Perspectives in Atopic Dermatitis: Optimizing Outcomes

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Current Issues in Atopic Comorbidities and Preventing the Atopic March
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Understanding and Managing Atopic Dermatitis in Adult Patients
Improving the Patient-Clinician and Parent-Clinician Partnership in Atopic Dermatitis Management
Personal Care Plan
CME Post-Test and Evaluation

Original Release Date: September 2012
Most Recent Review Date: September 2012
Expiration Date: September 30, 2013
Estimated Time to Complete Activity: 2.0 hours
Medium or Combination of Media Used: Written Supplement
Method of Physician Participation: Journal Supplement

This activity is supported by an educational grant from Valiant Dermatology.
Perspectives in Atopic Dermatitis: Optimizing Outcomes

The estimated prevalence of atopic dermatitis (AD) in the United States ranges from 10% to 20%, with a current estimated prevalence of new diagnoses of AD (or eczema) of 11% each year. The disease is most commonly diagnosed in childhood, and most cases resolve before adulthood. Although most cases of AD that persist into adulthood tend to be milder than childhood AD, even mild AD can be a significant burden to adult patients, in terms of quality-of-life and psychosocial issues. Within the past decade, the increased appreciation of the role of the epidermal skin barrier and the discovery of the role of the filaggrin gene in the maintenance of this barrier has led to a new understanding of the pathogenesis of AD. Topical corticosteroids remain the mainstay of therapy for most cases of AD in both children and adults, and topical calcineurin inhibitors have proved to be a valuable addition to the roster of therapeutic options. Experience has shown that strategies such as rotational therapy can optimize the clinical benefits of both of these classes of topical medications. Clinicians need to remain up-to-date on the benefits and risks, as well as the appropriate selection, of all of the available treatments, both topical and systemic. Health practitioners also must be informed about new and emerging developments in the pathogenesis of AD and other atopic diseases. These advances hold promise for future developments in the diagnosis and management of AD.

ACKNOWLEDGMENTS
The authors would like to thank Global Academy for Medical Education, LLC, and Joanne Still for assistance with the preparation of this supplement.

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LEARNING OBJECTIVES
After participating in this continuing medical educational activity, clinicians should be able to:
- Discuss the most recent information on the epidemiology and pathogenesis of AD, and how this is likely to affect the management of patients with AD.
- Explain how the current and emerging understanding of the role of the epidermal skin barrier should affect—and continue to improve—the day-to-day care of patients with AD.
- Describe the role of mutations in the filaggrin gene (FLG) in the pathogenesis of AD, and use this understanding to evaluate the results of ongoing clinical studies that address FLG mutations.
- More effectively individualize patient treatment strategies by considering the full range of current therapeutic options.
- Reassure patients and/or parents by providing updated information about the risks and benefits of using topical corticosteroid and topical calcineurin inhibitors.
- Incorporate discussions of quality-of-life and potential psychosocial comorbidities into clinical encounters with adult patients with AD, and be prepared to provide interventions or refer patients for appropriate counseling and therapy.
- Have improved confidence in using systemic therapy when indicated, and incorporate recommendations for clinical and laboratory monitoring into treatment plans for the duration of such treatment.

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Atopic dermatitis (AD) has a substantial impact on both patients and their families. This issue of *Seminars in Cutaneous Medicine and Surgery* highlights newly recognized aspects of AD pathogenesis as well as the evolution in therapy that offers opportunities for improved outcomes. The faculty members convened for this supplement provide up-to-date evidence that supports some long-held concepts; they also review other recently published data that challenge clinicians to reconsider long-standing ideas about the pathogenesis and treatment of AD. The major topics concerning AD that are addressed in this supplement include epidemiology, pathogenesis, microbial colonization and infection, comorbidities, disease in adults, prevention and treatment strategies, and improving the patient-clinician/parent-clinician partnership in AD management.

**Epidemiology and Pathogenesis**

The prevalence of AD has been increasing worldwide over the past several decades, with a current reported prevalence of 10% to 20% among children in industrialized countries. As the authors discuss in the article by Eichenfield et al., relatively new data from the United States show a prevalence of AD of 8.7% to 18%, with interesting prevalence differences from state to state—higher rates are found in Idaho, Nevada, Utah, and the East coastal states. In the past, discussions of AD pathogenesis focused on immune dysregulation. Now, however, recent research advancements have led to an understanding that sets of mutations in skin cell genes are associated with skin barrier defects in AD. Data discussed by Eichenfield et al. demonstrate that mutations in these genes—especially in the filaggrin gene—are strongly predictive of AD as well as immunoglobulin E sensitization and allergy. These findings have challenged us to consider sensitization and allergy not as primary causes of AD, but as secondary consequences of skin barrier dysfunction. This newer information about pathogenesis is changing approaches to the care of patients with AD.

**Colonization and Infection in AD**

It has long been known that *Staphylococcus aureus* is an important organism in AD, being associated with high rates of colonization and infection and being responsible for impetiginized dermatitis, pustules, and, occasionally, more significant skin, bone, or systemic infections in patients with AD. The paper by Eichenfield et al. discusses perspectives on the bacterial and viral complications in AD, as well as some of the intriguing data on how normal skin flora—such as *Staphylococcus epidermidis*—contributes to innate immune reactions. This raises the question whether changes in usual commensal microbes on the skin in patients with AD may affect the cutaneous innate immune system, as well as how *S. aureus* colonization develops and influences the course of AD over time.

As Paller et al. note, studies have shown that twice-weekly bathing with sodium hypochlorite solution (“bleach baths”) can markedly improve AD by decreasing microbial colonization and reducing the risk for infection. Increasingly, clinical experience also supports the benefit of bleach baths.

**Comorbidities in AD**

Simpson and colleagues highlight the very important emerging information on comorbidities in AD. Although it has long been recognized that AD is associated with the development of asthma, allergic rhinitis, and food allergy, evidence regarding behavioral, emotional, and psychological comorbidities has been increasingly reported. Particularly interesting are the data...
demonstrating that children with AD may have increased rates of attention-deficit/hyperactivity disorder (ADHD). Autism also may be associated with AD. It is unknown whether AD is a causal factor in ADHD or other psychological effects, but the data appear to be very strong that there is a significant association. This emerging evidence should strengthen clinicians’ conviction to optimize treatment of AD, minimizing its impact on pruritus, skin inflammation, and sleep disturbance, all of which may be contributing to these secondary disabilities.

Adult AD

Although AD in adults is not uncommon, a paucity of studies has been devoted to this topic, particularly adult-onset AD. Adult-onset AD is discussed in the paper contributed by Ellis and colleagues, who address the clinical presentation of AD beginning in adulthood, as well as some of the immunologic differences that are found in these patients. The paper also highlights infectious comorbidities in adult AD and the significant psychiatric and psychological effects of AD in this population. Depression, suicidal ideation, a substantial impact on quality of life, choice of occupation, and psychosexual issues are all reported with adult AD.

Considerations for treatment of adults with severe AD that does not respond to topical therapy can include phototherapy and systemic immunosuppressive agents, but we look forward to more-specific, biologic-based strategies in the future.

AD Prevention and Treatment Strategies

The article by Simpson et al highlights strategies for AD prevention. We await future publication of the results of the work of investigators who are studying early-intervention skin care targeting abnormal skin barrier function to determine whether this can minimize the development or improve the course of AD.

To optimize AD outcomes, a broad knowledge of skin management strategies and regimens is required, including bathing, nonprescription topical agents, and prescription topical and systemic agents. The article by Paller et al discusses strategies for optimizing available therapeutic options for successful treatment of AD.

Bathing and appropriate use of emollients and moisturizers, including targeted barrier-repair products, can be useful as part of the mainstay of therapy for AD. Anti-inflammatory medications, including topical corticosteroids and topical calcineurin inhibitors (TCIs), can be crucial in AD care. New information on the relative safety of the TCIs has emerged, including long-term registry data and multiple epidemiologic studies.

