The pathogenesis of atopic dermatitis (AD) is not fully understood, but ongoing discoveries continue to expand our knowledge of the condition. We know that epidermal barrier dysfunction is an integral component of AD, and this understanding has allowed us to reassess our understanding of AD and its management.

For example, the skin of patients with atopic dermatitis may be described as “irritable” or “hyper-sensitive.” We now recognize that these characteristics may not truly reflect a state of the skin. Instead, they are symptoms of epidermal barrier dysfunction and associated cutaneous inflammation. Given the accumulated evidence that barrier dysfunction may be present even in clinically normal appearing skin of AD patients,1,2 it makes sense that patients may experience skin sensitivity even when they do not have an active flare.

Similarly, AD patients may experience dry skin and pruritus as a consequence of epidermal barrier dysfunction and may have a lower threshold to perceive itch with a variety of stimuli, such as contact with coarse fibers like wool.3 This is not an allergic or “irritant” reaction, per se; rather, such sensitivity may be a symptom of the patient’s underlying disease.

While it is important to work with patients and families to identify and avoid any patient-specific AD triggers, this can be a daunting task; isolating a trigger can be difficult, there is a good deal of confounding misinformation available to families, and avoiding known triggers is not always simple. We have come to recognize that when standard therapeutic interventions are in place to control atopic dermatitis, extreme avoidance tactics are rarely necessary. A comprehensive long-term strategy for AD management should include education, identification and avoidance of true triggers (patient-specific), excellent skin care, and treatment (pharmacologic and non-pharmacologic measures).4

Much has been written about the management of mild to moderate atopic dermatitis with topical corticosteroids and topical calcineurin inhibitors (and I would direct the reader to our 2008 publication in Pediatrics4), but the issue of skin-care remains challenging for some clinicians and for families. It is widely accepted that skin moisturization is crucial for the AD patients, but it is less clear what agents patients should use and when.

WHEN TO APPLY MOISTURIZERS

Patients with AD should apply moisturizers as often as possible, at a minimum twice per day (I recommend three times a day in the hopes it actually gets accomplished one to two times a day). The timing is less important than the frequency of applications, relatively new data suggest. Results from a small study conducted at Rady Children’s...
Hospital and Health Center and the University of California San Diego suggest that frequent and liberal application of moisturizers may be more important for maintaining skin hydration than the frequency of bathing. The question of bathing frequency and timing of moisturizer application has been long debated. The study involved patients with AD as well as controls. The study showed that the skin of patients who had bath soaks but did not apply moisturizers was less hydrated than the skin of patients who applied moisturizer only but did not bathe. The skin of patients who took soaking baths and then applied moisturizer remained well-hydrated for the 1.5-hour observation period following application.5

Among patients who applied moisturizer without pre-bathing, the skin had a higher moisture status at 1.5 hours than the bathing plus moisturizer group.6 It is clear that moisturizer application is tremendously important in AD management. Patients should always apply moisturizer after bathing, and those who bathe less frequently should apply moisturizer regularly to improve skin hydration.

MOISTURIZER VERSUS BARRIER REPAIR

The stratum corneum, which traps moisture to prevent dry skin and protects against the entry of foreign substances, also coordinates an immunologic defense against pathogens that bypass the barrier. Its structure is often described as a “bricks” (covalently bonded corneocytes arranged in compact, overlapping layers) and “mortar” (ceramides, cholesterol, and lipids) structure. Dysfunction of the barrier prompts immediate production of cytokines, including TNF-α, IFN-γ, IL-1, and GM-CSF, and it is now widely accepted that activation of cytokines, chemokines, T-cells, antigen-presenting cells and other inflammatory cells within the epidermis contributes to the onset and proliferation of atopic dermatitis.6

A genetic defect in filaggrin production in the skin is also implicated in AD, contributing to compromised barrier function characterized by increased transepidermal water loss (TEWL). There is even evidence of decreased barrier function (as indicated by increased TEWL) in non-involved skin of patients with AD.7

Barrier repair therapies (considered medical devices by the FDA, learn more at PracticalDermatology.com) currently on the market seek to enhance epidermal barrier function and reduce TEWL and inflammation by replenishing lipids and ceramides shown to be absent from atopic skin. Examples of these prescription formulations include: Mymix (palm-tamide monoethanolamine (PEA) cream, Stiefel), Atopeclear (hydrolipidic cream MAS063DP, Sinclair), Epiceram (3:1:1 ratio ceramides, cholesterol, and free fatty acids, PuraCap Pharmaceutical), Eletone (Mission Pharmaceutical), and NeoSalus (Quinnova). An increasing database demonstrates the utility of these agents for atopic dermatitis and other barrier defect diseases. These agents may improve the symptoms of atopic dermatitis, help reduce patient use of topical corticosteroids, and possibly offer therapeutic benefits comparable to those of low-potency topical corticosteroids.8 These agents are not associated with the long-term side effects associated with topical corticosteroids, such as atrophy or adrenal axis suppression; however, insurance coverage varies and financial expense may be cost-prohibitive for certain patients paying “out-of-pocket.”

