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# TECHNOLOGICAL ADVANCES IN ROSACEA TREATMENT - A COMPREHENSIVE REVIEW

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## ABSTRACT

Rosacea is a chronic inflammatory dermatosis characterized by recurrent facial erythema, flushing, telangiectasia, papules, pustules and in some individuals, phymatous or ocular involvement. Its global prevalence is estimated at approximately 1-3%, with substantial geographic variability and increasing recognition in individuals with skin of color. Although its precise etiology remains multifactorial, contemporary research highlights a complex interplay of neurovascular dysregulation, innate and adaptive immune activation, microbial factors, genetic predisposition, and environmental triggers. Dysregulated cathelicidin expression, kallikrein-5 activity, inflammasome activation, and TRP-channel-mediated neurovascular responses represent key mechanistic pathways.

Clinically, rosacea presents with heterogeneous phenotypes encompassing persistent erythema, episodic flushing, inflammatory lesions, phymatous changes, and ocular manifestations, necessitating individualized diagnostic and therapeutic strategies. Evidence-based management integrates phenotype-directed treatment algorithms and data from randomized controlled trials, demonstrating efficacy of topical azelaic acid, ivermectin, and brimonidine, as well as systemic agents such as doxycycline. Recent advances include the introduction of novel topical and systemic therapies, targeted immunomodulators, and combination regimens that address multiple pathogenic pathways. Novel therapies - such as  $\alpha$ -adrenergic agonists, topical minocycline formulations, enhanced-delivery topical agents and laser-based technologies - represent promising advancements for phenotype-directed and mechanism-targeted treatment.

This review synthesizes current evidence on epidemiology, pathogenesis, clinical features, diagnostic considerations, and contemporary treatment strategies for rosacea, integrating findings from consensus guidelines, clinical trials, and recent translational research.

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## KEYWORDS

Rosacea, Chronic Inflammatory Dermatitis, Neurovascular Dysregulation, Ocular Rosacea, Phenotype-Based Treatment, Azelaic Acid, Ivermectin, Doxycycline, Emerging Therapies

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## CITATION

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## Introduction

Rosacea is a chronic inflammatory skin disorder characterized by recurrent or persistent centrofacial erythema, telangiectasia, papules, and pustules. The condition affects a substantial proportion of adults worldwide, with higher prevalence reported in individuals with fair skin, and typically manifests between mid-adulthood and older age [6,15]. Women are diagnosed more frequently, although men often present with more severe phymatous changes [6,14].

Current understanding indicates that rosacea arises from a complex interplay of dysregulated innate immunity, neurovascular instability, increased Demodex density, microbiome alterations, and genetic susceptibility [2,3]. Key pathogenic mechanisms include overexpression of inflammatory mediators, heightened cathelicidin activity, oxidative stress, and aberrant neurovascular signaling, all contributing to episodic flushing, persistent erythema, and inflammatory lesions [2,3,5]. Environmental and lifestyle factors - such as ultraviolet exposure, heat, cold, alcohol, and emotional stress - can further amplify these pathways and worsen symptoms [1,10].

Rosacea is also associated with systemic comorbidities, including cardiovascular, gastrointestinal, and psychiatric conditions, suggesting broader inflammatory and neurovascular involvement [14]. Recent clinical frameworks, including the ROSCO diagnostic recommendations, emphasize a phenotype-based approach that supports individualized assessment and tailored therapeutic strategies [1,5,9]. Advances in topical agents and systemic therapies have significantly refined modern management strategies, supported by recent consensus and clinical evidence [4,8]. Emerging research on immune and microbiome-targeted approaches further expands potential therapeutic options [11,13].

## Methodology

This narrative review was developed using a structured literature search and selection process, modeled after contemporary academic standards applied in similar reviews. A comprehensive search of PubMed, Scopus, and Web of Science was performed to identify relevant publications addressing epidemiology, pathogenesis, clinical features, diagnosis, and treatment of rosacea. The search covered the years 2012-2025 and was limited to peer-reviewed, full-text articles published in English.

## Search Strategy

The search strategy incorporated combinations of keywords and their synonyms, including: rosacea, facial erythema, papulopustular rosacea, ocular rosacea, pathogenesis, innate immunity, neurovascular dysregulation, Demodex, cathelicidin, brimonidine, ivermectin, doxycycline, and phenotype-based management. Boolean operators (AND/OR) were used to refine the results. Additional sources were identified manually through screening reference lists of selected publications.

