A topic dermatitis (AD) is a common, complex inflammatory skin disorder characterized by pruritus and eczematous dermatitis (Figures 1-3, see page 202; also see image at right). Epidemiologic data have shown a significant rise in prevalence of atopic dermatitis in Western and developing countries worldwide.

Estimates range between 15% to 20% for the lifetime prevalence of atopic dermatitis in young schoolchildren in the United States and Western Europe, a twofold to threefold increase during the past 30 years. This rise cannot be explained on the basis of genetics alone.¹² There has been an evolution in the understanding of the pathogenesis of atopic dermatitis, and with the introduction of new therapeutic agents, an evolution in treatment as well.

**DIAGNOSIS OF ATOPIC DERMATITIS**

As with other diseases with a wide spectrum of clinical presentation, a complex and still largely unclear pathophysiology, and multifactorial etiology, the diagnosis of atopic dermatitis may not be straightforward. The goal to establish consensus on the criteria for atopic dermatitis has been a continuous endeavor of various expert panels of the American Academy of Dermatology and multiple national and international consensus groups. Expanding on the initial ground-breaking work by Hanifin and Rajka,³ AD is best viewed as a syndrome consisting of essential, important, and associated features that determine the diagnosis (Sidebar, see page 203).⁴

---

**EDUCATIONAL OBJECTIVES**

1. Provide a rationale for early treatment intervention given our current knowledge of the epidemiology and pathophysiology of atopic dermatitis (AD).
2. Review the currently available treatment modalities for AD, their indications, and their limitations.
3. Discuss practical treatment algorithms for AD that incorporate education, skin care, and both traditional and new therapeutic agents.

---

*Dr. Dohil is assistant professor of pediatrics and medicine (dermatology), University of California San Diego School of Medicine, and attending physician, Pediatric and Adolescent Dermatology, Children's Hospital and Health Center, both in San Diego, CA. Dr. Eichenfield is professor of pediatrics and medicine (dermatology), University of California San Diego School of Medicine, and chief, Pediatric and Adolescent Dermatology, Children's Hospital and Health Center, San Diego.*

*Address reprint requests to: Lawrence Eichenfield, MD, Children's Hospital and Health Center, 8010 Frost St, Ste 602, San Diego, CA 92123*

Dr. Eichenfield has served as a clinical investigator and consultant to Fujisawawa, Novartis, Connetics, GlaxoSmithKline, Hill Dermaceuticals, Ferndale, Galderma, Ortho-Neutrogena, and Dermik. He is a consultant with Connetics, Novartis, Medicis, and Dermik and serves on the Speaker's Bureau for Novartis, Fujisawawa, and Dermik. Dr. Dohil has no industry relationships to disclose.

---

Magdalene A. Dohil, MD; and Lawrence F. Eichenfield, MD
Figure 1. Infant with atopic dermatitis with extensive facial involvement, demonstrating the clinical features of impetiginization with erythema, scaling, erosions, oozing, and crusting.

Figure 2. Atopic dermatitis in a patient with a darker complexion, demonstrating lichenification with fresh erosions and moderate erythema on the anterior neck.

Figure 3. Dorsum of hands illustrating erythema, infiltration, excoriation and early lichenification.

A comprehensive review of the numerous factors in atopy and their complex interplay, including genetic, environmental, immune, metabolic, neuroendocrine and infectious triggers, is beyond the scope of this article. However, recent research has focused on the close epidemiologic and pathophysiologic links among atopic dermatitis, asthma, and allergic rhinitis as part of the “atopic triad.” Similar to the rise in atopic dermatitis, there has been a surge in the incidence of asthma. Among children up to age 4, asthma prevalence has increased 160% since the early 1980s. Current epidemiologic data and linkage studies show that atopic dermatitis generally precedes the development of asthma and allergic rhinitis. It appears to represent the “entry point” for allergic disease; 50% to 80% of children with atopic dermatitis eventually may manifest other atopic symptoms.

