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## Diagnosis and Treatment of Rosacea

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### Abstract and Introduction

#### Abstract

**Background:** Rosacea is a common skin disorder affecting middle-aged and older adults. Many patients mistakenly assume that early rosacea is normally aging skin and are not aware that effective treatments exist to prevent progression to permanent disfiguring skin changes.

**Methods:** The medical literature was reviewed on the pathophysiology, diagnosis, and treatment of rosacea. MEDLINE was searched using the key search terms "rosacea," "rhinophyma," "metronidazole," "*Helicobacter pylori*," and "facial redness."

**Results and Conclusions:** Rosacea is easily diagnosed by physician observation, and physicians should initiate discussion of rosacea treatment with patients. Effective treatment of rosacea includes avoidance of triggers, topical and oral antibiotic therapy, both topical and oral retinoid therapy, topical vitamin C therapy, and cosmetic surgery.

#### Introduction

As the general population ages and the baby boomers increasingly dominate clinical practice, a frequent complaint is the red face. Of the many causes of the red face, rosacea will be the diagnosis for approximately 13 million Americans.<sup>[1]</sup> Although not a life-threatening condition, rosacea produces conspicuous facial redness and blemishes that can have a deep impact on a patient's self-esteem and quality of life. Rhinophyma, the most prominent feature of advanced rosacea, is often mistakenly associated with alcoholism, as caricatured by W.C. Fields, further stigmatizing rosacea patients. A survey by the National Rosacea Society reported that 75% of rosacea patients felt low self-esteem, 70% felt embarrassment, 69% report frustration, 56% felt that they had been "robbed of pleasure or happiness," 60% felt the disorder negatively affected their professional interactions, and 57% believed that it adversely affected their social lives.<sup>[2]</sup> Much of this suffering is unnecessary, however, because rosacea is a condition that can be easily diagnosed and effectively treated in most patients.

#### Methods

We undertook a literature review on the pathophysiology, diagnosis, and treatment of rosacea using MEDLINE. Key search terms included "rosacea," "rhinophyma," "metronidazole," "*Helicobacter pylori*," and "facial redness."

#### Diagnosis

Rosacea develops gradually. Many patients, unaware that they suffer from a treatable skin condition, assume that the intermittent facial flushing, papules, and pustules are adult acne, sun or wind burn, or normal effects of aging. Correct diagnosis and early treatment of rosacea are important because, if left untreated, rosacea can progress to irreversible disfigurement and vision loss.<sup>[3]</sup> Rosacea is a vascular disorder of distinct, predictable symptoms that follows a remarkably homogenous clinical course. Rosacea generally involves the cheeks, nose, chin, and forehead, with a predilection for the nose in men.<sup>[4]</sup>

There are four acknowledged general stages of rosacea ([Table 1](#)).<sup>[4]</sup> Stage I can be described as pre-rosacea. This stage is characterized by frequent blushing, especially in those who have a family history of rosacea. Blushing as a symptom of rosacea can start in childhood, although the typical age of onset for rosacea is 30 to 60 years.<sup>[5]</sup> There might be increased frequency of facial flushing or complaints of burning, redness, and stinging when using common skin care products or antiacne therapies. The second stage of rosacea is vascular. At this point in the disease progression, transitory erythema of midfacial areas, as well as slight telangiectasias, become apparent.<sup>[4]</sup> In the third stage of rosacea, the facial redness becomes deeper and permanent. Telangiectasias increase, and papules and pustules begin to develop. During this stage, ocular changes, such

as conjunctivitis and blepharitis, can develop.<sup>[6]</sup> Edema can develop in the region above the nasolabial folds. In the fourth stage, there is continued and increased skin and ocular inflammation. Ocular inflammation can progress to keratitis and result in loss of vision. Multiple telangiectasias can be found in the paranasal region. It is at this point that fibroplasia and sebaceous hyperplasia of the skin produces the nasal enlargement known as rhinophyma.<sup>[4]</sup>

Several skin conditions share some clinical features with rosacea. Acne vulgaris causes comedones, papules, pustules, and localized inflammatory nodules but not the generalized erythema, telangiectasias, and other vascular features of rosacea. Seborrheic dermatitis, perioral dermatitis, and the malar rash of lupus can all cause mild erythema, but these conditions will not produce the characteristic flushing, telangiectasias, papules, and pustules of rosacea.<sup>[1]</sup> Sarcoidosis can closely mimic rosacea by producing red papules on the face, but the disease will usually manifest itself in other organs as well. In addition, a biopsy will show sarcoid granulomas.<sup>[7]</sup> A more complete listing of the differential diagnosis appears in [Table 2](#).