## Eligibility Criteria

Inclusion criteria:

- peer-reviewed, full-text clinical studies, including randomized controlled trials, observational studies, meta-analyses, and systematic reviews;
- mechanistic and translational studies relevant to the biological basis of rosacea;
- clinical guidelines, consensus statements, and high-quality narrative reviews;
- articles addressing epidemiology, pathophysiology, clinical presentation, diagnostic approaches, or treatment strategies.

Exclusion criteria:

- case reports and small case series (unless providing essential mechanistic insights);
- experimental animal studies not directly applicable to clinical understanding;
- conference abstracts without full text;
- non-English publications;
- articles unrelated to dermatologic or ocular rosacea.

## Data Extraction and Selection Process

Eligible studies were screened for methodological quality, clinical relevance, and contribution to current understanding of rosacea. Data extracted included study type, population characteristics, primary outcomes, mechanistic findings, diagnostic frameworks, and therapeutic approaches. Sixteen key publications fulfilling predefined methodological and thematic criteria were selected for final synthesis.

## Review Approach

Given the heterogeneity of study designs and outcomes, data were synthesized descriptively without meta-analysis. Emphasis was placed on integrating clinical evidence with mechanistic insights and aligning findings with current consensus-based frameworks. The final review provides an updated, clinically oriented summary of rosacea grounded in contemporary dermatologic literature.

## Epidemiology

Rosacea is widely recognized as a common chronic inflammatory condition of adults, with a global prevalence estimated at approximately 1–3% across population-based studies [6]. Considerable geographic variation exists: lower rates have been reported in some Asian regions, while significantly higher prevalence has been described in Northern and Eastern European populations, particularly among fair-skinned individuals of Celtic or Northern European descent [1,8,14]. Despite this distribution pattern, rosacea occurs in all ethnic groups, and recent data emphasize that the condition is frequently underdiagnosed in individuals with darker skin phototypes due to the subtle clinical visibility of erythema [1].

Most patients are diagnosed between 30 and 60 years of age, although symptoms may persist lifelong, and earlier onset-including in adolescence-has been described [6,14]. Women are diagnosed more frequently, likely reflecting both biological and healthcare-seeking differences; however, men more commonly develop phymatous changes, particularly rhinophyma, which is associated with more advanced disease [1,16]. Ocular involvement may appear at any stage and can occur independently of cutaneous signs, making timely detection essential [15].

Several epidemiologic studies highlight consistent risk factors associated with rosacea. These include family history, lighter skin phototypes, tendency to flush, cumulative ultraviolet exposure, and environmental or lifestyle triggers such as heat, emotional stress, alcohol, and spicy foods [3,6]. Associations with

comorbidities have also been described, including gastrointestinal disorders, migraine, cardiovascular disease, and metabolic abnormalities, although causal relationships remain unclear [5,7].

Overall, current epidemiologic evidence supports rosacea as a multifactorial disease with broad demographic reach and significant underrecognition in specific populations. The heterogeneous presentation and variable severity underscore the need for individualized evaluation and early identification of high-risk phenotypes.

### **Pathogenesis**

The pathogenesis of rosacea is multifactorial and reflects the interaction of dysregulated neurovascular responses, innate and adaptive immune activation, microbial factors and individual genetic susceptibility [2]. Modern research indicates that disease expression results from an exaggerated cutaneous response to external and internal stimuli, leading to persistent inflammation, vascular instability and tissue remodeling [3,7].

A central component of rosacea biology is innate immune dysregulation. Increased expression of toll-like receptor 2 (TLR2) on keratinocytes enhances sensitivity to environmental triggers, amplifying downstream inflammatory pathways. Upregulation of kallikrein-5 promotes aberrant processing of cathelicidin into highly pro-inflammatory peptide forms, which stimulate leukocyte recruitment, angiogenesis and vasodilation [2,10]. Elevated matrix metalloproteinase activity and inflammasome activation further contribute to chronic inflammation and dermal matrix degradation [3,5].

Neurovascular dysfunction plays a major role in symptoms such as flushing and persistent erythema. Enhanced activity of transient receptor potential (TRP) channels, including TRPV1 and TRPA1, lowers the threshold for vasodilatory responses to heat, UV radiation, spicy foods and emotional stress [2,7]. Sensory nerve overstimulation leads to release of vasoactive neuropeptides, which promote vasodilation and neurogenic inflammation. These mechanisms explain the characteristic triggers described by patients and the chronicity of vascular symptoms [11].