Many individuals affected with AD may have persistent or frequently flaring eczema. The concept of rotational therapy, or intermittent treatment to minimize flares of the disease, has been very helpful in management. Rotational therapy may involve the use of topical corticosteroids, with switching to a TCI, or relatively long-term intermittent application of corticosteroids or TCIs. A subset of patients with AD is insufficiently controlled even with excellent topical therapy. The approach to severe refractory AD can include hospitalization to remove the patient from the environment and ensure adherence with therapy, or phototherapy, or systemic immunosuppressive therapy.

The Patient/Parent-Clinician Partnership

The art of achieving high-quality, optimally effective AD care involves working with patients and/or their family to understand their disease and to feel comfortable with interventions for control of their disease. Commonly, treatment failure or response that is poorer than expected is secondary to poor adherence. Optimal management of AD involves not only choosing the right therapeutic agents but also effectively explaining regimens of care to patients and their families, encouraging appropriate use of medications, dealing with patient concerns or fears about their products, and having appropriate follow-up to assess their therapeutic efficacy.

The article by Mancini et al discusses the patient-clinician/parent-clinician partnership in AD management. Unfortunately, there is tremendous evidence showing poor adherence to care of patients with AD. There has been an evolution in AD management, recognizing that appropriate therapeutic education can make a huge impact on the course of a disease. This article also includes a helpful personal-care-plan information page and form; the care plan may be copied by clinicians and distributed to parents and patients free of charge. (This page also will be posted on the Website, www.globalacademycme.com/sdef using an interactive design to permit computer generation of the personalized care plan.)

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References

Atopic Dermatitis: Epidemiology and Pathogenesis Update

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**The prevalence of atopic dermatitis (AD) has increased markedly in the United States over the past 5 decades, with current reports varying from 10% to 20% prevalence in US children, and new diagnoses are estimated at almost 11% per year. Recent research in AD pathophysiology and pathogenesis has demonstrated that AD is associated with epidermal barrier dysfunction and that mutations in the filaggrin gene are implicated in barrier defects. These discoveries hold promise for future breakthroughs in the diagnosis and management of AD.**

Semin Cutan Med Surg 31(suppl 3):S3-S5 © 2012 Published by Elsevier Inc.

Worldwide, the prevalence of atopic dermatitis (AD) has increased approximately threefold since the 1960s. In the United States, the reported prevalence of AD currently ranges from 10% to 20% of children. In a recent study of US children 17 years of age or younger derived from National Surgery of Children’s Health data from 2003, Shaw and colleagues1 reported a 10.7% prevalence of new diagnoses of AD or eczema within the previous year. (These prevalence data from the study by Shaw et al are similar to those reported in previous studies involving smaller US populations.2-4)

Of additional interest are two observations from the study by Shaw et al.1 One is that the prevalence rates ranged from 8.7% to 18.1% from state to state, with a higher prevalence along the East coast states and in Nevada, Utah, and Idaho. The other observation is that significantly higher disease prevalence was associated with metropolitan living (P = 0.008), black race (P = 0.005), and education levels in the household greater than high school (P = 0.004). These data clearly suggest that social or environmental factors can affect

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Publication of this CME article was jointly sponsored by the University of Louisville Continuing Health Sciences Education and Global Academy for Medical Education LLC in affiliation with Skin Disease Education Foundation and is supported by an educational grant from Valeant Pharmaceuticals North America Inc. The faculty have received an honorarium from Global Academy for Medical Education for their participation in this activity. They acknowledge the editorial assistance of Joanne Still, medical writer, and Global Academy for Medical Education in the development of this continuing medical education journal article. Joanne Still has no relevant financial relationships with any commercial interests.

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the expression of AD, although the specific factors have not been identified.

**Immunologic and Inflammatory Pathways: Newer Concepts, Emerging Evidence**

AD was once thought to be related to keratinocyte dysfunction, but over the past 2 decades, the understanding of AD pathogenesis focused on AD as a disease of immunologic dysregulation. Immunologic studies have demonstrated that even clinically unaffected skin in patients with AD can show mild epidermal hyperplasia and sparse perivascular T-cell infiltrates. Acutely eczematous skin is associated with spongiosis, which is a manifestation of intercellular edema. In addition, androgen-presenting dendritic cells are thought to be of potential importance in immunologic responses that manifest in atopic skin. However, the most recent evolution in understanding AD concerns genetic mutations that cause barrier dysfunction in AD. These developments have called to question the contributors to AD pathogenesis.

These advances in understanding AD pathogenesis occurred following the identification of a set of mutations in the skin that are associated with barrier defects, specifically, mutations in the filaggrin gene (FLG). Interestingly, as early as 1985, Sybert and colleagues had proposed that filaggrin abnormalities were the cause of ichthyosis vulgaris, which is a condition that was known to be present in a subset of patients with AD. However, the significance of this work was not appreciated until the revolution in genetics occurred within the past decade, with the mapping of the human genome and the identification of the FLG. When the work of Sybert’s group and others was revisited, it became clear that FLG mutations were, in fact, the cause of ichthyosis vulgaris. (For a comprehensive commentary on this breakthrough, Segre’s article, “Epidermal differentiation complex yields a secret: Mutations in the cornification protein filaggrin underlie ichthyosis vulgaris,” is recommended.)

To review briefly, the stratum corneum layer, also referred to as the epidermal skin barrier, has several major functions, including the prevention of invasion of the body by environmental pathogens and the control of water loss across the epithelium (ie, transepidermal water loss [TEWL]). The stratum corneum consists of between 10 and 30 layers (depending on anatomic site) of keratinocytes that have differentiated to become anucleated corneocytes; in these cells, the plasma membrane is replaced by a layer of large protein molecules—the cornified envelope. Filaggrin, an essential structural protein in the cornified envelope, is expressed first as profilaggrin, which plays an important role in “packing” the keratinocytes into the stratum corneum.

In addition to its contribution to creating a mimeticlike, impermeable structure, filaggrin is also broken down, through proteolysis, into humectants—hygroscopic amino acids referred to as natural moisturizing factor. Filaggrin deficiency can adversely affect these functions, impairing stratum corneum adhesion, enhancing TEWL, and causing dysregulation of the skin pH resulting in increased skin permeability.

Loss-of-function mutations in the FLG are quite common: 10% of individuals of European ancestry carry such mutations, which are associated with a reduction of about 50% in filaggrin protein production. Clinically, loss-of-function mutations have been associated with the development of AD. In addition, patients who have AD and the FLG mutation also have a greater tendency than those without the mutation to have more severe or persistent AD, an increased risk for acquiring herpesvirus infection (eczema herpeticum), and an increased risk for early sensitization and multiple allergies (including peanut allergy) and asthma.

It is now recognized that a variety of cytokines may mediate inflammation in atopic skin. Acute AD may be associated with T-helper type 2 (Th2) cytokines, including interleukin (IL)-4 and IL-13, which influence immunoglobulin E synthesis and adhesion molecule expression. In addition, IL-31 has been identified as a unique Th2 cytokine that is associated with the development of dermatitis and pruritus in experimental animals.

Further, recent studies have demonstrated that thymic stromal lymphopoietin (TSLP) may be expressed in keratinocytes, affected by skin barrier defects. TSLP may mediate inflammation of the skin and other organs, including the bronchial tree.

**Microbes in AD: Recent Findings**

Colonization with *Staphylococcus aureus* is very common in AD, and patients with AD are at increased risk for impetiginized lesions, pustules, and, occasionally, more significant skin or systemic infections.

With the emergence of community epidemics of methicillin-resistant *S. aureus* (MRSA), concern was raised that patients with AD might be particularly susceptible to such infections. However, several studies have found that the actual rates of MRSA infections in patients with AD are not especially high; in fact, compared to clinical infections seen in nonatopic community members, patients with AD more commonly have methicillin-sensitive staphylococcal infections than MRSA.

It has also been shown that the cutaneous immune defense is influenced by innate defense proteins in the skin and that a relative deficiency of antimicrobial peptides can be seen in the skin of patients with AD compared to patients with other inflammatory skin diseases. This deficiency may be associated with staphylococcal colonization.

