Rethinking Skin Hydration from a Clinical and Molecular Level

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In recent years, understanding of epidermal barrier function and its role in modulating skin health has been enhanced exponentially. With the increased attention to epidermal barrier function and strategies to help normalize it, there has also come some confusion about the impact of topical skincare, clinical signs and symptoms of barrier dysfunction, and the objective markers studied to assess barrier function and repair. To help clarify current thinking for clinicians and encourage more effective communication with patients, it is important to understand some of the differences that may exist in available OTC skincare formulations.

IDENTIFYING THE PROBLEM

The most obvious clinical sign of barrier dysfunction is xerosis: skin clinically characterized by a dry, rough, scaly texture.[1,2,3] Patients may describe such skin as "sensitive" or "chapped" and may note a tendency to easily develop small tears and fissures. Xerotic skin is marked by both a deficiency of natural moisturizing factor (NMF) in the outer layers of the stratum corneum (SC)[4,5] and dysregulation of SC hydration, ultimately impacting proper SC exfoliation, resulting in retention and hyperkeratosis.[3,4,6]

In fact, it is now understood that common dermatoses, such as atopic dermatitis (AD) and ichthyosis vulgaris are characterized by an inability of the SC to maintain hydration as a result of inherent defective elements of the cornified envelope. These flaws result in epidermal barrier dysfunction, which both allow for increased transepidermal water loss (TEWL) and penetration of a broad array of antigenic material inducing an inflammatory response. Together, these factors ultimately result in further impairment of the barrier, inhibiting the ability to generate instrumental lipids and filamentous proteins, and resulting in rough, scaly, or hyperkeratotic skin.[7] Taking a step away from inherent skin disease, even in apparently healthy skin, xerosis is associated with/results from increased TEWL and reductions in NMF levels.[8]

COMING TO TERMS

From patient complaints of dry skin to underlying pathologies, like AD, epidermal barrier dysfunction is a common concern in the dermatology clinic. A plethora of skincare products are currently on the market to manage "dry skin" and support epidermal barrier repair, across a range of price points and with various different ingredients and vehicles. Many have no published studies to support their benefit. Some moisturizer formulations provide temporary improvement of signs of dryness (eg, scaling), due to emollients, but do not provide sustained and therapeutically relevant moisturizing benefits.[5]

Physicians and patients often speak of the importance of moisturizing the skin. The terms "moisturizer" and "moisturizing" are marketing terms with no scientific significance,[9,10] therefore the selection of a topical barrier support formulation should be made based on an assessment of the ingredients and any available data demonstrating their effects on barrier homeostasis. In fact, moisturizers historically were more "moisture-blockers," serving as occlusive films to prevent TEWL more than anything else. It can be inferred that the marketing appeal of this terminology was not as favorable as "moisturizer."

Most dermatologists are familiar with TEWL, which has been suggested to be a sensitive indicator of damage to the epidermis.[11] While it is true that a disrupted barrier is marked by increased TEWL, the utility of TEWL as a marker for epidermal barrier health is coming into question. For example, topical formulations may help to modify TEWL in the short-term via one or both primary mechanisms: creating an endogenous barrier to the diffusion of water out of the stratum corneum (in essence an artificial barrier) or the delivery of moisture to the stratum corneum.[10,12,13] In the former instance, when the moisturizer is ultimately removed, so is the artificial barrier to TEWL. In the latter case, it is not clear that simply bringing moisture into the SC will meaningfully improve barrier function in the long-term. Patients frequently present to our offices complaining that they have used moisturizers daily for weeks with no prolonged improvement in their skin.

"Skin hydration" is another imprecise concept that, for patients, may be conflated with "dry skin." In fact, many patients will remark that they drink plenty of water, which actually has an impact on turgor, not SC fluidity and functionality. Itchy, tight, scaly skin is a physical manifestation of underlying barrier dysfunction and insufficient epidermal hydration.[3] However, the effects of insufficient stratum corneum hydration at the cellular level are complex. Insufficient stratum corneum hydration results in epidermal barrier dysfunction, which may allow the entry for microbes, allergens, and other pro-inflammatory stimuli, which can cause further inflammation.[2,7]

NMFs have gained increase attention lately, from researchers, clinicians, and marketers. Much of the roughly 20 percent water that comprises the healthy stratum corneum is bound to these hygroscopic molecules.[3,14] NMFs are largely comprised of amino acids and their derivatives that are byproducts of the breakdown of various epidermal elements, such as filaggrin.[15] While it is impossible to exogenously replenish NMF, per se, it is possible to replace certain NMF cofactors. For example, urea, a component of NMF, is a common ingredient used in OTC and Rx formulations that can be applied exogenously to xerotic skin, conferring multiple beneficial effects. It can function as a humectant as well as a keratolytic depending on concentration, stabilize intercellular SC lipids, enhance SC water uptake, and importantly regulate genes required for proper barrier function (i.e., stimulate the production of key SC lipids).[3,16]

Finally, the issue of skin pH or the so-called "acid mantle" deserves consideration. Although skin pH has been well studied for years, only relatively recently have dermatologists begun to appreciate the clinical significance of pH in healthy SC function or the effects of topical pH modulation.[17,18] The acid pH of normal skin (pH values of 4–6) has been shown to be favorable for key enzymes involved in the synthesis and maintenance of a competent skin barrier as well as for formation of lamellar structures and processing of lipids secreted by lamellar bodies; Ceramide production is pH dependent.[19,20] Topical emollients have been shown to be able to modify skin pH and help improve SC barrier function.[17,20] Importantly, research has shown that topically applied keratolytics such as urea can increase skin acidity and improve epidermal barrier function.[21]

COMPLEX PROBLEMS, THOUGHTFUL SOLUTIONS

The epidermal barrier is a complex and dynamic structure. Therefore, even mild disruption can result in significant changes at the molecular level, leading to functional changes and visible manifestations of xerosis, and potentially contributing the cycle of dermatoses, such as atopic dermatitis.

Supporting epidermal barrier repair requires more than simply "using a moisturizer." The type and concentration of ingredients used in topical skincare can determine the benefit of a given formulation. For example, the inclusion of select NMF components in topical formulations has been shown to regulate TEWL and restore the SC's capacity to attract and maintain hydration.[22] Routine use of a moisturizer may prevent the progression of dry skin pathologies involving epidermal hyperproliferation and inflammation.[23]

Formulations that offer soothing occlusion, reduction of TEWL, and moisturizing humectants in non-irritating, easy-to-use vehicles are ideal for patients. Integrating established and multifunctional NMFs like urea, in combination with emollients and occlusive ingredients, continues to offer affordable, effective, and widely-assessable benefit for epidermal barrier support.[3,24] ■

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