Growing evidence supports the contribution of microbial factors, particularly *Demodex folliculorum*. Increased mite density may stimulate inflammation through bacterial antigens and direct activation of TLR2 on epidermal cells [3]. Other proposed triggers include *Helicobacter pylori*, although findings remain inconsistent and the association appears indirect rather than causal [6]. Alterations in the skin microbiome may further modulate inflammatory responses.

Genetic susceptibility and environmental exposures influence disease expression and severity. Polymorphisms affecting immune signaling, vascular regulation and skin barrier function have been identified in genome-level analyses [7]. UV radiation, oxidative stress, temperature extremes and lifestyle triggers such as alcohol or spicy foods can exacerbate inflammatory cascades and neurovascular instability [6,14].

In some patients, especially those with long-standing disease, chronic inflammation contributes to tissue remodeling and fibrosis, resulting in phymatous changes. These changes reflect fibroblast activation, extracellular matrix overproduction and persistent vascular dilation [4].

Ocular rosacea is thought to arise from similar mechanisms, involving dysfunction of the meibomian glands, tear film instability and chronic inflammation of the eyelid margin and ocular surface [15]. Neurovascular dysregulation and altered innate immunity appear to drive both cutaneous and ocular manifestations.

Overall, rosacea pathogenesis reflects a complex interplay of innate immune activation, neurovascular dysregulation, microbial triggers and genetic predisposition. This integrated model supports modern phenotype-based diagnostic and therapeutic strategies [9,12,16].

### **Clinical Features**

Rosacea presents with a wide spectrum of cutaneous and ocular manifestations, most frequently involving the central face, including the cheeks, nose, chin and forehead. Symptoms typically fluctuate over time and are often intensified by environmental factors such as heat, temperature extremes, spicy foods, alcohol, emotional stress and ultraviolet exposure [1,6]. The disease is clinically heterogeneous, and most individuals exhibit more than one dominant feature simultaneously.

The most characteristic manifestations include persistent centrofacial erythema, episodic flushing and telangiectasia, features that reflect underlying neurovascular instability. Many patients also report burning, stinging and heightened cutaneous sensitivity, which may be accompanied by dryness, roughness or mild scaling [2,7]. Inflammatory papules and pustules represent another common presentation and are particularly useful in distinguishing rosacea from acne vulgaris, as the latter is characterized by comedones, which are

absent in rosacea [1,3]. Long-standing inflammation and tissue remodeling may lead to skin thickening and surface irregularities, most prominently rhinophyma, although phymatous changes can also develop on the chin, forehead, ears or eyelids [4]. Ocular involvement is frequently observed and may manifest as dryness, burning, foreign-body sensation, photophobia, blepharitis, lid-margin telangiectasia, conjunctival hyperemia or keratitis. Importantly, ocular findings may precede or occur independently of cutaneous symptoms, underscoring the need for careful evaluation in patients with eye discomfort [15,16].

#### **Phenotypic Classification of Rosacea**

Recent international consensus recommendations have shifted from the traditional subtype-based classification toward a phenotype-oriented model, which more accurately reflects the clinical diversity of rosacea and supports individualized therapeutic strategies [4,9]. Unlike the historical system, in which patients were assigned to a single subtype, the phenotypic approach acknowledges that most individuals express multiple overlapping features of varying severity.

Two clinical features - persistent centrofacial erythema and phymatous changes - are recognized as diagnostically sufficient when present independently. Persistent erythema represents a long-standing redness of the central face caused by chronic vasodilation and neurovascular dysregulation and is considered the hallmark manifestation of rosacea [1,6]. Phymatous changes, characterized by progressive skin thickening, nodularity and enlargement of sebaceous regions, reflect late-stage tissue remodeling and may involve the nose, chin, forehead, ears or eyelids [4].

Other major phenotypes support the diagnosis when occurring alongside a diagnostic feature or in combination with one another. These include inflammatory papules and pustules, flushing episodes triggered by environmental or emotional stimuli, telangiectasia resulting from chronic vasodilation, and ocular involvement such as blepharitis, conjunctival erythema, meibomian gland dysfunction or keratitis [1,9]. Secondary features - including burning, stinging, sensitivity to topical products, dryness, roughness or episodic edema - do not establish the diagnosis alone but contribute to the overall clinical profile and may influence therapeutic decisions [11].