Interestingly, recent studies have shown that there is an interaction between resident commensal microbes on the skin and antimicrobial peptides. In fact, there appears to be a degree of microbial symbiosis with the innate immune system. For example, *Staphylococcus epidermidis* in normal skin causes keratinocytes to produce antimicrobial peptides, and these suppress cytokine release after minor epidermal injury. Thus, *S. epidermidis* contributes as a barrier against coloniza-
tion of pathogenic microbes. This begs the question of how *S. aureus* has developed colonization in AD skin, as well as the possible sequence of events that changes the standard commensal microbes in this patient population.

**Conclusion**

AD is a common skin disease, and its prevalence continues to increase worldwide. Over the past 2 decades, research regarding the pathogenesis of AD and related conditions has implicated skin barrier dysfunction and, in turn, that mutations in the FLG adversely affect barrier function. The emerging data on fundamental defects in barrier function have raised the question of whether these barrier defects allow secondary changes in immunologic response that mediate the development of both AD and other atopic conditions. This increasing body of knowledge also has fueled interest in whether early interventions could modulate the development of the secondary atopic phenomena.

**References**


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The individual, family, and public health burden of atopic dermatitis (AD) is considerable. The prevalence of AD is high, the signs and symptoms of the disease adversely affect quality of life for patients and their families, and the comorbid conditions associated with AD can increase considerably the negative impact of the disease. These comorbid conditions patients with AD are susceptible to include skin infectious, IgE-mediated diseases, and mental health disorders. New research identifies the skin barrier as not only an important initiator of atopic dermatitis but may even be a site for allergic sensitization to protein antigens. The skin barrier represents a potential new target for novel atopic prevention strategies.

Semin Cutan Med Surg 31(suppl 3):S6-S9 © 2012 Elsevier Inc. All rights reserved.

A topic dermatitis (AD) is a common disorder, becoming more prevalent in developing countries around the world. AD often negatively affects the lives of children and has a major impact on an entire family. AD also predisposes a child to multiple comorbid conditions, such as skin infections, food allergy, asthma, and psychological issues. Because of the high disease prevalence and its impact on patients and families, finding a way to prevent the development of AD has become a focus of intensive research. Additionally, preventing AD may prevent or reduce the burden of multiple comorbidities that often occur in children who develop AD. Herein, we discuss recent advances regarding AD comorbidities and present a novel skin barrier approach to prevent the atopic march.
Atopic Comorbidities

Mechanisms of Sensitization

In the past, the clustering of IgE-mediated conditions led to the assumption that AD is a disease driven by allergic mechanisms. Indeed, several single nucleotide polymorphisms in genes encoding for immune elements have been found in AD populations. However, in light of the robust data implicating the skin barrier gene filaggrin as a strong predictor of AD development, IgE sensitization and allergy are no longer viewed as causes of AD, but as possible consequences. Protein exposure through a defective skin barrier may be an important mechanism of IgE sensitization in young children, although more direct human data are needed to better understand the importance of transcutaneous sensitization.

Gideon Lack and his team of pediatric allergists conducted one of the first clinical studies to suggest IgE sensitization and allergy may be associated with protein exposure to the skin. This group demonstrated that the strongest predictor of peanut allergy in a cohort of children in the UK was the use in infancy of topical moisturizers containing peanut oil. This suggested IgE sensitization to peanut proteins was occurring via a transcutaneous route. Lack and colleagues also demonstrated that food protein concentrations in house dust was strongly associated with an increased risk for peanut allergy.

Studies in both the murine model and in humans support this concept of transcutaneous sensitization. In mouse models, Beck and Leung showed that applications of protein allergen to abraded skin would produce high levels of IgE to that protein, to a degree greater than that found with sensitization via other routes. In clinical studies, it has been demonstrated that a filaggrin skin barrier gene defect not only increases the risk for AD, but also increases the risk for asthma and allergic sensitization. Most recently, Brown and colleagues reported that filaggrin defects increase the risk for developing peanut allergy even in the absence of AD development, further highlighting the importance of the skin barrier in peanut sensitization.

Food Allergy

The prevalence of food allergy is increased in patients with AD compared to control populations, although the strength of that risk is not clear. Recent population-based studies show that previous estimates of 30% to 60% may be too high, and the risk is probably closer to 15%. In addition, several papers have been published recently indicating that positive allergy tests in AD have poor predictive value—that is, the presence of a positive test is not a reliable predictor of either an immediate or delayed clinical reaction. Indeed, an estimated 50% of the U.S. population will have positive results on an allergy test with no history of allergy.

Recently, the National Institute of Allergy and Infectious Diseases published new guidelines on the diagnosis of food allergy with recommendations for the management of food allergy for patients with AD. Among the changes incorporated by the independent panel of allergists and dermatologists responsible for updating the guidelines is that the diagnosis of allergy should not be based solely on positive results of allergy testing, but also requires demonstration of an “adverse health effect.” The updated NIAID guidelines further state that patients with AD should not be routinely tested for food allergy unless signs are evident of a type 1 reaction (for example, vomiting, urticaria, or angioedema), or unless a patient has been adequately treated with appropriate topical skin care without significant improvement.

Asthma

There is at least a two-fold increase in asthma risk in children with AD. In addition, asthma severity is known to be worse in patients who also have AD. The type of asthma that is most common in patients with AD is allergic asthma. The mechanisms of asthma development in AD are not clear. One possibility is that IgE sensitization, either through immune dysregulation or transcutaneous sensitization, drives allergic asthma. Several studies have suggested that early exposure to respiratory syncytial virus may dramatically increase the risk for asthma, especially in patients predisposed to atopic disorders.

Behavioral/Emotional/ Psychological Issues

General clinical experience and numerous published studies have shown that children with AD have an increased prevalence of emotional, behavioral, and psychological issues compared to children without AD. These issues include irritability, fussiness, clingy behavior, restlessness, and scratching the skin as an attention-getting behavior.

In addition, accumulating evidence suggests that children with AD may be at increased risk for defined mental health disorders, including attention deficit-hyperactivity disorder (ADHD) and autism. Prompted by epidemiologic evidence demonstrating an increased prevalence of asthma in children with ADHD, Schmitt and colleagues hypothesized that the immunologically related condition of AD might be linked to ADHD symptoms. They studied the possible relationship in a study of more than 1400 German children. These investigators found that the prevalence of ADHD in the subjects with AD was 5.2%, and in controls, it was 3.4%, a statistically significant association (odds ratio, 1.54; 95% CI, 1.06-2.22; p = 0.02), and possibly indicating a severity-related independent association between AD and ADHD.

However, the authors also point out that their results “require cautious interpretation,” noting that even if the association is a real one, it may relate to atopy in general and may not be specific for AD. In addition, they delineate methodologic issues that prevent the establishment of a causative relationship between AD and ADHD. Finally, they indicate that AD-related pruritus, sleep disturbance, and other factors may have been factors in their results.

Our group recently conducted a study of mental health disorders in children with AD in large populations in the United States that confirm the initial study from Europe. This study demonstrated that pediatric AD is associated with
ADHD, depression, anxiety, and autism with the greatest risk being associated with more severe skin disease.18

A prevailing opinion regarding the underlying mechanisms of behavioral/psychological problems in children with AD is sleep disturbance. Studies have shown that children with AD commonly experience disturbed sleep, both in duration and quality. Disturbed sleep for just a few consecutive nights can manifest in behavior that resembles that associated with ADHD, and children with AD often experience many months and years of poor-quality sleep. It is not yet clear whether the behavioral/psychological problems in children with AD are fully explained by sleep disturbances, or are the result of other mechanisms entirely.

One other proposed mechanism that may explain—or contribute to—the link between AD and ADHD or autism is systemic inflammation. The theoretical possibility must be considered that cutaneous inflammation may lead to a systemic inflammatory state leading to altered brain development. Children with ADHD and autism have elevated levels of proinflammatory cytokines.19,20 Proinflammatory cytokines have been thought to influence brain development, as cytokine receptors can be found in the developing brain.