Several studies in animals have suggested skin sensitization to allergens may affect the development of airway sensitization. Cutaneous antigen-presenting cells play a key role in stimulating a predominantly Th2 immune response, which is known to be significantly elevated in atopic disease. Memory Th2 cells reach the lung and nasal mucosa via the circulatory system, promoting an allergic response at these distant sites.

While these studies have not been reproduced in humans, many children seem to display an evolution in atopy. Some “outgrow” their atopic dermatitis while developing respiratory allergy or asthma. In many, the atopic phenomena coexist, and these children appear to have more severe asthma. Ongoing studies are testing the hypothesis that early, effective treatment intervention for atopic dermatitis in an infant or young child may modify the risk of developing other atopic disease or alleviate its effects.
TREATMENT CONCEPTS IN ATOPIC DERMATITIS

An effective treatment strategy for atopic dermatitis needs to incorporate education, basic skin care (including appropriate bathing practices and moisturization), and use of topical antiinflammatory and systemic medications when necessary. A standardized approach can be used, while care plans can be individualized to promote plan adherence and to address individual beliefs and expectations.

In general, management aims at repair and maintenance of the compromised skin barrier, interruption of the itch-scratch cycle, and reduction of inflammation. Therapeutic interventions can include preventive measures such as efforts to eliminate precipitating factors, reactive use of topical, oral, or other systemic anti-inflammatory agents, and institution of maintenance strategies to minimize dermatitis persistence or recurrence.

TRIGGER AVOIDANCE

Extrinsic provocation factors may be irritant or allergic in nature and may include either nongeneric or specific triggers. A focused history covering potential environmental factors may be useful, though identifying triggers and determining clinical relevance is quite challenging. Common observations cite factors such as environmental temperature and humidity, texture and cleaning of fabrics relating to their breathability, abrasiveness and chemical residue content, and repetitive exposure to otherwise innocuous agents such as plain water, particularly in conjunction with rubbing.

True allergens may include foods, animal dander, preservatives and fragrances in toiletries, or medicated and nonmedicated topical preparations. Food allergens have been implicated in a subset of patients with atopic dermatitis, particularly in very young infants, and are more common in children with AD than those without. Food allergies may induce dermatitis and contribute to the severity of skin disease in some patients, while in others, urticaria or noncutaneous symptoms such as nasal congestion or wheezing are elicited. In 90% of cases the offending foods are milk, egg, peanut, soy, wheat, or fish.

It is reasonable to avoid foods that have been identified clearly to be relevant by food challenges. However, it is equally important to ascertain clinical relevance of allergy testing, due to false-positive results. Extreme restriction diets imposed by worried parents have been associated with malnutrition, including kwashiorkor. Assay of specific IgE levels to particular food allergens has been found to have predictive value as to clinical relevance and may help determine when a food can be reintroduced, although confirmation of valid clinical correlation between food allergy and degree of dermatitis is highly recommended.

The issues of usefulness of breastfeeding or other dietary manipulation to prevent AD often are raised by parents. Despite several prospective studies suggesting some benefit of exclusive and prolonged breastfeeding, results remain inconclusive overall.

Aeroallergens, specifically dust mites and animal dander, may be triggers of established AD. However, more recent research has indicated that there may be an early window of opportunity during the first 2 years of life when exposure to animal dander may paradoxically infer a protective effect on the immune system and prevent the development of sensiti-
TABLE 1.  
Potency Rankings for Topical Corticosteroids

