Skin Disorders

Hit Atopic Dermatitis On Several Fronts

Cleansers, emollients, topical steroids, antihistamines, baths, and topical calcineurin inhibitors all can help.

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — Atopic dermatitis is a multifactorial disease requiring multimodal treatment, Jeffrey Sugarman, M.D., said at a meeting on clinical pediatrics sponsored by the University of California, San Francisco.

Dr. Sugarman of the university offered a number of tips to assist the clinician in treating atopic dermatitis (AD), the key dermatosis in children:

- ▶ Be sure of the diagnosis. "Pruritus is a universal feature," Dr. Sugarman said. "If your child with atopic dermatitis is not itchy, you may want to rethink the diagnosis."
- ▶ Barrier dysfunction contributes to AD, and the barrier is typically abnormal, even

will put it out of	the reach o	t many pa-
tients, he said.		

- ▶ "Drooling dermatitis," AD around an infant's mouth, is caused by mechanical irritation in messy eaters from nursing or the bottle. Tell parents to keep the barrier up by applying Vaseline or Aquaphor on the perioral skin before meals. Assure them that drooling dermatitis will disappear as the infant gets older.
- ▶ A child or adolescent who has had "athlete's foot" that has not responded to topical antifungals may actually have juvenile plantar dermatosis or "toxic sock syndrome," he said.

These children typically will have sweaty feet and a history of atopic disease. Look closely at the bottom of the feet. Juvenile plantar dermatosis is characterized by inflammation on the weight-bearing surfaces

of the big toes.

The web spaces are spared, which is the opposite distribution you would see from a fungal infection. Treatment includes a frequent change of socks and the use of emollients and a mid-potency steroid cream.

► To minimize pruritus with AD, recommend warm—not hot—baths, and avoid overheating. Keep the body covered with soft, non-wool clothing. Use emollients. Hydroxyzine is Dr. Sugar-

man's favored antihistamine, at a dose of 1- 2 mg/kg per day.

Consider rotating antihistamines, such as cyproheptadine, doxepin, and diphenhydramine, if one stops working. Topical diphenhydramine is of little use, and the newer nonsedating antihistamines also appear to be relatively ineffective in reducing pruritus.

- ▶ For decades, the use of intermittent topical corticosteroids has been the standard of care for AD, despite their well-known side effects including burning, redness, dryness, and thinning of skin with long-term use.
- ▶ Topical calcineurin inhibitors (TCIs) such as tacrolimus and pimecrolimus also work, and are especially valuable for intertriginous and eyelid lesions. They decrease the need for topical corticosteroids and improve quality of life.

The FDA apparently is concerned about the potential risk of cancer with long-term use of TCIs, but Dr. Sugarman said they're safe if used properly.

They should be reserved for second-line use for short-term and intermittent long-term use in AD. TCIs should be avoided in children younger than age 2 and in immunocompromised patients. Reinforce the need for adjunctive treatment such as gentle skin care, controlling itch, and treating infections. And advise parents that treated areas also need sun protection.

Agent	pH
Johnson's Baby Wash	11.0
Basis soap	10.6
Ivory soap	10.1
Neutrogena Transparent Facial Bar	9.6
Antibacterial soaps	9.0-10.0
Cetaphil Gentle Cleansing Bar	7.3
Dove Beauty Bar	7.3
Aveeno Cleansing Bar for dry skin	4.9

in nonlesional skin. This results in an increased permeability to bacterial pathogens, allergens, and nonspecific irritants.

- ▶ Gentle skin care is important, and one way to accomplish that is to use a cleanser with a neutral or slightly acidic pH. Surprisingly, some popular cleansers, even those marketed for infants, have highly alkaline pH, which exacerbates barrier dysfunction. (See chart.)
- ▶ Recommend the use of emollients, hydrophobic lipids that replace or supplement subcutaneous lipids. These form a temporary hydrophobic shield on the surface, which promotes immediate barrier repair.
- ▶ Most emollients, such as petrolatum and lanolin, are nonphysiologic and have a limited duration of benefit (less than 6 hours).

Physiologic lipid emollients, which now are coming on the market, contain correct molar ratios of ceramide, cholesterol, and free fatty acids.