Infections

Patients with atopic dermatitis are at increased risk for Staphylococcus aureus colonization and infections. In addition, patients with AD also get exaggerated presentations of viral infections, particularly to herpes simplex virus (eczema herpeticum), which is associated with a dramatic spreading of viral lesions over the skin, lymphadenopathy, fever, and malaise. Eczema herpeticum can be severe and even life-threatening. Patients with AD also are at increased risk for eczema vaccinatum, a viral skin infection that results from direct vaccination with the smallpox vaccine or, more likely, from close contact with another individual who has been vaccinated.

Understanding of the role and nature of microbial skin infections has been enhanced recently by the work of Capone and colleagues21 and of Kong et al.,22 groups who published groundbreaking articles on the human skin microbiome in infants21 and in patients with AD. The skin microbiome is, essentially, the genetic signature of all microorganisms on the skin. These microbiome studies have provided a richer understanding of the microbial diversity and dynamic nature of skin microbes in patients with AD. Kong et al.22 demonstrated that flares of AD actually are correlated with a lack of microbial diversity. Staphylococci appear to proliferate in the setting of reduced microbial diversity, although the exact order of events is unclear. Studies of the microbiome provide opportunities for the development of novel strategies in patients in whom recurrent cutaneous infections may be a problem.

Strategies for Prevention

A systematic review determined that 91% of previous eczema prevention strategies were based on allergen avoidance or on attempts to alter allergic responses. Some of these examples include the use of hypoallergenic formulas, dietary allergen avoidance, environmental allergen avoidance, and dietary supplements to alter immune reactions in the gut. Unfortunately, after decades of research and more than 100 published studies, no generally accepted prevention strategy for AD exists.23

The use of probiotic supplementation and hypoallergenic formulas have shown some recent promising results, but these strategies have not been consistently effective.24,25 In part, this may be because allergic mechanisms are not an important driving factor in atopic dermatitis as previously discussed. Attempting to repair a defective skin barrier early in life represents a new strategy for preventing AD.

In the first study examining a skin barrier approach to AD prevention, Simpson and colleagues used full-body emollient to prevent the initial flare of AD. This approach was studied in a cohort of 22 babies at high risk for developing eczema (one first-degree relative with a history of atopic disease).26 After over 1 year of treatment, the cumulative incidence of AD was lower than what would be expected using historical controls. These open-label results were recently confirmed in a small, controlled feasibility trial—the Barrier Enhancement for Eczema Prevention (BEEP) study, a collaborative effort between the U.K. and the U.S. involving 124 neonates.27 Although the study was not powered to assess efficacy, the results indicated that the approach appears to be safe, feasible, and was associated with significant efficacy in reducing the incidence of AD. The caveats to these results include the fact that it was only a 6-month study and three different emollients were used. However, the results provided a basis on which to further explore this strategy.28

Conclusion

Atopic comorbidities include IgE-mediated diseases, infections, and behavioral and emotional problems. An obvious goal in prevention of AD is to avoid the skin signs and symptoms, but also to prevent these various allergic, infectious, and mental health comorbidities.

Although currently there are no generally accepted, or objectively proven, prevention strategies for AD, results from the BEEP feasibility study suggest that measures to protect and enhance the skin barrier from birth may be a promising avenue for future research.

References


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Successful treatment of atopic dermatitis (AD) depends on accurate diagnosis and the development of individualized treatment plans. However, achieving these clinical goals does not ensure the best possible treatment outcome unless compliance is also maximized. Too frequently, less-than-optimal response to therapy or treatment failure can be attributed to adherence issues. For example, Krejci-Manwaring and colleagues used microprocessor stealth monitoring of medication use to assess adherence in an AD patient population. These investigators found that overall adherence was only 32%. In another paper from that same study, Feldman and coworkers described how adherence to topical medication regimens markedly increased during the 8-week period surrounding the clinic visit, increasing right before and decreasing a few weeks afterward.

Eric L. Simpson, MD, MCR, has served as a consultant, investigator and speaker for Galderma.

The faculty have received an honorarium from Global Academy for Medical Education for their participation in this activity. They acknowledge the editorial assistance of Joanne Still, medical writer, and Global Academy for Medical Education in the development of this continuing medical education journal article. Joanne Still has no relevant financial relationships with any commercial interests.

Address reprint requests to Amy S. Paller, MD, Walter J. Hamlin Professor and Chair, Department of Dermatology, Northwestern University Feinberg School of Medicine, 676 North St. Clair Street, Suite 1600, Chicago, IL 60611, email: APaller@nmff.org
It is important for clinicians to spend time not only educating patients and parents but also exploring the lifestyles of patients’ families to determine which factors might influence medication use and so should be considered in devising a treatment plan. Some areas of discussion should include the time of day when the patient’s bath can be done, how often topical emollients can be applied and when this can be done, and the patient’s and/or caregivers’ preference regarding the type of vehicle in topical medications.

Finally, the concept of written action plans is also critically important. The treatment plan should be discussed, but that information also should be imparted in writing.5

Treatment recommendations in AD are based on the current understanding of pathogenesis—i.e., the role of skin barrier dysfunction and of the inflammatory processes that drive the condition.

**Bathing and Moisturization**

The importance of bathing has long been recognized. Bathing removes some bacteria from the skin, results in some exfoliation, and, importantly, provides hydration. A crucial element of therapy is application after the bath of an appropriate moisturizing agent. Ointments are generally preferred because they reduce transepidermal water loss and, unlike some creams, do not contain preservatives that may sting or burn.

In extremely warm weather, ointments may be too occlusive, and emollient creams are a good alternative in these circumstances. Emollient creams also may be preferred by patients or parents who have strong objections to the greasy feel of ointments. Based on the finding that ceramide tends to be reduced in the skin of patients with AD, some newer emollient agents have been developed that contain this lipid. The amount of ceramide in these products varies. To date, ceramide’s mechanism of action and how much ceramide may be needed to affect barrier function have not been clearly established.

Lotions have a high water content and are appropriate for cases in which dryness is not severe or in very warm weather when excess occlusion from ointments or even emollient creams is a concern.

Several medical devices have become available that are primarily designed to improve the skin barrier. These include N-palmitoylethanolamine, a lipid-based ceramide-dominant cream, and MAS063DP. These have largely been tested in patients with mild to moderate eczema and appear to be superior to vehicle. In more severely affected patients, these may be helpful as adjuvant agents.4

**Anti-inflammatory Modalities**

*Topical corticosteroids* remain the mainstay of therapy for bringing AD under control. These are available in a wide variety of strengths, formulations, and vehicles. They range in potency from very-low-strength over-the-counter hydrocortisone to superpotent formulations of various agents (Table 1). Class 2 corticosteroids are the strongest usually used in children; stronger topical formulations are sometimes used in adults and may be used selectively for older children.

When used appropriately, topical corticosteroids are associated with few side effects. The risk for side effects—most commonly, atrophy and striae—increases with excessive use of corticosteroids (in duration of use or in frequency of applications) and when potency is too high, particularly when applied to intertriginous areas or the face. Systemic absorption is a rare possibility with the use of low- or medium-strength corticosteroids, particularly when their application is limited through use of a rotational strategy.

Occasionally, response to a topical corticosteroid may diminish over time in a previous responder, a phenomenon referred to as tachyphylaxis. Reduced or failed response to an agent after initial efficacy suggests the need for a change in the topical regimen, usually to a different corticosteroid of similar potency or to a stronger-potency formulation of the same agent.

However, one of the worst problems associated with topical corticosteroid use is the failure to use the medication, commonly as a result of what has been termed “steroid phobia.” Steroid phobia is the fear on the part of patients’ parents—and even some clinicians—that topical corticosteroids cause significant local and, possibly, systemic side effects. In fact, in one study, steroid phobia accounted for treatment nonadherence in 36% of patients or families.5 This unwarranted fear has an unfortunate adverse impact on the prescription of and/or adherence to use of what are appropriate first-line medications.

*Topical calcineurin inhibitors (TCIs)—*specifically, tacrolimus ointment and pimecrolimus cream—have been available for the past decade and are indicated as second-line therapy for intermittent use. However, they commonly are used off-label as first-line therapy for facial dermatitis because, unlike corticosteroids, TCIs have not been associated with ocular problems or cutaneous atrophy.

