Update on Rosacea Classification and Its Controversies

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PRACTICE **POINTS**

- Rosacea therapy is based on a phenotype classification system, in which patients can have major and minor features across all previously denoted subtypes. This system allows for greater flexibility in treatment regimens.
- Despite mention of progression between subtypes, there has not been convincing evidence that patients can progress or regress from one end of the rosacea spectrum (erythematotelangiectatic) to the other (phymatous).

Rosacea is an inflammatory skin condition that, despite its prevalence, remains imperfectly understood. Without "gold standard" laboratory markers, the diagnosis depends greatly on clinical judgment and the nomenclature used. Throughout the years, the classification schemas for rosacea have changed as clinicians and researchers study the condition. Herein, we highlight the fundamental differences between the proposed classification systems for rosacea, emphasize the areas for improvement, and discuss the implications on clinical decision-making and patient care.

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Rosacea is an inflammatory skin condition that affects approximately 5% of the adult population, with the highest prevalence in Europe and North America.[1] Despite its prevalence, rosacea remains poorly understood from a pathophysiologic perspective, with no diagnostic laboratory markers.[2] Because diagnosis relies on clinical judgment, the nomenclature for describing and characterizing rosacea becomes paramount in ensuring that patients are given an accurate diagnosis and subsequent treatment. We review the shortfalls in the recent history of rosacea classification and discuss their implications.

Subtype to Phenotype Classification

In 2002, the National Rosacea Society (NRS) Expert Committee published a standardized classification schema for rosacea (Table).[3] The authors described primary and secondary diagnostic criteria. The presence of 1 or more primary features in a central facial distribution was indicative of rosacea. Primary characteristics included flushing (transient erythema), nontransient erythema, papules and pustules, and telangiectasia. Secondary features, which could occur with or independently of primary features, included burning or stinging of the face, dry appearance, facial edema, ocular manifestations, peripheral (nonfacial) occurrence, phymatous changes, and red facial plaques. Whereas these features often present simultaneously in a characteristic pattern, they were grouped into 4 main subtypes—erythematotelangiectatic (ETR), papulopustular, phymatous, and ocular—and 1 variant, granulomatous rosacea.[3]

To enhance clinical and research applications of this categorization system as well as offer further standardization, the NRS released a supplementary clinical grading scorecard in 2004 in which each of the primary and secondary characteristics could be assigned a subjective severity score of absent, mild, moderate, or severe. The goal was that the subtype classification and clinical grading system, when used in conjunction with each other, would establish a common language for patients, clinicians, and researchers to describe and further investigate rosacea.[4]

The 2002 categorization system was certainly an impactful first step in the organization of rosacea. It

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Rosacea Classification Schemas

Group (Year)	Diagnostic Criteria	Primary or Major Features	Secondary or Minor Features	Subtype Classification	Variants	Exclusions
NRS Expert Committee[3] (2002)	One or more primary feature	Flushing (transient erythema), nontransient erythema, papules and pustules, telangiectasia	Burning or stinging, dry appearance, facial edema, ocular manifestations, peripheral (nonfacial) location, phymatous changes, red facial plaques	Erythematotelangiectatic, papulopustular, phymatous, ocular	Granulomatous	Perioral dermatitis, rosacea fulminans (pyoderma faciale), steroid-induced acneform eruption
ROSCO panel[9,11] (2017)	Persistent centrofacial erythema, phymatous changes *or* 2 or more major features	Flushing (transient erythema), inflammatory papules and pustules, centrofacial telangiectasia, ocular manifestations	Burning or stinging, dry sensation of skin edema	None	None	None
NRS Expert Committee[12] (2018)	Fixed centrofacial erythema, phymatous changes *or* 2 or more major features	Flushing (transient erythema) within seconds or minutes of neurovascular trigger, papules and pustules, telangiectasia, ocular manifestations	Burning or stinging, dry appearance, edema	None	Ocular rosacea can occur independently of skin findings, granulomatous variant was eliminated	Drug-induced flushing, lupus erythematosus, seborrheic eczema, steroid-induced rosacea

Abbreviations: NRS, National Rosacea Society; ROSCO, ROSacea COnsensus.

was not without its critics, however, namely rosacea-oriented dermatologists who were concerned about its lack of specificity.[5-7] For instance, the NRS Expert Committee did not address the time frame for flushing, which typically has a long duration in rosacea patients, or for the nontransient erythema; telangiectasia secondary to heliodermatitis; or the often-observed periocular sparing. Additionally, the schema did not account for conditions such as gram-negative folliculitis (pustules characteristically located on the central face) or discuss the need to rule out carcinoid, mastocytosis, or connective-tissue disease, which can lead to nontransient facial erythema. Without strict definitions and exclusions, nonrosacea disorders could be incorrectly labeled as rosacea.