When these barrier repair devices came to market, they were met with much excitement. However, some patients and prescribers remain skeptical. Studies of various barrier repair agents have not always had optimal design or large cohorts, but taken together they suggest that barrier repair agents may reduce epidermal barrier dysfunction and help decrease inflammation.9 Further complicating matters, there are data to suggest that an OTC petroleum-based moisturizer may be as effective as a barrier repair cream for the management of atopic dermatitis, at a significantly lower cost.10 Nonetheless, prescription barrier repair devices may offer benefits over OTC formulations, including optimized formulations to address the needs of atopic skin and enhanced cosmetic elegance and patient acceptability. If they act to reduce the number or severity of AD flares, they may also allow for overall therapeutic cost savings for the AD patient.

One of the most studied prescription barrier repair devices is a specific ceramide-dominant, physiologic lipid-based barrier repair emulsion (EpiCeram Skin Barrier Emulsion, PuraCap). This formulation has a 3:1:1 molar ratio of ceramides, cholesterol, and free fatty acids—suggested to be an optimal ratio to help skin barrier repair.11 It is formulated with a controlled release mechanism that is intended to permit once-daily application.

This ceramide-dominant, physiologic lipid-based barrier repair emulsion was compared to fluticasone propionate cream 0.05% in pediatric patients with moderate to severe AD, and was shown to reduce clinical disease severity, decrease pruritus, and improve sleep habits at two and four weeks. Although fluticasone cream provided a significantly greater improvement in SCORAD, pruritus, and sleep habits at two weeks, the two agents showed comparable efficacy for all measures by four weeks.9 Barrier repair therapies have also shown some efficacy as monotherapy for AD.12 Eletone cream monotherapy was found to have comparable efficacy to pimecrolimus cream in a small study.13 The trial involved 20 patients who applied barrier repair cream to a lesion on one side of the body three times daily and the TCI to a similar lesion on the contralateral side twice daily for four weeks. At four weeks, 75 percent of lesions treated with each
agent were rated clear or almost clear by Physician Global Assessment (PGA).

Beyond lesion clearance, topical barrier repair formulations may provide symptomatic relief. In one study, in addition to improvement in AD severity as measured by patient global assessment, Atopiclair was shown to provide symptomatic improvement in pruritus with use three-times per day.15 Barrier repair devices are available in a variety of formulations, allowing for selection of an agent to optimize adherence. In an open-label study in which about half of patients using EpiCeram achieved a score of clear or almost clear on investigator global assessment scores, 75 percent of subjects and 77 percent of investigators reported satisfaction with therapy.16

In practice, barrier repair devices are not typically considered alternatives to topical corticosteroids or topical calcineurin inhibitors for acute AD flares. Prescription barrier repair agents are safely used in conjunction with these medications, and combination therapy is exceedingly common.17 When the flare is brought under control and the TCI or steroid are decreased, then the barrier repair agent may be used to aid in chronic maintenance.

**CONCLUSION**

Frequent and liberal use of moisturizers is essential to AD care. Prescription barrier repair devices may be especially useful in the management of AD. When used in conjunction with standard topical therapies they may help to ease acute flares, and when used as maintenance to normalize barrier function, they may reduce the frequency and severity of flares.

As prescription agents, barrier repair devices are more costly than OTC moisturizers. To minimize financial expense, patients may be provided a barrier repair agent to use once daily and can augment their care with the use of OTC moisturizers throughout the day. Also, keep in mind that manufacturers also frequently offer coupons on their corporate websites. Data showing that certain petroleum-based formulations may offer similar barrier-enhancing benefits to prescription creams suggest that such agents can be recommended to patients with barriers to access to prescription devices. These OTC ointment formulations may, however, not be cosmetically elegant, and patients may not apply them as often as they should. Discuss these factors with your patients in order to design an AD regimen that encourages optimal adherence.

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