<table>
<thead>
<tr>
<th>Group*</th>
<th>Generic name (brand name: vehicle, concentration)</th>
</tr>
</thead>
</table>
| **Group 1** (Most potent) | Clobetasol propionate (Temovate: cream/ointment/lotion, 0.05%)  
Clobex lotion 0.05% (Cormax: cream/ointment, 0.05%)  
Betamethasone dipropionate (Diprolene: gel/ointment, 0.05%)  
Diflorasone diacetate (Psorcon: ointment, 0.05%)  
Halobetasol propionate (Ultravate: cream/ointment, 0.05%) |
| **Group 2** | Fluocinonide (Lidex: cream/ointment/gel/solution, 0.05%)  
Mometasone furoate (Elocon: ointment, 0.1%)  
Betamethasone dipropionate (Diprosone/Maxivate: ointment, 0.05%)  
Aminophylline (Cyclocort: ointment, 0.1%)  
Desoximetasone (Topicol: cream/ointment, 0.25%; gel, 0.5%)  
Diflucan diacetate (Psorcon: cream, 0.05%; Psorcon E: ointment, 0.05%) |
| **Group 3** | Triamcinolone acetonide (Aristocort: ointment, 0.1%)  
Aminophylline (Cyclocort: cream/ointment, 0.1%)  
Betamethasone dipropionate (Diprosone: cream, 0.05%)  
Betamethasone valerate (Vilosone: ointment, 0.1%)  
Fluticasone propionate (Cuttivate: ointment, 0.005%)  
Diflucan diacetate (Psorcon E: cream, 0.05%)  
Desoximetasone (Topicol LP: cream, 0.05%) |
| **Group 4** | Mometasone furoate (Elocon: cream/ointment, 0.1%)  
Triamcinolone acetonide (Kenalog Aristocort: cream, 0.1%)  
Fluocinolone acetonide (Synalar: ointment, 0.025%)  
Hydrocortisone valerate (Westcor: ointment, 0.2%) |
| **Group 5** | Fluticasone propionate (Cuttivate: cream, 0.05%)  
Fluocinolone acetonide (Synalar: cream, 0.025%)  
Betamethasone valerate (Vilosone: cream, 0.1%)  
Hydrocortisone valerate (Westcor: cream, 0.2%)  
Betamethasone dipropionate (lotion, 0.05%)  
Prednicarbate (Dermatop: cream, 0.1%) |
| **Group 6** | Fluocinolone acetonide (Dermasmothe F5: oil, 0.01%; Synalar: solution, 0.01%; Capex shampoo 0.01%)  
Betamethasone valerate (lotion, 0.05%)  
Triamcinolone acetonide (cream, 0.1%)  
Desonide (DesOwen: cream/ointment/lotion, 0.05%; Tridesilon: cream)  
Adcetansone dipropionate (Acloven: cream/ointment, 0.05%) |
| **Group 7** (Least potent) | Hydrocortisone (Hytone: cream/ointment/lotion, 1%/2.5%)  
Dexamethasone, prednisolone, methylprednisolone  
Pramoxine hydrochloride (1.0%, 2.5%) |

*Categories defined by vasodilator assay.

Dust mite-impermeable covers for pillows and mattresses are considered by some to be a practical measure that may improve AD in an individual patient, although there are conflicting data. Complete avoidance of all allergens is impossible. Some encouraging results were seen with orally administered antihistamines which appeared to protect at-risk infants against sensitization in a large prospective European study. Other preventive efforts include the administration of the probiotic *Lactobacillus rhamnosus* strain GG to at-risk children during the first 2 years of life, with some protective effect noted. Studies have been performed on only a small number of children, and further studies are warranted.

**TOPICAL TREATMENT OPTIONS**

Historically, topical treatment of atopic dermatitis has relied on skin hydration and moisturization in combination with corticosteroids of varying strengths and delivered in various vehicles. Calcineurin inhibitors are newer anti-inflammatory medications that have expanded the available choices for topical therapy.

**Skin Hydration**

Atopic skin shows enhanced transepidermal water loss and impaired skin barrier function, leaving the skin susceptible to irritants and microbial colonization. Frequent rehydration of the skin is essential in any treatment regimen. Ointments and oil-based vehicles with a high lipid content and a thick consistency, but preferably still with good spreadability, are superior in their ability to restore skin surface lipids. This is in contrast to creams or lotions, which have a higher water content and are generally less moisturizing. They may be indicated, however, during extremely hot and humid weather conditions, to prevent occlusive folliculitis and miliaria.
Moisturizers containing urea have been shown to improve skin capacitance, indicating increased skin hydration. Promising results have been noted in an open-label study of a ceramide-dominant emollient cream resulting in improved stratum corneum integrity, and as well with alpha-hydroxy acids improving skin barrier function.

