

A Role for Vascular Pathogenic Mechanisms in Rosacea: Implications for Patient Care

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Rosacea is one of the most common dermatoses about which surprisingly little is known. Notions of the pathogenesis of the condition and the relationship among several of its subtypes, namely erythematotelangiectatic, papulopustular, phymatous, and ocular, provoke disparate views among dermatologists. My position is that rosacea often may be driven by a vascular disorder, with lymphedema, which is facilitated by UV damage. I find support for this view from clinical experiences with 3 groups of patients, including patients with severe systemic flushing disorders who developed progressive erythematotelangiectatic rosacea and phymatous changes (because crops of papules and pustules occurred in a few patients but not all, an additional factor may be required for the papulopustular lesions); patients with erythematotelangiectatic and papulopustular changes that coincided with the onset of menopausal hot flashes; and patients with onset or worsening of rosacea associated with vasodilator drug therapy.¹

Recent findings fit well with the notion of rosacea as a facial cutaneous vasculature disorder. First, Yano et al² demonstrated a UVB-induced angiogenic switch mediated by up-regulation of vascular endothelial growth factor. Calcium channel blockers have been associated with the development of photodistributed facial telangiectasia, plausibly because of their potent cutaneous vasodilatory activity.^{3,4} Aloï et al⁵ documented the striking parallel in histologic characteristics between rhinophyma and elephantiasis caused by chronic lymphedema. Bender et al⁶ showed that tetracyclines may exert their effects, at least in part, by inhibiting the human dermal microvascular endothelial release of chemokines. Finally, Yamasaki et al⁷ demonstrated an association between the clinical signs of rosacea and abnormal cathelicidin expression and subsequent processing by substantially increased serine protease activity. They also pointed out that cathelicidins and related peptides may stimulate cytokine release, chemotaxis,

and angiogenesis, and tetracyclines indirectly inhibit serine proteases.⁷

Even if a vascular basis is not the ultimate point of origin for all manifestations of rosacea in all patients, in my view, it is a sufficiently profound factor in the course of rosacea for many patients to warrant consideration in strategies for patient care. Accordingly, it is important to assess if the patient has flushing reactions. Does the patient take vasodilator medications; have menopausal hot flashes; or describe flushing from foods, beverages, or overheating? In a recent article, rosacea was listed among the causes of flushing, and the authors referred in the text to “[a]cne rosacea, another common cause of flushing.”⁸ Although patients with rosacea may be more prone to flushing, there is no convincing evidence to suggest that the causes of flushing in patients with rosacea are different from the causes of flushing in patients without rosacea. The physician should not accept rosacea as a cause for flushing but should seek a specific diagnosis for the flushing to remove the causative agent or prescribe specific therapy.

Similarly, the physician should explore with the patient the possible topical exposures that lead to erythematous and/or stinging reactions. Lonne-Rahm et al⁹ reported near ubiquity of stinging reactions in patients with erythematotelangiectatic rosacea when challenged and elicited a high frequency of reported stinging reactions to topical products and cosmetics. Draelos¹⁰⁻¹³ provided insight regarding specific ingredients that should be avoided and the importance of moisturizers. In my experience, many patients who report stinging are already careful to avoid their personal list of offending agents based on their own observations. In addition to identifying and avoiding products that actually cause stinging in individual patients, the cornerstone of my therapeutic approach has been to displace unwanted exposures to the offending agents through a daily facial skin cleansing ritual that avoids irritation. The regimen advises patients to do the following¹⁴:

1. Wash the face with lukewarm water.
2. Use a gentle cleanser that is soapless.

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3. Use the fingertips and not a washcloth or sponge.
4. Blot dry with a thick-pile cotton towel but do not rub.
5. Initially, wait 30 minutes and then apply the prescribed topical agent. With subsequent cleansing, the 30 minutes may be reduced by 5-minute increments until any stinging sensation occurs when the topical product is applied. The patient should then select a time after which such stinging never occurs.
6. Wait 5 to 10 minutes after applying the topical product before applying cosmetics or moisturizers.

Feldman et al¹⁵ confirmed that nearly 70% of patients with rosacea are women; thus, dermatologists cannot avoid discussing cosmetics with many of their patients with rosacea. While I emphasize the avoidance of topical products that cause stinging reactions and/or redness, such as cosmetics, moisturizers, and sunscreens; the substitution with nonirritating products; and the use of a nonirritating facial cleansing ritual, I avoid any reference to cosmetic or cosmeceutical efficacy. Although there is no doubt that some products marketed as cosmetics may contain ingredients that at some concentration may exert a pharmacologic effect in human skin, possibly even a beneficial effect, my preference is to direct patients to topical products that do not irritate or otherwise harm the skin. I am concerned with some of the marketing pitches that might be taken literally to mean that rosacea can be controlled or treated with cosmetics. The last thing our patients with rosacea need is the trivialization of their rosacea as a cosmetic condition. Not only is this a direct insult to patients, but more importantly, it may be an indirect insult that affects both the perceived risk-benefit calculus of therapeutic decisions by nondermatologists and product-approval decisions by regulatory authorities.

Published reports on the efficacy and safety of topical drug products often do not describe the evaluation for ocular rosacea in the selection process for patients or within the inclusion and exclusion criteria. Simply stated, every patient with rosacea should benefit from a careful assessment of the presence of ocular rosacea. Ghanem et al¹⁶ have shown that the most common complaints by patients with ocular rosacea not initially diagnosed by an ophthalmologist include itchy or watery eyes and foreign body sensations. In addition to asking about these symptoms, it can be revealing to query patients on the use of prescription or over-the-counter eyedrops, any contact lens intolerance, and a sensation of dry eyes. Anamnestically less reliable

is the patient's recollection of how the eye symptoms may have changed during prior systemic antibiotic use; however, if a systemic antibiotic is needed for cutaneous rosacea, it is useful to alert the patient to its anticipated effectiveness for ocular rosacea and record the ocular signs and symptoms before and during therapy. Key areas to examine are the lid margins for dilated vessels and the interpallebral conjunctivae for hyperemia, both vascular features that in the presence of cutaneous rosacea suggest referral to an ophthalmologist. If you know of an ophthalmologist who is interested in treating ocular rosacea, it is my experience that he/she may send you more patients than you refer, and the real winners are the patients.

Attention to (1) flushing reactions, (2) topical products and facial cleansing methods that cause reddening, and (3) vascular clues on lid margins for ocular rosacea can result in improved care of patients with rosacea.

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