Beyond the lack of specificity, there was additional concern if a subtype system was the ideal way to capture disease presentation and severity. By subtyping, there was unnecessary division of interrelated disease into individual disorders; an individual's clinical presentation might fall along a spectrum rather than within a discrete box.[8]

Furthermore, from a research standpoint, subtyping rosacea could hinder or confuse epidemiologic studies. For instance, if patients present with phenotypes from different subtypes, into which subtype would they fall?[8-10]

The global ROSacea COnsensus (ROSCO) panel, comprising 17 international dermatologists and ophthalmologists, convened in 2016 to address this matter. The

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panel proposed a new system (published in 2017) based on individual phenotypes.[9] In this new system, diagnostic features include persistent centrofacial erythema with periods of increased intensity and phymatous changes. Major features, which are diagnostic when there are at least 2, include flushing (transient erythema), inflammatory papules and pustules, centrofacial telangiectasia, and ocular manifestations. Each feature could then be graded on a severity spectrum independent of concurrent phenotypes (Table).[8]

The panel concluded that this system would provide a stronger foundation for standardization as new knowledge of rosacea continues to be elucidated.[8] In support of their argument, ROSCO also released a treatment algorithm that depended on a phenotype scheme.[11] The panel emphasized that by focusing on individual lesions rather than a subtype encompassing many characteristics, treatment could be tailored to the patient. Using this à-la-carte therapy option, physicians could choose those rosacea aspects that are particularly concerning to the patient and manage only those aspects or overlap treatments to improve multiple aspects.[11]

In 2017, 15 years after the original classification system was proposed, the NRS updated their classification system (published in 2018), taking into consideration some of the criticisms as well as new scientific data on rosacea. Similar to the schema proposed by ROSCO, this system was based on phenotype. Inclusion and exclusion criteria were more robust in this update compared to the original classification in 2002. The criteria provide a timeline for transient flushing—it must occur within seconds or minutes in response to a neurovascular stimulant—and state that it is characteristically prolonged (Table).[12]

However, the Expert Committee still did not define either the length of time of flushing or nontransient erythema. It also did not specify convex surfaces of the face with periocular sparing as the characteristic pattern or provide additional information on how photoaging fits into the definition. The updated classification stated that centrofacial erythema must not be from cutaneous lupus or seborrheic eczema, and steroid-induced rosacea was still excluded.[12] However, there is still the need to exclude other systemic conditions, such as mastocytosis, carcinoid, polycythemia vera, and dermatomyositis. Therefore, the potential for subjective error and inclusion of nonrosacea diseases persists.

A critical change was elimination of the granulomatous rosacea variant. In 2002, this variant was defined by monomorphic, yellow-brown to red papules and nodules that led to scarring. This variant, however, did not share the commonalities of the other subtypes, including persistent facial erythema, limitation to convex surfaces, periocular sparing, and transient flushing.[3,13] At the time, Crawford et al[6] proposed that the variant be recategorized as granulomatous facial dermatitis. In the updated NRS classification, this variant and phenotypic description was eliminated from the schema.[12] It is unclear if it was removed because of these discrepancies or if the NRS panel felt it had a distinct pathogenesis from the proposed rosacea pathophysiology; however, we applaud this change.

Subtype Progression

Both the ROSCO and NRS classification schemes mention progression between the various phenotypes,[10,12] suggesting that rosacea phenotypes exist along a continuum, progressing and regressing with disease severity. The main study addressing this point was based on the self-reported retrospective patient memory of disease features in rosacea patients. The authors used a modified criterion of centrofacial erythema alone to define ETR; therefore, a person who began their disease with this finding but then acquired inflammatory lesions or phymas was defined as progressing along a spectrum.[14] Given that persistent erythema of convex surfaces of the face is common in all subtypes, we do not find it surprising that the authors found (using their modified criteria) that ETR appeared to progress to papulopustular and phymatous subtypes in a small number of patients. We strongly disagree with their interpretation and conclusion.