Moisturizers generally are applied immediately after a warm bath while the skin is still damp, to allow for maximum penetration and epidermal hydration, known as the “soak and seal” method. Most patients benefit from the complementing effects of a relaxing and cleansing tepid soaking bath followed immediately by the use of emollients. In fact, many patients with mild atopic dermatitis may be managed on a strict moisturizing treatment schedule alone, decreasing the frequency and severity of flares and the need for topical prescription medication.

Topical Corticosteroids

For the past 50 years, topical corticosteroids have been the mainstay in the management of atopic dermatitis requiring medical intervention. They are effective in reducing acute and chronic inflammation through the suppression of inflammatory cell lines, and cytokines and are able to reduce the density of *Staphylococcus aureus* on affected skin.

The choice of topical steroid preparation depends on the severity and distribution of disease as well as the age of the particular patient. Topical steroids are divided into seven potency classes, with class 1 representing the strongest and class 7 the lowest potency (Table 1, see page 204). Patients need to be informed about these classifications so they understand treatment instructions and limitations regarding potential side effects. In particular, it is helpful to explain to patients that the numbers at the end of the steroid label do not correlate to the relative strength of the corticosteroid. For example, triamcinolone 0.1% is much stronger than hydrocortisone 1%. Generally, the least potent steroid that is effective at achieving prompt disease control is recommended.

It is helpful to educate the caregiver about the long-term treatment plan at the initiation of treatment. Parents need to understand that the goal is controlling, not curing, the disease. It also should be clarified that rescue treatment during an acute flare will be very different from inhibition or blunting of flare development, and that treatments, in turn, will vary from achieving stability to finally maintenance during remission. Given this perspective, parental “steroid phobia” can be overcome, and parents can be actively involved in the step-down treatment plan, improving patient compliance.

Although topical corticosteroids traditionally are not considered appropriate for maintenance therapy in AD, several recent studies with fluticasone propionate in infants as young as 3 months have shown that long-term control can be achieved with twice-weekly therapy on normal-appearing skin. Common fears regarding thinning of the skin, stretch marks (striae), and systemic absorption of corticosteroids should be addressed openly but put into perspective, given the intention of limiting the duration of treatment. The differences between topical steroid products and anabolic steroids used for building muscle also may be discussed.

An important question is how much steroid medication should be applied. In children, the fingertip unit (FTU), known as the amount of topical medication extending from the tip to the first joint on the palmar aspect of the index finger, has been an established measure. Depending on the patient’s age, 1 FTU covers approximately one hand, 2 FTUs are sufficient for the face or a foot, 3 FTUs for an arm, 6 FTUs for the leg.

---

it is helpful to educate the caregiver about the long-term treatment plan at the initiation of treatment. Parents need to understand that the goal is controlling, not curing, the disease.
or may only respond minimally. In these scenarios, it is helpful to review patient compliance. Possible exacerbating factors also should be examined closely. These may include ongoing exposure to irritants or allergens, concomitant bacterial superinfection, or, rarely, steroid allergy or insensitivity.

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCIs) represent a new class of immunosuppressant and anti-inflammatory drug therapy for AD. They interfere with the production of a number of inflammatory mediators by inhibiting the enzyme calcineurin in immune cells, which in turn inhibits the dephosphorylation of the nuclear factor of activated T-cell (NFAT) protein. These medications were first developed after it was noted that systemic cyclosporine A, primarily used for the prevention of organ transplant rejection, was efficacious in eczema and psoriasis patients. Cyclosporin itself shows poor efficacy as a topical medication, and its systemic use often is limited due to its known systemic toxicity.\(^{21}\) In clinical trials, and tacrolimus 0.03% ointment has gained approval from the Food and Drug Administration (FDA) for the treatment of moderate to severe AD in children 2 and older.\(^ {23}\) Currently, safety and efficacy data are available on more than 13,000 patients worldwide spanning a 4-year period. Relevant adverse events include a fairly common (and temporary) local burning sensation, and pruritus, usually reported at initiation of therapy. Less common adverse events reflected on the product label include varicella zoster infections and vesiculobullous rashes. Long-term, open-label studies in both children and adults are ongoing.