## Pathophysiology

Although the exact pathogenesis of rosacea is unknown, the pathologic process is well described. The erythema of rosacea is caused by dilation of the superficial vasculature of the face.<sup>[1]</sup> It is thought that atrophy of the papillary dermis provides for easier visualization of the dermal capillaries.<sup>[9]</sup> Edema can develop as a result of the increased blood flow in the superficial vasculature. This edema might contribute to the late-stage fibroplasia and rhinophyma.<sup>[1]</sup> It has been suggested that *Helicobacter pylori* infection is a cause of rosacea. *H pylori*, originally implicated as the cause of gastric ulcers, has more recently been associated with urticaria, Henoch-Schöndonlein purpura, and Sjögren syndrome. In a 1999 study, however, Bamford et al<sup>[10]</sup> found there was no benefit in the eradication of *H pylori* compared with placebo in the treatment of rosacea, although both subjects and controls experienced improvement in the rosacea symptoms. Thus the role of *H pylori* in rosacea remains uncertain, and the cause of rosacea remains elusive.

## Treatment

The most important first step in the treatment of rosacea is the avoidance of triggers. Triggers are both exposures and situations that can cause a flare-up of the flushing and skin changes in rosacea. Principal among these is sun exposure. Rosacea patients must be advised always to apply a nonirritating facial sun block when outdoors. Stress, through autonomic activation, can also increase the flushing. Alcohol consumption, while not a cause in itself, can aggravate this condition through peripheral vasodilation. Spicy foods can also aggravate the symptoms of rosacea through autonomic stimulation. Finally, care must be taken to use only those facial cleansers, lotions, and cosmetics that are nonirritating, hypoallergenic, and noncomedogenic.

Rosacea should be treated at its earliest manifestations to mitigate progression to the stages of edema and irreversible fibrosis. Antibiotics have traditionally been considered the first line of therapy, although their success is considered to be primarily due to anti-inflammatory effects rather than antimicrobial ones.<sup>[4]</sup> Topical metronidazole, which is effective for stage I and stage II rosacea and avoids the toxicity of systemic treatment, is considered first-line therapy.<sup>[11]</sup> Metronidazole is available in a twice-daily application of 0.75% cream or gel and in a newer once-daily 1.0% formulation.<sup>[4]</sup> No significant difference in efficacy has been found between the once-daily 1.0% medicine and the twice-daily 0.75% medicine.<sup>[12]</sup> Sulfacetamide lotion can also be used in place of metronidazole. In certain patients, sulfacetamide might be less irritating than metronidazole.<sup>[4]</sup>

Rosacea responds well to oral antibiotics. Starting treatment with simultaneous oral and topical therapy reduces initial prominent symptoms, prevents relapse when oral therapy is discontinued, and maintains long-term control.<sup>[6]</sup> Oral therapy is generally continued until inflammatory lesions clear or for 12 weeks, whichever comes first.<sup>[12]</sup> Tetracycline is the primary oral antibiotic prescribed for rosacea therapy, at a dosage of 1.0 to 1.5 g/d divided into 2 to 4 daily doses. Minocycline at 100 mg two times a day is an acceptable alternative.<sup>[13]</sup> Doxycycline is another acceptable alternative, although the monohydrate formulation, in a dosage of 100 mg once daily, is more consistently effective and has fewer gastrointestinal side effects than the hyclate form.<sup>[13,14]</sup> Clarithromycin, 250 mg to 500 mg twice daily, has been found to be as effective as doxycycline but with a more benign side effect profile.<sup>[15]</sup>