Tacrolimus ointment, 0.03%, and pimecrolimus cream, 1%, are indicated for use in patients 2 years of age or older. In addition, tacrolimus ointment is available in a 0.1% strength, indicated for adults and children more than 15 years of age. The indications for tacrolimus were based on early studies suggesting that the 0.03% and 0.1% strengths were equally safe and effective.6 However, the subsequent widespread clinical experience accumulated with the off-label use of the 0.1% formulation of tacrolimus in children shows that it is actually more effective than the 0.03% formulation for pediatric patients. In addition, evidence supports the safe and effective use of the 0.03% formulation of tacrolimus ointment7 and pimecrolimus in children less than 2 years of age, including infants.8 9

In 2005, a committee convened by the US Food and Drug Administration (FDA) discussed the possibility of adding a black box warning in the prescribing information for TCIs. The discussions centered on the two areas of concern. The first was that high-dose oral calcineurin inhibitors, given as immunosuppressants in patients who received organ transplants, was associated in a minority of these patients with post-transplant lymphoproliferative disorder, in addition to their increased potential for causing ultraviolet-light–induced nonmelanoma skin cancer. The second area of concern was that administration
### Relative Potencies of Topical Corticosteroids

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### Therapy Strategies

#### Rotational and Intermittent

The concept of rotational therapy emerged with the increased understanding of and attention focused on the skin barrier in AD. Studies of the effects on skin barrier function of topical corticosteroids, but not TCIs, in the AD population. The other study shown between lymphoma and high-potency topical corticosteroids.

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corticosteroids and TCIs have demonstrated that corticosteroids compromise skin barrier function with long-term therapy and that this compromise actually may happen fairly quickly—within as little as 2 to 3 days with some of the higher-potency agents.\textsuperscript{14,17} In contrast, repair of some of the corticosteroid-induced barrier has been seen with TCIs.\textsuperscript{16}

Taking advantage of these mechanisms, rotational therapy involves the initial use of a medium-strength topical corticosteroid for AD flares, then switching to a TCI (rather than a lower-strength corticosteroid) when the flare is under control.\textsuperscript{18}

To minimize long-term, chronic application of corticosteroids—and the risk for chronic impairment of barrier function—intermittent therapy should be considered as maintenance treatment. Hamfin and colleagues\textsuperscript{19} tested this strategy with twice-weekly applications of flucetasone cream as maintenance and found it to be effective. This concept of “dialing down” was subsequently tested using tacrolimus ointment to decrease corticosteroid use for maintenance. Several studies have demonstrated that, once a flare is under control with corticosteroids and the skin in that area is clear or almost clear, the application of tacrolimus two to three times weekly provides an effective means of extending the corticosteroid-free periods between recurrent flares.\textsuperscript{18,20,21} A maintenance schedule of twice-weekly application of TCIs to clear or almost-clear areas is currently indicated in Europe.\textsuperscript{22}

**Preventing and Managing Infections**

Infection in patients with AD, heralded by crusting or pus-tules, is treated with systemic antibiotics; topical antibiotics have been tried but have not proved to be effective. Interestingly, decades of experience with certain systemic agents—for example, cephalaxin—has shown that antimicrobial therapy often results in dramatic improvement of inflammation as well as control of an infection. To date, however, no good clinical trial has been published that supports this clinical observation.

It is not uncommon for patients to experience an AD flare within a few days to a few weeks following completion of the oral antibiotic regimen. The timing of this flare tends to correlate with the severity of a patient’s disease and reinfection. Presumably, the flare and reinfection tendency relates to *Staphylococcus aureus* overgrowth, and several groups currently are investigating ways to prolong improvement following oral antibiotic therapy.

One relatively new technique that has become the standard of care in the United States for infection-prone patients with AD is the dilute bleach bath—that is, adding sodium hypochlorite (chlorine bleach) to bath water. Huang and colleagues\textsuperscript{20} conducted a study of 31 children with moderate to severe AD and skin infections, in which decreasing *S. aureus* colonization in the nose and on the skin was associated with a decrease in severity of AD. In this study, nose and skin cultures were obtained prior to initiation of oral cephaloxin treatment. Patients were then randomized to receive either bleach in their bath water plus a monthly course of intranasal mupirocin or no bleach in their bath water and a placebo for intranasal administration. Family members of the bleach bath group also received intranasal mupirocin; family members of the no bleach group were given intranasal placebo.

With twice-weekly bathing, both eczema severity and the affected body surface area (BSA) had dramatically decreased in the bleach bath/intranasal mupirocin group, reaching statistical significance by 1 month ($p = 0.02$ for Eczema Area and Severity Index [EASI]; $p = 0.05$ for BSA) and even greater significance by the end of the study at 3 months ($p = 0.004$ for both EASI and BSA). A post hoc analysis showed that these differences were evident only on the limbs and trunk—the areas of the body submerged in the bath; no differences were noted between the two groups in AD sites on the head and neck, which were not submerged. Cultures performed throughout the study demonstrated the persistence of *S. aureus* colonization; thus, the number of organism was suppressed, but *S. aureus* was not eliminated.

Dilute bleach baths must be continued as a maintenance treatment for *S. aureus* overgrowth to remain suppressed. The current recommendation for the concentration of bleach in the bath is 0.005%. The typical concentration of sodium hypochlorite in common household bleach (used in laundry, for example) is 6%, so ¼ cup of bleach added to a half-filled, standard, 40-gallon bathtub (or ½ cup added to a full bathtub) will yield the proper concentration. If a baby bathing basin is used, the proper concentration can be achieved by adding 3 cc of household bleach to each gallon of water.

Other steps should be considered to minimize *S. aureus* exposure in patients with AD, particularly in those who have already experienced one or more infections. One possible source of *S. aureus* contamination that has been discovered in recent years is unpreserved topical agents (prescription and nonprescription) used in AD. In one study, Carr and colleagues\textsuperscript{23} cultured bacteria from the rims, nozzles, and containers of ointments, emollients, and topical corticosteroid medications. About half of the containers were contaminated by bacteria, and, of these, *S. aureus* was cultured in half. Keeping in mind the ubiquitous nature of *S. aureus*, clinicians should consider advising parents to keep moisturizers and topical medications in the refrigerator (warming them by floating them in the bathtub prior to after-bath application). Parents also should be instructed to use a tongue blade or a clean spoon to remove medications and moisturizers from their containers, thereby avoiding hand contamination of the remaining product.

Furthermore, in cases in which infections are recurrent, it may be helpful to have family members use mupirocin intranasally and also to use mupirocin ointment on the hands. In one study of bacterial cultures from skin and nares, 65% of parents also showed *S. aureus* colonization, and in 84% of these isolates, the *S. aureus* characteristics were shared with those of their children with AD.\textsuperscript{24} In the future, other measures such as the use of alternative antiseptic products (cur-
Refra
ty AD

In patients who do not respond as expected to appropriate
management and in whom tachyphylaxis has been ruled
out by changing topical medications, the possibility of an
incorrect diagnosis must be considered. Many conditions
mimic AD and range from genetic disorders such as Neth-
erton syndrome, hyper–immunoglobulin E syndrome,
and Wiskott-Aldrich syndrome to conditions like allergic
contact dermatitis, secondarily eczematized scabies, and
tinea incognito.

In addition, studies have shown that contact dermatitis
can coexist with AD.25 Beattie and colleagues26 showed that 6% to
22% of patients with AD had a positive patch test beyond
nickel, and half of them were sensitive to agents in their
emollient. Thus, it is important to be mindful that additives
used in emollients, skin cleansers, and even topical cortico-
steroids can be contact sensitizers.

After considering and ruling out these alternative explana-
tions for failure to respond adequately, more aggressive ap-
proaches can be considered. One of these is hospitalization,
during which patients can receive careful monitoring and
intensive attention, including ready access to consultants.
Hospitalization has the added advantage of providing respite
for the family, as well as a focused opportunity for them to
receive further education about the proper use of medicati-
ons. Of course, hospitalization itself presents certain risks,
including that of exposure to bacterial infection, so the dura-
tion of the stay should be minimized.