Pimecrolimus is an ansamycin derivative that appears to work by a similar mechanism to tacrolimus, binding to “FK binding protein” macrophilin 12 and inhibiting calcineurin.\(^ {24}\) Only low levels of systemic absorption have been seen in clinical studies, and long-term pharmacokinetic studies have not reported significant systemic accumulation of the drug. Multiple clinical studies have demonstrated pimecrolimus 1% cream options for short-term and long-term management for patients who traditionally have relied on topical steroids. The role of TCIs in disease management is still evolving. While the agents appear to be safe in studies and clinical use to date, the local cutaneous immunosuppression raises concerns about potential risks of increasing skin cancer and potential long-term risks such as lymphoma. Recommendations for both agents include sun avoidance and use of sunscreen and sun protection because of studies indicating a shorter time to squamous cell carcinoma development in a standard ultraviolet-irradiated mouse model.

**Combination Topical Therapy**

Clinical studies of topical tacrolimus and pimecrolimus show their efficacy and safety as monotherapy. Clinical experience with both medications supports their usefulness, particularly in the less acute disease phase, focusing on the inhibition or blunting of a flare-up of the dermatitis, or the induction of skin clearing and rescue therapy at earliest sign of a breakthrough flare. For moderate to severe eczema flares, however, mid- to high-potency steroids may induce more rapid disease control than the TCIs. Both TCIs and corticosteroids may be useful for long-term intermittent therapy to maintain the skin disease-free or with reduced disease activity.

Clinical studies are currently focusing on the use of TCIs in combination or in sequential therapy with topical corticosteroids, rather than as first- or second-line monotherapy. Calcineurin inhibitors also are being studied for prolonged maintenance therapy. Sequential therapy generally relies on mid- to high-potency corticosteroids for management of acute disease flares, followed by tapering according to disease activity, and eventual substitution with calcineurin inhibitors for maintenance therapy. Combination therapy with different

---

**Relevant adverse events of tacrolimus include a fairly common (and temporary) local burning sensation and pruritus, usually reported at initiation of therapy.**

Tacrolimus (FK 506), developed for systemic use to prevent graft rejection, has been shown to be efficacious in topical preparations. It is a macrolide lactone that inhibits the activation of T-cells and the release of histamine from mast cells in the inflammatory skin response, which is clinically manifested as AD.\(^{22}\) Tacrolimus 0.03% and 0.1% ointments have been studied extensively to be safe and efficacious in both pediatric and adult patients with AD. Localized burning and stinging of the skin were the most commonly reported adverse events. Long-term studies evaluating its efficacy and safety are ongoing, and pimecrolimus 1% cream has FDA approval for the treatment of mild to moderate AD in patients older than 2.\(^ {25}\)

Both TCIs offer alternative treatment
### TABLE 2.

Algorithm for Severity-based Step Therapy of Atopic Dermatitis

<table>
<thead>
<tr>
<th>Mild Dermatitis (Extent or persistence)</th>
<th>Moderate Dermatitis (extent or persistence)</th>
<th>Severe Dermatitis (extent or persistence)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STEP 1</strong></td>
<td><strong>STEP 2</strong></td>
<td><strong>STEP 3</strong></td>
</tr>
<tr>
<td>Emollient twice daily; avoidance</td>
<td>Emollient twice daily; avoidance</td>
<td>Emollient twice daily; avoidance</td>
</tr>
<tr>
<td></td>
<td>Intermittent low-potency TCS for flare control</td>
<td>Mid-potency TSC for flare control</td>
</tr>
<tr>
<td></td>
<td>(TCI alternative)</td>
<td>TCI alternative</td>
</tr>
<tr>
<td></td>
<td>±Antihistamines</td>
<td>±Antihistamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Step forward if necessary, back to step 1 if controlled. Maintenance Rx beyond step 1 if frequent recurrence or persistence of disease.</td>
</tr>
</tbody>
</table>