## New Therapies

Azelaic acid is a naturally occurring, dicarboxylic acid possessing antibacterial activity. It is available as a 20% cream and is generally used as an alternative treatment for acne vulgaris. In 1999 Maddin<sup>[16]</sup> compared once-daily applications of azelaic acid with topical metronidazole 0.75% cream for treatment of papulopustular

rosacea. Maddin concluded that both medicines were equally effective in reducing the number of inflammatory lesions and the associated signs and symptoms of rosacea. When the study physicians' rating of the overall improvement was considered, however, the azelaic acid was considered to be considerably more effective. The patients involved in the study also preferred the azelaic acid.<sup>[16]</sup>

Topical retinoic acid has been shown to have a beneficial effect on the vascular component of rosacea.<sup>[17]</sup> The drawbacks of retinoic acid therapy include delayed onset of effectiveness, dry skin, erythema, burning, and stinging.<sup>[17]</sup> Retinaldehyde is intermediate in the natural metabolism of retinoids, between retinal and retinoic acid, and is generally well tolerated while retaining most of the therapeutic activity of retinoic acid.<sup>[17]</sup> Daily application of a 0.05% retinaldehyde cream for 6 months was found to yield positive and statistically significant outcomes in 75% of those patients undergoing treatment.<sup>[17]</sup> Specifically, improvements were found in erythema and telangiectasias, the vascular components of rosacea.

Topical vitamin C preparations have recently been studied in the reduction of the erythema of rosacea.<sup>[18]</sup> Daily use of an over-the-counter cosmetic 5.0% vitamin C (L-ascorbic acid) preparation was used in an observer-blinded and placebo-controlled study. Nine of the 12 participants experienced both objective and subjective improvement in their erythema.<sup>[18]</sup> It was suggested that free-radical production might play a role in the inflammatory reaction of rosacea, and that the antioxidant effect of L-ascorbic acid might be responsible for its effect. These promising preliminary results still need to be confirmed in larger, long-term studies.

### Treatment of Advanced Disease

Recalcitrant rosacea can respond to oral isotretinoin therapy. In a recent study of 22 patients with mild to moderate rosacea, major reductions in erythema, papules, and telangiectasias were noted by the ninth week of treatment.<sup>[19]</sup> Isotretinoin reduces the size of sebaceous glands and alters keratinization. Recalcitrant cases of rosacea have been successfully treated with 0.5 mg/kg/d of isotretinoin.<sup>[12]</sup> Isotretinoin, of course, has serious side-effects, most notably its teratogenic potential. Female patients of childbearing age must be strongly advised to use effective birth control. Stage IV of rosacea, involving irreversible fibrotic changes, such as rhinophyma, does not respond well to medical therapy. At that point, the patient should be referred for cosmetic surgery, such as cryosurgery and laser therapy.

In the aging US population, rosacea is an increasingly common disorder. Although rosacea causes only limited physical effects, the prominent visibility of these changes often yields intense psychosocial distress. Although the exact cause of rosacea is unknown, its progression, signs, and symptoms can be readily alleviated by the primary care physician.

Tables      Table 1. Rosacea Staging

Stage	Symptoms and Signs
I	Pre-rosacea
	Frequent blushing
	Easy irritation and erythema of facial skin
II	Vascular stage
	Transitory erythema of midfacial areas
	Early telangiectasias
III	Deeper facial erythema
	Increased telangiectasias
	Papule and pustule formation
IV	Tissue hyperplasia
	Rhinophyma
	Possible ocular inflammation

Table 2. Brief Differential Diagnosis of Rosacea

Flushing, autonomic mediated	
	Exercise
	Spicy food
	Emotions
	Horner syndrome
Rosacea	
Atopic dermatitis	
Seborrheic dermatitis	
Systemic lupus erythematosus	
Dermatomyositis	
Acne vulgaris and steroid-induced acne	
Perioral dermatitis	
Physical erythema	
	Mechanical
	Thermal
	Electromagnetic
Contact and photocontact dermatitis	
Medications	
Sarcoidosis	

Adapted from Murray.<sup>[8]</sup>

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