Systemic intervention is an option in some patients, and
the patient’s and family’s quality of life should be included as
factors when considering such a decision. The process must
include a discussion with the family concerning the risks for
infection and neoplasia, particularly lymphoma.

No large comparative trials have been published, and no
detailed treatment guidelines currently exist on the use of
systemic immunosuppressants for AD in children. Some case
series have been published.27-32 These studies all show the
potential efficacy and limited toxicity of these immunosup-
pressants when used for limited periods and with careful
monitoring (as described below).

In general, topical anti-inflammatories should be contin-
ued during initiation of systemic immunosuppressant ther-
apy, and these topicals subsequently phased out, if possible.
If topical therapy is continued, a rotational strategy should be
considered. Side effects from appropriately used topical
agents are unusual, even with concomitant use of systemic
immunosuppressants.

Nonsteroidal immunosuppressants are preferred because
of the potential side effects associated with the use of systemic
corticosteroids. In addition, rebound flare of AD is a common
problem in children when systemic corticosteroids are dis-
continued.

More commonly, cyclosporine, azathioprine, mycopheno-
late mofetil, and methotrexate are used. Among these immu-
nosuppressants, cyclosporine has the most rapid onset of
action. A meta-analysis that included 15 studies showed that
cyclosporine administration was associated with a decrease
in disease severity by 55% at 6 to 8 weeks.27 In addition,
open-label studies have been done in children, specifically,
using 5 mg/kg/day, adjusted as needed for therapeutic effect.
This regimen has yielded reductions in severity of scores
ranging from 50% to 60% after 6 to 8 weeks of treatment.28,29
Continuous administration of cyclosporine, tapered to the
lowest therapeutic level, seems to yield approximately the
same clinical results as administration of intermittent 12-
week courses of therapy.30 The effective dose should be
maintained for a few months and then tapered gradually,
with exposure to cyclosporine limited to 1 year.

Azathioprine has received greater attention recently30,31
and is the treatment of choice in the United Kingdom. In a
study of 48 children, Murphy and Atherton32 found an
excellent response in about 60% of children with severe
AD at 3 months. Azathioprine has a delayed onset of effi-
cacy of 4 to 6 weeks, so some clinicians begin concurrent
treatment with azathioprine and a corticosteroid, tapering
off the corticosteroid starting 1 month later. In general,
the optimum dosage is 2.5 to 3.5 mg/kg/day of azathioprine;
however, if an intermediate level of the erythrocyte thio-
purine methyltransferase (TPMT) enzyme is obtained (see
the discussion of monitoring, below), that dosage can be
adjusted downward to 1 mg/kg/day. An effective dose
should be maintained for about 3 months, then tapered
gradually; azathioprine can be used for 2 years before
transitioning to an alternative therapy.

Another option is mycophenolate mofetil, which is
among the least toxic (although costlier) systemic immu-
nosuppressants for AD. As with azathioprine, mycophe-
nolate mofetil’s onset of efficacy is delayed for 4 to 8
weeks. The maximal effect is seen at 8 to 12 weeks after
initiation, so, here again, concurrent administration of
corticosteroid at the start of therapy, followed by tapering
and then discontinuation, is advisable. In a study by Heller
et al,33 58% of patients showed greater than 90% improve-
ment, and 93% of patients showed greater than 60% im-
provement. In children, a dosage of 40 to 50 mg/kg/day
(or 600 to 1,200 mg/m²) is the usual dosage. For adoles-
cents, a dosage range of 30 to 40 mg/kg/day will yield a
maximum level of 3 g/day. The use of mycophenolate
mofetil should be limited to 2 years.

Finally, methotrexate has been found to be helpful, par-
icularly once a flare has subsided. In fact, methotrexate
probably is most suitable for maintenance in severe AD.
For this use, the dosage is 0.5 to 0.6 mg/kg/week, with a
maximum of 20 mg. This can be administered in a single
dose each week, although some clinicians have found that
efficacy is greater if the dosage is divided over several
consecutive days. Concomitant administration of folic
acid is important during methotrexate therapy. No studies
of methotrexate have been done in children with AD. In a
study of adults, Weatherhead et al34 demonstrated that
methotrexate resulted in a decrease in severity of 52% from baseline over a 24-week period.

Clinical and laboratory monitoring is crucial during treatment with systemic immunosuppressants (Table 2). Among the four agents discussed here, cyclosporine is associated with the greatest number of potential side effects. Neoplasia is a potential long-term risk. Shorter-term, increased risks for infection, renal and hepatic toxicity, and hypertrichosis are associated with cyclosporine. During treatment, blood pressure should be monitored weekly for 1 month, then monthly thereafter. Baseline laboratory tests should include complete blood count (CBC), liver function tests, and blood-urea-nitrogen and creatinine levels; these tests should be repeated monthly for at least the first few months, then every other month thereafter.

With the use of azathioprine, a baseline level of erythrocyte TPMT should be obtained; inadequate levels of this enzyme are associated with the greatest risk for myelosuppression. Baseline CBC and liver function tests also are important. These studies should be repeated every 2 weeks for 1 month, then monthly for 2 months, and every 2 months thereafter for the duration of treatment.

For mycophenolate mofetil and methotrexate therapy, monitoring should include baseline CBC and liver function tests, repeated monthly for 2 months, then every 3 months for the duration of treatment.

An alternative to systemic immunosuppressive treatment is phototherapy, preferably with narrowband ultraviolet B (UVB) light. Clayton and colleagues35 presented a retrospective review of 50 children with severe AD who were treated with at least 10 exposures to narrowband UVB. Complete clearance was seen in 40% of patients, with good improvement in 23% and moderate improvement in 26%; the median length of remission was 3 months.

There are several disadvantages to using narrowband UVB in children. First, it requires cooperation by the child, either alone or with a parent in the phototherapy booth. Second, the time commitment required for treatments is often difficult to secure, conflicting with parents’ work schedules and children’s school and recreational activities. Third, the potential risks for skin cancer and premature aging are unknown at this time.

**Adjuvant Therapy**

Wet wraps are a traditional method for decreasing inflammation and pruritus and increasing comfort, particularly during an AD flare. Some centers, such as the Mayo Clinic, have used
inpatient wet-wrap therapy for rapid control of pediatric AD. The method has gained renewed and more widespread interest in recent years, and several authors have provided evidence of efficacy and guidelines for use in AD.

This technique is simple enough to use at home. Following a bath and application of medications and moisturizers, the affected areas are wrapped in wet gauze and topped by a dry layer. If the AD is widespread, it is more convenient (and cost-effective) to dress the child in wet pajamas, followed by warmed, dry towels or blankets. Wet wrapping used at night can decrease pruritus and help children sleep. This technique usually is more successful in infants and toddlers; older children may refuse to leave the wet wraps in place or may refuse to allow the treatment at all. One needs to keep in mind that when using a topical corticosteroid, wrapping will increase the potential absorption.

Antihistamines are not particularly useful for decreasing pruritus associated with AD, but can be very helpful to promote sleep when used at sedating dosages—for example, hydroxyzine given at 1 mg/kg/day.

**Conclusion**

A number of effective and safe agents are available to manage AD flares and extend periods of remission between flares. However, no single regimen will work for all patients with AD. Treatment strategies must be individualized and modified over time as patient needs require and, in the case of children, as caregiver adherence permits. Sufficient time must be spent educating patients and parents about the risks and benefits of therapy as well as allaying unfounded fears about medication side effects, particularly regarding topical corticosteroids.

**References**


continued on page 29
Atopic dermatitis (AD) in adults is an important dermatologic disease. Even in patients in whom the clinical presentation is mild, the burden of disease can be considerable. Relatively little has been published on adult AD compared to the body of literature devoted to AD in children, although adults with severe AD are greatly affected by the disease. Even when AD is a mild clinical disease in adults, the psychosocial and economic burden of the disease can be profound. Patients are likely to find it useful if these nondermatologic comorbidities of AD are addressed by health care providers in clinical encounters. The treatment options for AD in adults are the same as those for children with AD, with some modifications.

**Why Does AD Persist in Some Patients?**

The reason for resolution of childhood AD in most patients or for persistence of AD into adulthood in some patients has not been established, but recent research demonstrates that—

**References**

like the predisposition to develop AD itself—persistence or resolution of the disease is genetically determined.

