin biopsy should differentiate the conditions.[9]

Carcinoid syndrome is a reasonable consideration for patients with a sudden onset of severe flushing. The diagnostic test for carcinoid syndrome is the 24-hour urinary excretion of 5-hydroxyindoleacetic acid.

TREATMENT

The primary treatment for rosacea is either oral antibiotics or topical metronidazole. Other therapies include topical antibiotics, isotretinoin, surgical ablation of telangiectasia and rhinophyma, and avoidance of provocative "triggers." The goal of therapy is remission.

The papular/pustular component of rosacea responds well to **oral antibiotics**, specifically tetracycline (initially 1.0 to 1.5 g/day, tapered after 1 to 2 months), doxycycline (100 mg once or twice daily), or minocycline (100 mg twice a day). Tetracycline and doxycycline are also used to treat ocular rosacea[13]; the doses used are the same as for the dermatologic manifestations. The effect of antibiotic therapy in rosacea is more anti-inflammatory than antibacterial.

Topical metronidazole, available as a 0.75% aqueous gel, lotion, or cream (MetroGel/Cream/Lotion), is safe and effective for moderate-to-severe disease. Applied twice daily, it reduces papules and pustules, but has no effect on telangiectasia or flushing.[14] Regular use promotes remission. A new 1% formulation of metronidazole (Noritate), applied once daily, may improve patient compliance.[15] Topical metronidazole can be used as monotherapy or, in more severe disease, in combination with oral antibiotics.

Isotretinoin (Accutane), 0.5–1.0 mg/kg/day for 1 to 3 months, is an alternative for patients with severe or resistant rosacea. Adverse effects include mucosal dryness,

TABLE 1

Rosacea triggers

Weather
- Sun
- Strong winds
- Cold
- Humidity

Emotional influences
- Stress
- Anxiety

Temperature-related factors
- Saunas
- Hot baths
- Simple overheating
- Excessively warm environments

Physical exertion
- Exercise
- "Lift and load" jobs

Beverages
- Alcohol, especially red wine, beer, bourbon, gin, vodka, or champagne
- Hot drinks, including hot cider, hot chocolate, coffee, tea

Foods
- Liver
- Dairy products, including yogurt, sour cream, and some cheeses
- Chocolate and vanilla
- Soy sauce and vinegars
- Vegetables, including eggplant, tomatoes, spinach, lima and navy beans, and peas
- Fruits, including avocados, bananas, red plums, raisins, figs, and citrus fruits
- Hot and spicy foods

Skin care products
- Cosmetics and hair sprays that contain alcohol, witch hazel, or fragrances
- Topical steroids
- Any substance that causes redness or stinging, such as soaps and astringents

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myalgias, hair loss, and elevated lipids. Because the drug is a known teratogen, female patients must practice birth control while taking the drug and undergo rigorous follow-up.[16] The package insert recommends using two birth control methods and undergoing monthly pregnancy tests. Ophthalmic rosacea may worsen with isotretinoin therapy.

Rhinophyma and telangiectasia require **surgical treatment**. A CO_2 laser can remove excess tissue and recontour the nose; the pulse dye laser can eradicate telangiectasia.[17,18]

Other skin care suggestions

Most rosacea patients have sensitive skin. As such, they should discontinue or minimize their use of all irritants such as soaps, cleansers that contain alcohol, and astringents. They should use a nonirritating, broad-spectrum UVA and UVB sunscreen with a sun protective factor (SPF) of 15. Patients can help control their symptoms by avoiding triggers (TABLE 1). A diary of symptoms may help to identify such triggers.

For more information on rosacea, contact the National Rosacea Society at 800 South Northwest Highway, Suite 200, Barrington, IL 60010; (800) 66-25874 (NO-BLUSH). The organization also has a website at www.rosacea.org.

Patients may help control symptoms by avoiding triggers

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