In our experience, ETR patients have fine textured skin without sebaceous quality or a history of extensive acne (Figure 1). Flushing is common and usually lasts 10 minutes to 1 hour. There might be concurrent burning or stinging; however, there is no associated sweating, lightheadedness, palpitations, or diagnostic laboratory findings, which distinguishes ETR from other common causes of flushing. The persistent centrofacial erythema involves convex surfaces, spares periocular skin, and can be best defined as present for longer than 3 months.

In contrast, phymas occur commonly in patients with thick and sebaceous (glandular) skin (Figure 2).[6,15-17] Men are most often affected and usually have a history of moderate to severe acne. It is not uncommon to observe nodules, cysts, and scarring in addition to papules and pustules. These eruptions primarily cluster on the central face and present in areas of nontransient erythema. Flushing, although less prominent than in other phenotypes, also can be seen.

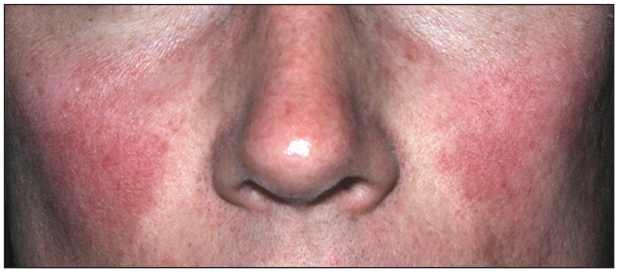

FIGURE 1. Erythematotelangiectatic rosacea.

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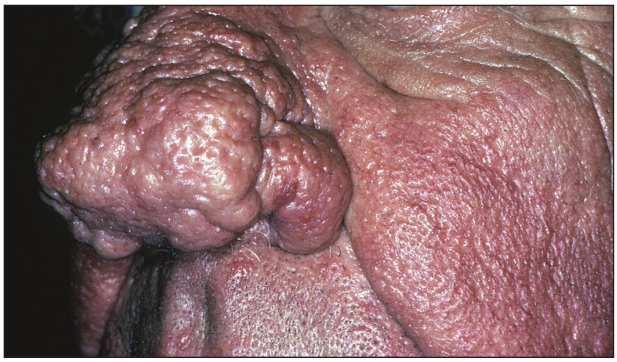

FIGURE 2. Phymatous rosacea.

Taken together, we find no convincing evidence from published studies or extensive experience caring for rosacea patients that classic ETR progresses to phymatous rosacea, or the other way around, as displayed in the ROSCO panel report.[8] The type of skin seen in Figure 1 will not "progress" to the type seen in Figure 2. Furthermore, treatment will not "reverse" the phymatous skin into thin, ETR-type skin. The implications are important: If a female patient is given a diagnosis of ETR, she will not develop an enlarged phymatous nose. Patients with thick sebaceous skin, as in Figure 2, usually tolerate treatments such as benzoyl peroxide that other rosacea patients do not and frequently respond well to such intervention.

Implications and Future Directions

We present an overview of 2 rosacea classification systems, hoping to stimulate further refinement. Looking forward, there are many directions for further investigation into the pathophysiology of rosacea. From a genetic standpoint, there needs to be continued molecular and epidemiologic data to determine the underlying genetic contributions to disease.

There has been some progress in the realm of understanding the mechanisms of inflammation; we urge further investigation to elucidate how "subclinical neuroinflammation" might lead to glandular hyperplasia.[12] We also see value in examining the genetic and hormonal contributions to phymas, as they may be different than those seen in the ETR-type patients. Last, more studies focusing on comorbidities that contribute to or arise from rosacea are welcomed.

The ultimate goal is to develop a classification system that integrates clinical descriptions, pathophysiologic mechanisms, and benchmark indicators of disease. Only then can we have a true gold standard for the diagnosis of rosacea, one that allows for improved personalized treatment and better outcomes.

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