Progress has been made within the last decade toward understanding the long-observed familial predisposition to develop AD, advances made possible by completion of the mapping of the human genome. Loss-of-function mutations in the filaggrin gene (FLG) have been identified as being strongly associated with the development of AD. Subsequent studies determined that the number of FLG copies within genes can vary, with alleles encoded for 10, 11, or 12 copies of the filaggrin monomer.

Based on this understanding, Brown and colleagues conducted a genetic study of more than 800 children with AD and determined that the number of copies of the filaggrin monomer affect how much filaggrin protein is expressed in skin. They demonstrated that the number of copies of FLG is associated with the tendency to develop AD, and speculated that the number of FLG copies might be associated with disease severity in a “dose-dependent” manner—fewer copies, more severe disease; more copies, less severe disease.

**Adult-Onset AD**

AD beginning in adulthood is an unusual presentation. In 2000, Bannister and Freeman noted that their extensive review of published articles yielded only occasional mentions of adult-onset AD in epidemiologic studies. In their own review of 2604 patients seen in a contact dermatitis clinic, 243 (9%) had onset of AD at 20 years of age or older and had no evidence of contact dermatitis. These authors note that clinicians encounter patients with adult-onset symptoms characteristic of AD, with cases being sometimes severe and disabling. Some of these patients are diagnosed with adult-onset AD because they have a clinical presentation that suggests AD (such as flexural involvement) or because their eczematous dermatitis is accompanied by a history of allergic disease (such as asthma or hay fever) or a family history of atopic disease.

Ozkaya argues that adult-onset AD may demonstrate the typical clinical pattern seen in adults who have maintained their childhood AD (which includes flexural involvement with lichenification), but also may affect the trunk and extremities, with or without flexural involvement. In a retrospective study of 376 consecutive patients with diagnoses of AD (according to the Hanifin-Rajka criteria), Ozkaya found 63 patients (17%) who reported onset of AD symptoms after 18 years of age (reported onset ranged from 18 to 71 years of age, with a mean of 28 years). Seven (11%) of the 63 patients had nonflexural involvement, and, in these patients, patch testing was done to exclude detectable contact dermatitis.

Additional studies are required to characterize further, delineate, and determine criteria for the diagnosis of adult-onset AD. Meanwhile, symptomatic therapy is indicated, following the same strategy that is used for patients with AD in whom the disease has persisted since childhood.

**Clinical Presentation**

The presentation of AD in adults may differ from that seen in children with the disease. As in childhood, the sites of involvement in adult AD can be anywhere on the body, but the most common areas of involvement in adults are the flexural areas of the arms and legs, the nape of the neck, and the hands. In adults, AD is characterized by a more lichenified, drier appearance than is usually seen in children with AD.

The psoriasiform presentation in adults might be explained by a shift in T helper (Th1) type 2 cells toward the Th1 phenotype. In a complicated study of 121 elderly patients (mean age, 69 years), Bozek and colleagues found that 25 (21%) of these patients had AD with negative allergy testing and low levels of total IgE. Patients in this group tended to have Th1 cytokine profiles. However, sensitivity to aeroallergens, especially dust mites, often persists in adults.

Although signs and symptoms tend to be less severe in adults than in children, milder presentations can be severely problematic for adult patients, particularly when the exposed areas of the body are involved, such as the hands, neck, and face. Moreover, a subset of adults can have severe AD that is challenging to manage (Figure 1).

![Figure 1 Atopic dermatitis in an adult](https://example.com/atopicdermatitis_in_an_adult.jpg)

This patient has had atopic dermatitis since childhood. At the time of this clinical visit, the patient complained of pruritus and the affected areas were dry and lichenified. In such cases, bacterial colonization is likely, particularly in crusted areas such as the periorificial region shown here. Photo courtesy of Charles N. Ellis, MD.
Infectious Comorbidities in Adult AD

Skin infection is not as common a problem in adults as in children. However, colonization with *S. aureus* in adult patients with AD is high—reported as 86% in one study—and is associated with the severity of disease. In addition, colonization with yeast organisms—typically, *Malassezia* species—is common in the head and neck areas.  

Eczema herpeticum (EH) can be a life-threatening or disfiguring complication of AD in adults as well as in children. The risk for this complication is increased in individuals with AD who have or acquire herpes simplex virus (HSV) infections. Patients with AD should take steps to avoid exposure to individuals with HSV infections, whenever possible. In addition, live vaccination for smallpox (for example, in the military) may generalize to cause eczema vaccinatum in patients with AD. Therefore, these individuals should avoid vaccinations, and those who share a residence with patients with should also avoid such vaccinations to prevent transmission to the patient with AD. Recently, Leung and colleagues reported that it may be possible to determine which patients with AD are at risk for EH infections. In a study involving 64 subjects with a history of this complication (ADEH-positive), 20 without such a history (ADEH-negative), and 20 nonatopic individuals—the investigators found that interferon-γ protein production was significantly lower in the ADEH-positive subjects than in the ADEH-negative and the nonatopic control groups.

Psychiatric and Psychological Comorbidities

The literature on comorbidity in AD has drawn attention to concomitant depression in teenagers and adults (well-established), as well as other mental disorders, including attention-deficit/hyperactivity disorder and autism (under investigation, with emerging evidence). AD is among the group of dermatologic conditions (also including psoriasis, chronic idiopathic urticaria, and alopecia areata) in which a number of psychiatric disorders—including depression—are considered comorbidities. At least 30% of patients with dermatologic diseases have been reported to experience psychiatric disturbances and psychosocial problems. Even mild degrees of severity of AD may be accompanied by a psychiatric comorbidity.  

Gupta et al examined the relationship between pruritus and depression in 252 patients with mild to moderate psoriasis (n = 77), AD (n = 143), or idiopathic urticaria (n = 32). Patients were asked to rate the severity of their pruritus on a 10-point scale devised by the investigators. They also completed psychologic rating scales to assess depression (Carroll Rating Scale for Depression), levels of anger, anxiety, and curiosity (Spielberger State-Trait Personality Inventory), and psychopathologic symptom dimensions such as depression, somatization, phobic anxiety, and paranoid ideation (Brief Symptom Inventory). In this study, the severity of pruritus in all groups of patients correlated with their levels of depression, which suggests that patients with more severe depression have a lower itch threshold, or that more severe pruritus results in higher depression scores.

Suicidal ideation is a risk in patients with depression, and Kimata reported that such ideation is common in patients with AD. Symptoms of major depression may be detectable during a brief office visit, but clinicians also should be alert to the possibility that patients with AD may be experiencing subclinical depression, characterized by less dramatic manifestations, such as a decrease in energy and interest in activities that usually bring satisfaction; individuals with subclinical depression often do not perceive themselves as feeling sad.  

In addition to frank psychiatric disturbances, AD is associated with psychosocial and quality-of-life impairment, a relationship that has long been recognized by clinicians and patients, and is supported by a large body of evidence in the literature.  

In the landmark International Study of Life with Atopic Eczema (ISOLATE), 38% of patients with AD said that their disease affected their choice of occupation, and even those with mild to moderate AD reported an increase the number of sick days taken from work, as well as early retirement. Ten percent of respondents said that they believed they had experienced discrimination in their workplace; one in seven patients said that their careers had been impaired by their disease.

Psychosexual issues also were common: 58% of individuals with AD reported that they had decreased desire for sex, and 37% of partners of those with AD said the condition adversely affected their sexual relationship. Forty-three percent of adults with AD said that they felt awkward about having a partner see or touch their body during a flare of the disease.  

Adults with AD also avoid other activities at work and in social- and home-life. The findings in ISOLATE have been supported by other studies.  

Unfortunately, such issues often are inadequately addressed in clinical encounters involving adult patients. Only 26% of patients in ISOLATE said that their physicians acknowledged and discussed such problems with them. Issues that may affect quality of life deserve more attention, and clinicians may wish to consider screening their patients with AD for possible clinical or subclinical psychiatric disturbances. Some patients may benefit from treatment with antidepressants or other psychotropic medications, as well as psychotherapy. Dermatologists and other clinicians who treat adult patients with AD also should be prepared to refer these patients to appropriate mental health professionals for evaluation and possible treatment when these issues are identified.