The phenotypic framework offers several advantages. It reflects the dynamic and overlapping nature of rosacea, aligns with contemporary understanding of neurovascular and immunologic mechanisms, and allows clinicians to target therapy toward the patient's most prominent manifestations. This model also enhances diagnostic accuracy in patients whose presentations do not fit neatly into traditional categories [4,9].

#### **Historical Subtypes of Rosacea**

Although phenotypes form the basis of modern classification, the traditional subtype system remains widely recognized and continues to provide a helpful descriptive structure in clinical practice and the literature [6,12]. Historically, rosacea has been divided into four subtypes.

The erythematotelangiectatic subtype (ETR) is characterized by persistent centrofacial erythema, episodic flushing, telangiectasia, increased warmth and marked cutaneous sensitivity. Patients frequently describe burning or stinging sensations, and the skin may appear dry or rough, with symptoms often triggered by heat, emotional stress or spicy foods.

The papulopustular subtype (PPR) presents with inflammatory papules and pustules on a background of persistent erythema. Lesions are typically dome-shaped, may be tender and often occur in clusters. In contrast to acne vulgaris, comedones are absent. More severe presentations may include numerous pustules, facial edema and pronounced sensitivity.

The phymatous subtype involves progressive skin thickening, coarse surface texture and sebaceous gland hypertrophy. Rhinophyma is the most common form, but similar changes may affect the chin (gnathophyma), forehead (metophyma), ears (otophyma) or eyelids (blepharophyma). These findings are more frequently observed in men and often reflect long-standing disease [4].

The ocular subtype encompasses a spectrum of ocular surface and eyelid abnormalities, including dryness, tearing, foreign-body sensation, photophobia, blepharitis, meibomian gland dysfunction, lid-margin telangiectasia and conjunctival hyperemia. Severe cases may develop corneal infiltrates, neovascularization, ulceration or scarring. Ocular manifestations may precede or occur without cutaneous disease, which highlights the need for careful ophthalmologic evaluation in affected individuals [15,16].

### **Diagnosis**

The diagnosis of rosacea is clinical and relies on the recognition of characteristic cutaneous and ocular features in the appropriate anatomic distribution. As the disease presents with considerable phenotypic variability, accurate diagnosis requires a systematic assessment of persistent centrofacial erythema, flushing tendencies, inflammatory lesions, phymatous changes and ocular symptoms [1,6]. A careful history is essential and should include evaluation of symptom duration, trigger factors, disease fluctuations, associated sensations such as burning or stinging, and any ocular complaints. Many patients report chronic sensitivity to heat, sunlight, spicy foods or emotional stress, all of which may support the clinical suspicion of rosacea.

Physical examination should focus on the presence of persistent erythema across the convex areas of the face, telangiectasia, inflammatory papules and pustules lacking comedones, skin thickening or irregularity, and any signs of ocular involvement. Persistent centrofacial erythema represents the most reliable primary diagnostic feature, while phymatous changes serve as a second diagnostic hallmark when present [1,4]. The coexistence of major phenotypes - such as papules, pustules, flushing episodes, telangiectasia or ocular disease - further strengthens the diagnosis and helps differentiate rosacea from other inflammatory dermatoses [4,9].

Ocular assessment is an important component of the diagnostic process, as ocular rosacea may precede or occur independently of cutaneous findings. Symptoms such as dryness, foreign-body sensation, burning, tearing, photosensitivity or blurred vision should prompt examination for blepharitis, meibomian gland dysfunction, conjunctival hyperemia or corneal involvement. When ocular symptoms are prominent, referral to an ophthalmologist may be necessary to evaluate for complications such as keratitis or corneal neovascularization [15,16].

No laboratory tests or imaging studies are required for routine diagnosis, as no specific serologic or histopathologic biomarkers have been identified. Skin biopsy is generally unnecessary and reserved for atypical presentations or to exclude other conditions such as cutaneous lupus erythematosus, sarcoidosis or sebaceous carcinoma [5]. Dermoscopy can assist in visualizing telangiectasia and vascular patterns, but its use is adjunctive rather than diagnostic.