| **STEP 2**                             | **STEP 3**                                  | **STEP 4**                                |
| Emollient twice daily; avoidance        | Emollient twice daily; avoidance             | Emollient twice daily; avoidance          |
| Intermittent low-potency TCS for flare control | Mid to higher potency TS for flare control (may be used instead of or in addition to TCI) | Higher potency TS for flare control       |
| TCI alternative                         | TCI long-term intermittent                   | TCI long-term intermittent                |
| ±Antihistamines                         | ±Antihistamines                              | ±Antihistamines                           |
|                                        | Antibiotic if clinical infection            | Antibiotic if clinical infection          |
|                                        | Step forward if necessary, back one step if controlled. Maintenance Rx as Step 2 if frequent recurrence or persistence of disease. Consider Step 5 if uncontrolled: photo-rx, other systemic rx. |

| **STEP 3**                             | **STEP 4**                                  | **STEP 5**                                |
| Emollient twice daily; avoidance        | Emollient twice daily; avoidance             | Emollient twice daily; avoidance          |
| Mid to higher potency TS for flare control (may be used instead of or in addition to TCI) | Higher potency TS for flare control         | Photo Rx or systemic Rx                   |
| TCI long-term intermittent              | TCI long-term intermittent                   | TCI long-term intermittent                |
| (Intermittent low- to mid-potency TS as alternative) | ±Antihistamines | ±Antihistamines                           |
| ±Antihistamines                         | Antibiotic if clinical infection            | Antibiotic if clinical infection          |
| Step forward if necessary, back one step if controlled. Maintenance Rx standard; Step 4 if uncontrolled; Step 5 as needed. |

**Changes in steps are in bold text. TS = topical corticosteroid; TCI = topical calcineurin inhibitor.**

Classes of drugs is a commonly applied principle in clinical practice, reflecting the effort to achieve disease control while minimizing the additive risk of adverse events for each agent. Combination therapy may be the use of a topical steroid and TCI applied at the same time, at different times on the same day, or on a fixed schedule (ie, 5 days for TCI, 2 days for steroid). Sequential therapy generally relies on topical steroids for the management of acute disease flares, with transition to TCIs. A combined approach may help patients recognize that they need not make a choice between long-term disease control and side effects, but rather that they have more options in adjusting their treatment adequately depending on disease activity. Disease algorithms incorporating topical corticosteroids and TCIs based on disease severity are discussed below.

**OTHER SYSTEMIC THERAPY**

**Oral Antihistamines**

Oral antihistamines commonly are used in AD, although there is a limited evidence basis for their efficacy. Oral antihistamines may be divided into sedating and nonsedating preparations and can be administered according to the child's daily schedule to help restore a restful, undisturbed sleep cycle or itch-free periods during school hours. Diphenhydramine and hydroxyzine are commonly used agents with an excellent safety record. Because of their sedating effects, bedtime dosing often is preferred. Doxepin, a tricyclic antidepressant and H1- and H2-receptor antago-
Oral Anti-infective Therapy

*S. aureus* commonly colonizes lesional and nonlesional AD skin, and secondary impetiginization of AD is common. First- or second-generation cephalosporins for 7 to 10 days commonly are prescribed commonly, with excellent clinical response.28

Alternatively, semisynthetic penicillins are effective. Erythromycin and macrolide antibiotics are often of limited utility due to staphylococcal resistance. Long-term systemic antibiotic prophylaxis is discouraged for the same reason, although topical mupirocin to affected areas and intranasally three times daily for 7 days may be helpful in controlling localized disease and reducing nasal carriage of *S. aureus*. The use of other broad-spectrum topical antibiotic preparations is not recommended, given concerns for resistance and skin sensitization, particularly common with neomycin.

With increased methicillin-resistant *S. aureus* (MRSA) in many regions of the United States, treatment of secondarily infected eczema has been evolving. Significant infection with resultant cellulitis, systemic symptoms, or infected eczema unresponsive to standard antibiotic treatment should prompt a bacterial culture and consideration for antibiotics that are effective against MRSA strains.

Children with atopic dermatitis carry an increased risk of eczema herpeticum. Systemic therapy with an oral antiviral drug (eg, acyclovir) is recommended; hospitalization for intravenous therapy may be necessary in some patients.