The skin handles physiologic emollients differently than their nonphysiologic counterparts. Physiologic emollients are taken up by keratinocytes, packaged into lamellar bodies, and resecreted to form lamellar bilayers.

TriCeram is one such emollient that's already on the market, and Dr. Sugarman expects others to become available soon. Unfortunately, the high price of TriCeram

Steroid, Calcineurin Inhibitor Best for AD at Different Times

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BY NANCY WALSH
New York Bureau

GLASGOW, SCOTLAND — A rational approach to the treatment of atopic dermatitis is to use calcineurin inhibitors and topical corticosteroids in different therapeutic niches, based on a scientific understanding of the effects of the drugs on the stratum

corneum and a recognition of the associated genetic-environmental interplay, Michael J. Cork, M.B., said at the annual meeting of the British Association of Dermatologists.

Topical corticosteroids, particularly the potent ones, have profound thinning effects on not only the dermis, but also the epidermis, including the stratum corneum.

In areas such as the face where the stratum corneum is normally thinner than on other body sites, corticosteroid-induced thinning of the skin can result in a low barrier reserve, leaving the skin vulnerable to insult such as from allergens and irritants, Dr. Cork said.

"Pimecrolimus appears to have no effect on the skin barrier. We have not yet looked at tacrolimus but we think it is a class effect," he said. The two drugs have similar molecular weights, but pimecrolimus is more lipophilic, appears to have a higher affinity to skin, and tends to remain trapped in stratum corneum. tacrolimus, the penetration through the stratum corneum and into the other layers of the skin into systemic circulation is greater than with pimecrolimus, but it still is low, said Dr. Cork, head of the academic dermatology group in the division of genomic medicine at the University of Sheffield (England).

These drug effects occur in normal as well as in abnormal skin, but in atopic dermatitis various other factors further contribute to skin vulnerability.

"Atopic eczema is a classic example of a gene-environment interaction, involving multiple genetic changes and multiple environmental factors," Dr. Cork said.

One of the primary genetic determinants in atopic dermatitis appears to be a change in the 3' untranslated region of the stratum corneum chymotryptic enzyme (SCCE) gene, which regulates protease activity

"We did a case-control study in our clinic and found a strong association with atopic eczema with the rare allele of the protease gene," he said (J. Invest. Dermatol. 2004;123:62-6).

Proteases are necessary for the shedding of corneocytes from the upper

layers of skin, a process that is achieved by cleavage of an adhesion protein within corneodesmosomes with SCCE.

This process, which is held in check by protease inhibitors, must be tightly regulated to prevent the skin barrier from breaking down.

The rare allele of the protease gene, which contains a repeat AACC, is like-

ly to increase the expression of messenger RNA for the SCCE gene. The result is an increase in production of protease leading to an excessive breakdown of the corneodesmosomes and the skin barrier.

Application of topical corticosteroids to even normal skin induces the expression of protease SCCE mRNA and increases the production of SCCE protein. In atopic

eczema the preexisting increase in SCCE can be further exacerbated by topical corticosteroids, inducing SCCE production, he said.

Exposure to environmental factors such as soap and detergent, which raise the pH of the skin from 5.5 to 7.5, can further contribute to skin breakdown, as proteases are pH sensitive, he said.

Further complicating the picture in the case of flare is the presence of secondary proteases from the inflammatory infiltrate.

This is the circumstance in which topical corticosteroids can be most useful and beneficial for protecting the skin barrier function. "Use of a topical steroid to suppress these high levels of secondary proteases during a flare has an overall positive, restorative effect on the skin barrier," Dr. Cork said.

But for milder, chronic use, corticosteroids can negatively affect the skin barrier, so pimecrolimus could reduce the number of flares and prevent their progression.

And there is very little systemic absorption, potentially about 0.2% of a dose, he said.

For patients with more severe eczema, who otherwise would need greater amounts of topical corticosteroids, rotating the steroid with tacrolimus can control the symptoms and minimize exposure to potent steroids.

"So, based on our understanding of the skin barrier and how topical corticosteroids and calcineurin inhibitors interact with the skin barrier, we can begin to carve out different niches where their benefits will be greater than the adverse effects," he said.

Dr. Cork disclosed that he has received research grants from Novartis and that he is on the company's advisory board.