The differential diagnosis includes acne vulgaris, seborrheic dermatitis, contact dermatitis, photodermatoses, facial erythromelalgia and systemic disorders presenting with facial erythema. The absence of comedones helps distinguish rosacea from acne, while the lack of greasy scaling and scalp involvement differentiates it from seborrheic dermatitis. In cases with prominent flushing, endocrine disorders such as carcinoid syndrome or mast-cell activation should be considered when symptoms are atypical or refractory to standard management.

Overall, diagnosis is based on the constellation of clinical findings, with emphasis on persistent centrofacial erythema and supporting phenotypes. Recognizing the diversity of presentations and incorporating the phenotype-based framework enhances diagnostic accuracy and guides individualized therapeutic planning.

### **Differential Diagnosis**

The differential diagnosis of rosacea is broad, as several inflammatory, vascular and photodistributed dermatoses may present with overlapping clinical features. Accurate distinction is essential, particularly in patients with atypical patterns of erythema, prominent flushing, or ocular symptoms, and in those whose presentation lacks the classic combination of persistent centrofacial erythema and papulopustular lesions.

A frequent diagnostic consideration is acne vulgaris, which may share inflammatory papules and pustules but is characterized by the presence of open and closed comedones-features absent in rosacea. Acne typically affects a wider distribution, including the jawline, temples, chest and back, and rarely presents with persistent centrofacial erythema or marked sensitivity. In contrast, rosacea lesions predominantly involve the central face and are often accompanied by burning, stinging and flushing.

Seborrheic dermatitis may also mimic rosacea due to erythema and scaling in the central face. However, seborrheic dermatitis typically presents with greasy, yellowish scale and more prominent involvement of the nasolabial folds, eyebrows and scalp. The absence of discrete inflammatory papules and pustules further supports distinction from papulopustular rosacea.

Contact dermatitis, whether allergic or irritant, may produce diffuse erythema, edema and burning similar to rosacea flares. A detailed history of new cosmetics, skincare products or occupational exposures is essential. Contact dermatitis tends to have a more acute onset, with sharp borders or involvement beyond classical rosacea locations; patch testing may be helpful in unclear cases.

Lupus erythematosus, particularly its cutaneous forms, is an important differential consideration, as the malar rash may resemble centrofacial erythema. The lupus rash, however, typically spares the nasolabial folds,

may be associated with photosensitivity or systemic symptoms, and often presents with fine scale or follicular plugging. When clinical suspicion persists, serologic testing or biopsy may be indicated.

Photodermatoses, including polymorphous light eruption and chronic actinic dermatitis, may cause diffuse facial erythema and discomfort. The distribution pattern-predominantly on sun-exposed areas with sparing of shaded regions - is useful in differentiation. These disorders often exhibit a seasonal pattern and lack the inflammatory papules characteristic of rosacea.

In patients with marked flushing, endocrine and neuroendocrine disorders such as carcinoid syndrome, pheochromocytoma or mast-cell activation syndromes should be considered. These conditions typically present with systemic manifestations such as diarrhea, palpitations or episodic hypertension, and laboratory evaluation may be necessary when flushing is severe, abrupt in onset or refractory to rosacea-directed therapy.

Other entities that may mimic rosacea include periorificial dermatitis, facial erythromelalgia, sarcoidosis, demodicosis and sebaceous carcinoma, the latter particularly in cases of recurrent or atypical eyelid lesions. Ocular rosacea must also be distinguished from blepharitis, meibomian gland dysfunction unrelated to rosacea, allergic conjunctivitis, and infectious keratitis. Comprehensive evaluation, including ophthalmologic assessment when needed, is crucial in such presentations.

Overall, differentiation relies on the pattern and distribution of erythema, presence or absence of comedones, specific ocular features, associated triggers, and the chronic fluctuating course typical of rosacea. A structured clinical assessment allows accurate exclusion of mimicking conditions and ensures appropriate management tailored to the underlying diagnosis.

### **Treatment**

Management of rosacea requires an individualized, phenotype-directed approach that reflects the heterogeneous clinical presentation of the disease. Contemporary consensus guidelines emphasize tailoring therapy to the dominant features - persistent erythema, flushing tendencies, inflammatory papules and pustules, phymatous thickening and ocular involvement - rather than relying on the historical subtype model [4,9]. Effective treatment often combines lifestyle modification, topical therapies, systemic agents, and procedural interventions, adjusted according to disease severity and patient preference.

Initial management includes identification and avoidance of personal trigger factors, which commonly include heat, ultraviolet exposure, emotional stress, spicy foods and alcohol. Many patients benefit from gentle skincare routines, avoidance of irritating cosmetics and daily use of broad-spectrum sunscreen, as barrier dysfunction and neurovascular reactivity contribute to symptom flares [1,6].

