Emerging Developments in the Management of Atopic Dermatitis

Research continues to provide support for common approaches while suggesting potential new avenues for patient care.

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New research on atopic dermatitis (AD) is changing our knowledge of disease pathogenesis, and influencing our therapeutic regimens. As new data are published, new therapies will develop, and it is necessary for dermatologists to keep up with these changes. Studies of the genetics of barrier dysfunction, infection and colonization by microbes, neuromechanisms of pruritis, and questions about how allergies may or may not play a role in skin inflammation are all areas of intense focus and debate.

Barrier Dysfunction, Allergens, Infections, and AD

There are multiple potential causes for defective epidermal barrier function in AD. These include abnormal lipid metabolism, increased protease activity (e.g. SCCE), serine protease inhibitor defects (e.g. LEKT1), and filaggrin mutations, which are also known to cause ichthyosis vulgaris (IV). Filaggrin mutations have generated the most interest in recent years. Studies have found that approximately one in 10 Europeans have some form of mild IV, caused by mutations in the filaggrin gene.1 Total absence of filaggrin leads to severe IV. Filaggrin mutations are clearly a significant risk factor for AD, as well as allergic sensitizations, asthma, and persistent AD.2,3

Allergens. Recently, researchers showed that 1-bp deletion mutation, 5303delA, analogous to common human FLG mutations, within the murine Flg gene occurred in the spontaneous mouse mutant flaky tail (ft). The application of allergen to the skin of mice homozygous for this mutation resulted in cutaneous inflammatory infiltrates and enhanced cutaneous allergen priming with development of allergen-specific antibody responses very similar to human atopic dermatitis. Given the data from mouse studies, and our current knowledge of AD, there are questions of whether early interventions to mediate allergy development may influence the course of AD. In one interventional study, infants with AD+ who had a family history of atopy but no food allergy or asthma were treated with either pimecrolimus 1% (Elidel, Novartis) cream or vehicle as a first line therapy, and a topical corticosteroid (Fluticasone cream) as a rescue therapy. After three years, results indicated no difference in rates of asthma or allergy between pimecrolimus-treated patients and controls. Both regimens were well tolerated, with the pimecrolimus appearing as safe as the vehicle.

Infections. Atopic dermatitis may be associated with staphylococcal colonization and clinical infections, including impetigo, pustules, and abscesses. However, cellulitis, sepsis, and osteomyelitis are rare complications. Recently, the link between MRSA and AD has been examined, suggesting regional variation in colonization throughout the U.S.10-11 Some studies have suggested lower MRSA colonization and infection rates than expected for a disease with such high staph colonization rates. For non-life-threatening or serious MRSA infections, initial therapy may be tailored to regional patterns/rates of MRSA. Treatment options may include cephalaxin, clindamycin, TMP/Sulfas, and most other tetracyclines for children over age eight. Of course, topical corticosteroids should be included in treatment regimens of secondarily-infected AD, as they can be useful in decreasing inflammation.

Bleach baths have been shown to be effective in improving AD, perhaps by influencing S aureus colo-
nization and infection. In one study, 0.5 cup of household bleach per full tub of water was used several times per week, in addition to mupirocin ointment twice daily to the nares for five days each month.

**What’s New**

**Wet Wraps.** Actually not new, wet wrap therapy has been a focus of renewed interest. It is important to note that the literature varies in terms of how to perform wet wrap therapy. Most experts advocate wet wrap therapy following application of topical corticosteroids, while others use emollients underneath the wet wraps. Much of the literature shows the utility of topical corticosteroids directly to wet skin, with wet wraps placed on top of the corticosteroids, often with a dry wrap. A discussion and “video training module” is available at the Rady Children’s Hospital Eczema Center Website (www.eczemacenter.org).

**TCIs.** New regimens for maintenance therapy with topical tacrolimus (Protopic, Astellas) have been studied, indicating that after “induction” of disease control, tacrolimus may be used two to three times a week, once a day. Compared to vehicle, tacrolimus 0.03% ointment led to fewer relapse days and more flare-free days. In a 12-month study, patients received twice-weekly application of 0.03% tacrolimus ointment as maintenance therapy. Treatment began with the application BID for up to six weeks until IGA was less than or equal to two. Then, patients were randomized to continue with the twice-weekly application of 0.03% tacrolimus for 12 months or no TCI. Results showed that 0.03% tacrolimus ointment significantly reduced disease exacerbation requiring substantial therapeutic intervention.

Long-term safety studies with TCIs have recently been reported. A recent prospective study has shown that the observed rate of malignancy among treated patients was half the rate of malignancy in the general US population. A “Pediatric Eczema Elective Registry” (PEER) for patients using topical pimecrolimus cream has shown no evidence of immunosuppression risk with normal use.

**Prescription Barrier Creams.** The use of non-steroidal barrier creams, or “targeted barrier therapy” may also be useful for patients with AD. Non-steroidal barrier creams may decrease the need for topical steroids or TCIs, can decrease AD symptoms, and can lengthen time between flares. Some studies have also shown that barrier creams can be superior to emollients in their ability to steroid-spare and in increasing the speed to clearing.

**Food Allergies.** Patients with moderate to severe AD may have higher rates of food allergies than the general population, with some data showing that 25-35 percent of patients have true food allergies. However, there is a poor correlation between specific IgE blood tests and skin prick tests, and clinically significant reactions. In one longitudinal study, positive specific IgE tests were seen in 63 to 74 percent of patients, but only 24 to 37 percent of these same patients had clinically significant food reactions.

Testing for food allergies in AD should be reserved for those patients who have a history suspicious for food reactions, though it may be considered in moderate to severe persistent atopic dermatitis patients who are not responding to standard therapies, and are less than five years of age. Patient and family reports of food allergies should be confirmed, because 50 to 90 percent of presumed food reactions are not actually clinically significant allergies.

New guidelines of care for the diagnosis and management of food allergies will soon be available. These guidelines were coordinated by the National Institute of Allergy and Infectious Disease, involving a set of experts from multiple specialties. The guidelines will likely acknowledge the limitations of allergy tests, and recommend considering food allergy testing in individuals with moderate to severe AD who are not responsive to standard therapy.

**Integrating Evolving Therapy**

It is reasonable to integrate our changing understanding of atopic dermatitis with our management regimens. It is reasonable to address skin barrier dysfunction early, to use anti-inflammatory medicine as needed, and to add anti-infective approaches judiciously, favoring broad, non-bacterially selective methods. Also, it is important to attend to concerns regarding allergies within a total-care regimen,
rather than just reacting to common “hype” of allergy concerns.

Dr. Eichenfield has served as a clinical investigator or consultant for Astellas, Galderma, Graceway, Hill, Johnson & Johnson, Medicis, Stiefel, and SkinMedica.

20. Simpson EL et al. 2009; SID

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