Phototherapy

Broadband UVB, narrowband UVB, broadband UVA, and psoralen plus ultraviolet A (PUVA) treatment have all been used as adjunctive treatment in an effort to control severe, generalized atopic dermatitis.29 Most patients are able to achieve a certain degree of improvement allowing for reduction of other systemic and topical treatment modalities and their particular side effects. Maintenance with once-weekly phototherapy in conjunction with moisteners and low-potency topical corticosteroids can be achieved reasonably. The immunologic response is thought to be mediated through Langerhans cells and eosinophils following UVA radiation, whereas UVB has immunosuppressive effects through the inhibition of Langerhans cells and altered keratinocyte production. Limitations of phototherapy are primarily related to their long-term adverse effects, including premature skin aging and cutaneous malignancies, and to the practicalities of delivering the treatment, which is frequently only available at certain treatment centers. Extended maintenance regimens are generally not feasible in pediatric patients.

Systemic Immunomodulatory Therapy

Severe, refractory atopic dermatitis may require additional systemic immunomodulatory therapy, to allow for disease control while other treatment modalities are being initiated. Recommended dosing is 2 to 5 mg per kilogram per day, or weight-independent dosing of between 150 and 300 mg daily in divided doses for older children and adolescents. Long-term treatment is hampered by potentially serious side effects, including renal impairment and the increased risk of malignancies.

Various other systemic agents have been used in a small number of patients with variable clinical success. All of these agents, including antimeatabolites, recombinant human interferon-gamma, tacrolimus, pimecrolimus, intravenous immunoglobulin, and the new biologic agents, carry significant risks and toxicities restricting their clinical usefulness.26

**TREATMENT ALGORITHM**

The understanding of AD as an inflammatory skin condition with
immunologic dysregulation has evolved along with therapeutic alternatives for atopic dermatitis. Asthma and AD, and their interrelationship as “atopic phenomenon,” were highlighted in recent reviews by United States specialists in dermatology, asthma, allergy and immunology, who reported on literature and evolving data. This group recommended the development of guidelines of care for AD.26,30,31

Algorithms of care should be clinically simple and useful. A severity-based algorithm, incorporating “levels” or “steps” of care dependent on disease extent, persistence and recurrence, has been published (Table 2, see page 207).32 Different severities of AD set up different prescriptions of base therapy, with movement forward or backward, dependent on disease response. It is hoped that algorithms of this type will allow incorporation of traditional therapies (eg, education, good skin care, emollients, topical corticosteroids) with newer therapies (eg, TCIs), enabling adequate disease treatment and control while minimizing overtreatment with prescription agents.27

Severity assessment for entry into the algorithm may be based on extent of disease or persistence of disease. It assigns “steps of therapy” similar to the National Heart, Lung, and Blood Institute and National Asthma Education and Prevention Program asthma guidelines.33 Differing severities of atopic dermatitis are treated with a different “base step” of therapy. This algorithm has not yet been evaluated in clinical practice.

Any algorithm using disease severity will require clinically simple and useful category assignments. Commonly used severity ratings scales are numerous, competitive, and variable in how objective they are.34-36 They pose difficulties in terms of their utility for clinical purposes, most of them using scoring systems that attempt to assign numbers objectively for components that usually are assessed subjectively. The most commonly used and validated scales, such as the Severity Scoring of Atopic Dermatitis and Eczema Area and Severity Index, as well as recently proposed scales based on transepidermal water loss and skin hydration (eg, the Objective Severity Assessment of Atopic Dermatitis, or OSAAD), are very difficult to use in clinical practice.6,7,37,38

In addition, most severity scales generally do not assess disease activity over time and cannot distinguish among patients. That is, patients with very intermittent flares of AD involving a moderate amount of body surface area that is easily controlled with several days of topical steroids and continued emollients are not distinct from those with persistent dermatitis over the same body surface area, or those with rapid recurrence upon discontinuation of steroids. One method is to assign severity (ie, mild, moderate, severe) by the medications needed to keep the disease in control. Another more practical method may be simple assignment into these categories based on disease extent and persistence.

REFERENCES