Topical medications represent the foundation of therapy for many patients. Agents such as azelaic acid and metronidazole have long-standing evidence supporting their efficacy in papulopustular rosacea, improving inflammatory lesions and background erythema with favorable tolerability profiles [13]. Topical ivermectin, which combines anti-inflammatory properties with activity against *Demodex* mites, has demonstrated superior efficacy to metronidazole in randomized trials and is widely used as a first-line option for inflammatory phenotypes [4,7]. For persistent erythema, alpha-adrenergic agonists such as brimonidine and oxymetazoline provide transient but clinically meaningful vasoconstriction, reducing facial redness for several hours without significant rebound phenomena in most patients [5,8].

Systemic therapy is indicated for moderate to severe inflammatory disease, extensive papulopustular flares or ocular involvement. Doxycycline, used at subantimicrobial anti-inflammatory doses, remains the systemic agent with the strongest evidence base and is effective in reducing inflammatory lesions, ocular surface inflammation and meibomian gland dysfunction [1,13,15]. Higher doses may be required for short-term control of more severe disease, although long-term therapy usually relies on low-dose regimens to reduce adverse effects. Azithromycin may serve as an alternative in patients unable to tolerate tetracyclines, while isotretinoin is reserved for refractory cases, particularly those with phymatous changes or severe inflammatory involvement [4,7]. Recent studies suggest that low-dose isotretinoin offers meaningful benefit with improved tolerability, although careful monitoring remains essential. Additionally, modern drug-delivery technologies - such as enhanced-delivery topical formulations and advanced carrier systems - are being explored to improve penetration, reduce irritation and increase therapeutic efficacy in rosacea management [13,16].

Procedural interventions provide additional benefit for selected phenotypes. Vascular laser therapy and intense pulsed light (IPL) effectively target telangiectasia and persistent erythema by causing selective photothermolysis of dilated vessels. These modalities are particularly helpful in erythematotelangiectatic phenotypes unresponsive to topical vasoconstrictors [5]. For advanced phymatous changes, surgical debulking, laser resurfacing or electrosurgical contouring may be required to restore normal nasal or facial architecture.

These interventions are often combined with medical management to limit progression and maintain long-term results. Recent technological innovations - including vascular-specific wavelengths, optimized pulse-duration engineering and improved energy-delivery systems - have further enhanced the safety and precision of device-based therapies for rosacea [5,8].

Management of ocular rosacea requires close collaboration between dermatology and ophthalmology. Lid hygiene, warm compresses and artificial tears are foundational measures, while topical antibiotics or anti-inflammatory agents may be required in more symptomatic cases. Doxycycline plays an important role due to its effects on meibomian gland function and ocular surface inflammation, and cyclosporine drops may improve tear film stability and reduce chronic inflammation [15,16]. Prompt recognition and treatment are essential to prevent complications such as keratitis or corneal scarring.

Across all phenotypes, treatment goals include reducing symptom burden, preventing progression, improving cutaneous and ocular function and addressing psychosocial impact. Patients often benefit from education regarding chronicity, trigger avoidance and realistic expectations, as many therapies require several weeks for optimal effect. Combination regimens are frequently necessary due to the multifactorial nature of rosacea, and long-term maintenance therapy is common.

Overall, contemporary management of rosacea integrates evidence-based pharmacologic and procedural options within a personalized, phenotype-oriented framework. Advances in understanding neurovascular and immune mechanisms have expanded therapeutic choices and improved outcomes, yet early recognition, consistent care and individualized planning remain the foundation of successful long-term management.

### **Discussion**

Rosacea represents a complex and heterogeneous chronic inflammatory disorder in which multiple pathogenic mechanisms converge to produce a wide range of cutaneous and ocular manifestations. The integration of neurovascular instability, innate immune dysregulation, microbial activity, genetic predisposition and environmental triggers provides a coherent explanation for the diversity of clinical phenotypes observed across populations [2,3,7]. Contemporary evidence supports the concept that rosacea is not a single entity but rather a spectrum of related processes with overlapping biological pathways, which accounts for the variable presentation and clinical course among affected individuals.

