Rosacea is a chronic skin condition affecting the face. It is characterized by background redness, as well as red bumps and pus pimples typically affecting the middle third of the face. Patients frequently complain of burning, flushing, and general skin sensitivity. The National Rosacea Society (www.rosacea.org) estimates that roughly 16 million Americans (or 5% of the population) suffer from rosacea. The typical age of onset is between 30 and 50 years. The most commonly affected individuals are Caucasian women, particularly those who are very fair-skinned. There is also some evidence suggesting that a family history increases your risk of developing rosacea.

The disease is categorized into four major subtypes: erythematotelangiectatic (ETR), papulopustular (PPR), phymatous, and ocular. PPR is the most common form, in which patients suffer from bumps and pus pimples. In addition, they may have central facial erythema along with telangiectasias. There is a characteristic sparing of the perioral and periorcular skin. In ETR, patients develop redness without the bumps. The phymatous subtype is characterized by sebaceous gland overgrowth, commonly affecting the nose, resulting in a bulbous nasal tip. Finally, rosacea can manifest in the eye, and patients complain of a gritty or “sand-in-the-eye” sensation.

ETIOLOGIC FACTORS

The pathogenesis of rosacea is complex and multifactorial. Skin barrier dysfunction, neurovascular dysregulation, and innate immune system hyper-reactivity all play a role. It has been demonstrated that the cathelicidin processing pathway is over-active along with high kallikrein-5 activity. Moreover, over-stimulation of toll-like receptor 2 (TLR2) and subsequent pro-inflammatory cytokine release promote inflammation in the skin of rosacea patients. Finally, adaptive immune defects include an abnormal response of B, T, and dendritic cells, and failure to tolerate commensal organisms. Demodex mites, for example, while a normal commensal organism, lead to an inflammatory response not seen in non-rosacea skin.

Histologic evaluation of the skin in rosacea is generally characterized by granulomatous inflammation. While patients with erythema only have a predominantly diffuse perivascular infiltrate, such as Th1 lymphocytes (CD4+), monocytes, and mast cells, those with PPR also have a perifollicular neutrophilic infiltrate.

Cathelicidins. Over-activity of the innate immune system is characterized by increased expression of antimicrobial peptides. High levels of stratum corneum trypsin enzyme (SCTE) promotes high cathelicidin levels. They are then abnormally processed into biologically active LL-37 cathelicidin and others by enzymes like KLK-5.

Yamasaki et al reported that LL-37 cathelicidin is associated with production of interleukin-8, vasodilation and erythema.

Toll-like Receptors. In acne, P. acnes bacteria stimulates TLR2 expression leading to release of proinflammatory cytokines (eg. IL-1β, IL-8, TNFα). In rosacea, TLR2 is similarly stimulated with subsequent TNF-alpha production. TLR2 stimulation is also associated with increases in KLK5 expression in keratinocytes, contributing to increased cathelicidin LL-37 levels.

Demodex. There is mounting evidence that demodex colonization plays a central role in the pathology of PPR. Rosacea patients have been shown to have higher levels of mites on the skin compared to controls. Moreover, the host response to the mite is elevated because of immune dysregulation. However, it is unclear whether it is the inflammatory response or demodex as a primary contrib-
“The pathogenesis of rosacea is complex and multifactorial. Skin barrier dysfunction, neurovascular dysregulation, and innate immune system hyper-reactivity all play a role.”

Rather than the mite itself, studies suggest that a bacteria in the demodex gut known as *bacillus oleronius* may be the causative factor. 16,17

Similar to rosacea, demodex folliculitis presents with papules and pustules on the face. It appears to be a separate entity from rosacea and should be considered when facial skin involvement is wide-spread and patients are unresponsive to traditional rosacea treatments.8,15

**CONCLUSION**

With a greater knowledge of the factors that cause rosacea, more targeted therapies can be developed. Treatment includes a combination of improving skin barrier function, reducing inflammation, eliminating demodex, and blocking vasodilation. A multi-pronged approach addressing as many pathogenic factors as possible is the key to improving treatment outcomes and patient satisfaction.

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