The increasing recognition of phenotypic diversity has important implications for both diagnosis and management. Traditional subtypes - erythematotelangiectatic, papulopustular, phymatous and ocular - remain clinically recognizable, but they do not adequately reflect the complexity of disease expression. The transition toward phenotype-based classification, endorsed by international consensus groups, emphasizes assessment of specific clinical features such as persistent erythema, flushing, inflammatory lesions, phymatous changes and ocular involvement [4,9]. This approach aligns more closely with contemporary understanding of rosacea pathobiology and enables clinicians to tailor therapeutic strategies to the dominant manifestations rather than fitting patients into rigid categories.

Diagnosis relies largely on clinical evaluation, and the absence of definitive laboratory or histologic markers underscores the need for careful assessment of symptom history, trigger patterns and characteristic morphologic findings. The potential for ocular involvement, which may precede or occur independently of cutaneous disease, highlights the importance of incorporating targeted ophthalmologic evaluation when indicated [15,16]. Distinguishing rosacea from mimicking conditions such as acne vulgaris, seborrheic dermatitis, contact dermatitis, cutaneous lupus or photodermatoses remains essential, particularly in patients with atypical features or persistent flushing, where systemic disorders must also be considered.

Therapeutic options have expanded significantly in the past decade. Topical agents such as azelaic acid, metronidazole and ivermectin remain central to the management of inflammatory phenotypes and have favorable safety profiles supported by high-quality evidence [4,7,13]. The introduction of alpha-adrenergic agonists, including brimonidine and oxymetazoline, provides additional benefit for persistent erythema through targeted vasoconstriction, although variability in response remains a clinical challenge [5,8]. Systemic therapies, primarily doxycycline in anti-inflammatory doses, play a crucial role in moderate to severe disease and ocular involvement due to their combined antimicrobial and immunomodulatory effects [1,13]. Isotretinoin offers an effective option for refractory inflammatory or phymatous disease, although careful selection and monitoring are required [4]. Procedural interventions, including vascular lasers and intense pulsed light, offer meaningful and often long-lasting improvement in telangiectasia and persistent erythema, particularly when medical therapy alone is insufficient [5].

Despite these advances, several challenges persist. Rosacea remains underdiagnosed in individuals with darker skin phototypes, in whom erythema may be more subtle, and in patients whose primary symptoms are burning, stinging or ocular complaints without prominent facial redness [1,14]. The chronic and relapsing nature of the disease requires ongoing management, patient education and realistic expectations regarding treatment outcomes. Psychosocial impact is often substantial, as facial symptoms may affect self-esteem, social interactions and quality of life, reinforcing the need for supportive counseling and individualized care planning [5].

Future research will likely continue to elucidate specific immune pathways, neurovascular mechanisms and microbial interactions that contribute to disease expression, highlighting opportunities for targeted therapeutics. Identifying reliable biomarkers for diagnosis or treatment response remains an important unmet need. Moreover, the development of standardized, phenotype-based outcome measures will be essential to improving treatment precision and guiding clinical decision-making.

Overall, rosacea should be approached as a multifactorial condition with diverse clinical manifestations requiring tailored, phenotype-directed therapy. The integration of mechanistic insights with clinical expertise has refined current management strategies, yet continued research and patient-centered approaches remain essential to further improving outcomes.

### Conclusions

Rosacea is a multifactorial chronic inflammatory disorder defined by a wide spectrum of cutaneous and ocular manifestations, driven by the interplay of neurovascular dysregulation, innate immune activation, microbial factors and genetic susceptibility. Contemporary evidence indicates that the phenotype-based framework provides a more accurate and clinically meaningful approach to diagnosis and management than the traditional subtype model, as it reflects the heterogeneous and overlapping nature of the disease. Early recognition of persistent centrofacial erythema, inflammatory lesions, phymatous changes and ocular involvement is essential for accurate diagnosis and timely intervention.

Advances in understanding rosacea pathobiology have expanded therapeutic options, with topical agents, systemic treatments and procedural interventions offering targeted benefits across phenotypes. Despite these developments, rosacea remains underdiagnosed in certain populations and continues to impose a substantial psychosocial burden. Long-term management requires individualized, phenotype-directed care, patient education and proactive identification of triggers to optimize outcomes.

Further research is needed to identify reliable diagnostic biomarkers, clarify the role of microbial and immunologic pathways and develop more precise therapeutic strategies. Integrating mechanistic insights with clinical practice will continue to refine the management of rosacea and improve quality of life for affected individuals.

### Disclosure

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