Treatment of AD in Adults: Special Considerations

With a few modifications, treatment options for adults with AD are the same as those for children with the disease (see the article by Paller et al on page S10 of this supplement). Because adult patients tend to have thicker, more lichenified skin, more aggressive measures may be needed to bring signs and symptoms under control. Unfortunately, only 25% of
patients and their caregivers in the ISOLATE study feel confident that they can manage AD flares adequately, and 75% reported that being able to have such control would be “the single most important improvement” in their quality of life. 39

For mild to moderate disease in adults, higher-potency topical agents (corticosteroids or topical calcineurin inhibitors [TCIs]) are the mainstays of therapy. However, the ISOLATE survey19 revealed that 58% of patients restricted their use of topical corticosteroids because of concerns about side effects, and 66% said they use these medications “only as a last resort.” Thus, it is evident that adult patients with AD require education from their health providers about the realistic risks and benefits associated with the use of topical medications, including both corticosteroids and noncorticosteroid agents such as TCIs.25,26

For adult patients with severe AD that does not respond to topical therapy, treatments include phototherapy—narrow-band ultraviolet B, ultraviolet A, or both.27-29 Systemic immunosuppressants also are recognized therapeutic options in severe cases of AD. Patients in whom these agents are used—including methotrexate, azathioprine, mycophenolate mofetil, and oral calcineurin inhibitors (cyclosporine or tacrolimus)—should be followed carefully, and laboratory monitoring should be performed, as described in the article by Paller et al.24

If the skin in an adult patient with AD looks superficially infected (for example, the presence of pustules or weeping of serous fluid), bacterial cultures should be obtained and appropriate antibiotic therapy instituted. In some patients, antibiotic treatment may be helpful, even in the absence of frank infection.

Emerging understanding of the underlying pathogenesis and related molecular processes of AD has led to attempts to influence these mechanisms. For example, based on the discovery of the association between IgE-mediated inflammatory responses and eczematous skin signs and symptoms, and on the success of treatment to reduce IgE serum levels in patients with asthma, some have proposed the potential benefit of reducing serum IgE levels in patients with AD. A study of a small group of adults with severe AD did not yield promising results.30 However, Vigo and colleagues31 studied the effects of anti-IgE treatment on skin symptoms in two pediatric and five adult patients with AD who were being treated with the anti-IgE monoclonal antibody omalizumab for their asthma. In this study, the anti-IgE strategy showed substantial benefit for the skin component.

Similarly, the association of IgE-mediated activation of skin mast cells in patients with AD, the advances in understanding of the roles of innate and adaptive immunity and skin barrier function/dysfunction,32 and the success of the leukotriene receptor antagonist montelukast in asthma and allergic rhinitis prompted the study of this agent in AD. However, a 4-week, randomized, double-blind, placebo-controlled trial of 59 adult patients with moderate to severe AD by Veien and colleagues33 failed to demonstrate a significant difference in efficacy between the montelukast and placebo-treated groups. A subsequent 8-week, randomized, placebo-controlled trial of montelukast in adults with AD conducted by Friedmann and colleagues34 also failed to demonstrate significant benefit.

Others have examined the potential benefits in AD of topical cromolyn sodium lotion35 (some success), probiotic treatment with microorganisms such as *Lactobacillus*36 and oral supplementation with essential fatty acids37 (no significant benefit likely), and Chinese herbal remedies38 (not enough evidence from clinical trials to establish or rule out benefit).

**Conclusion**

Relatively little has been published on AD in adults compared to the literature available regarding AD in pediatric patients. Treatment of AD signs and symptoms in adults is not radically different from that used in younger patients; all of the options available for children may be considered for adults, and modalities—such as ultraviolet therapy—that may not be suitable for some (especially the youngest) pediatric patients may be quite effective in adults.

A substantial gap exists in treatment of AD in adults with respect to the recognition and management of quality-of-life issues and psychiatric comorbidities. Addressing these comorbidities provides an important opportunity to improve the treatment of AD in adults.

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Perspectives in Atopic Dermatitis: Optimizing Outcomes


Long-term adherence to carefully developed, individualized strategies is necessary for the optimum treatment outcomes in patients with atopic dermatitis (AD). However, the parents of children with AD frequently lack sufficient information about the disease and its treatment, hold incorrect and sometimes harmful beliefs about these issues, and too often do not follow through consistently with the treatment plan. The health care provider is the primary source of such education, so an effective provider relationship is fundamental to adherence. In addition to the provision of correct information and the correction of misinformation, clinicians must be aware of and must address barriers to adherence with AD therapy, especially parent anxiety about the safety of topical medications (corticosteroids and topical calcineurin inhibitors).

Semin Cutan Med Surg 31(suppl 3):S23-S28 © 2012 Elsevier Inc. All rights reserved.

Adherence is an important issue that must be considered in any clinical encounter in which therapy is a component; with chronic diseases such as AD, which require long-term maintenance and care, low adherence on the part of the patient or parent can be especially problematic. Treatment outcomes can be improved with better understanding of, and improvement in, adherence. This article addresses the key components of topical treatment that must be implemented and

A ggressive topical therapy is one of the most important steps in the treatment of atopic dermatitis (AD). The efficacy of even the most careful and considered treatment regimens is only as good as the parents’ or patients’ ability and willingness to implement the clinical recommendations.
followed by caregivers or, in the case of older children and adults, by patients themselves.

**Obstacles to Adherence**

Adherence requires understanding, understanding requires education, and misinformation and unfounded fears are the main obstacles to both of these requirements. Parents of children with AD often have preconceived notions about triggers and “allergies” as well as concerns about toxicities of AD treatments.

Despite widespread professional and lay literature describing the evidence-based conclusions about the efficacy and safety of topical anti-inflammatory medications used in the treatment of AD, steroid phobia (or, as it is often called in the United Kingdom, “corticophobia”) and fear of topical calcineurin inhibitors (TCIs), both persist. The results of one recent study summarize the problem succinctly. Aubert-Wastiaux and colleagues distributed a 69-item questionnaire to 208 consecutive patients with AD attending the outpatient dermatology clinics of several centers. Completed questionnaires were received from 144 parents and 87 adult patients. Among the responders, 80.7% reported having fears about topical corticosteroids, and 36% admitted to treatment non-adherence. The investigators note correlations between steroid phobia and several factors, including the belief that topical corticosteroid agents pass through the skin into the bloodstream, a lack of trust in the practitioner, and discrepancies in the education received about their use.

**The Scope of the Nonadherence Problem**

Poor adherence to a prescribed treatment regimen should always be considered in patients in whom the response to therapy is suboptimal. A classic study by Richards and colleagues showed that medications prescribed for chronic conditions are not taken as prescribed an estimated 30% to 40% of the time.

In addition to phobias regarding the use of prescribed treatments (especially topical corticosteroids and TCIs, as described above), underlying reasons for poor adherence among patients and families of children with AD include family conflicts, parental involvement/caregiver fatigue, and misunderstandings regarding “toxicities” (for instance, the hypopigmentation often noted following inflammatory dermatoses, which parents may mistakenly identify as a toxicity of the topical medication [Figure 1]).

In a study of 37 children with mild to moderate AD treated with triamcinolone ointment twice daily, electronic monitors were used to measure adherence over the 8-week study period. Patients were unaware of the monitoring until they were informed at the conclusion of the study. In the 26 patients who completed the study, mean adherence was 32%. Interestingly—but not surprisingly—adherence was higher on or near office visit days and subsequently decreased rapidly.4

**Figure 1 Postinflammatory hypopigmentation in AD.** Post-treatment clearing of AD often reveals hypopigmentation or other skin discoloration. Parents should be reassured that these changes are the result of AD, are not a side effect of topical medication, and will gradually resolve over time without intervention. Photo courtesy of Anthony J. Mancini, MD.

**Bathing in Atopic Dermatitis**

Historically, bathing approaches have been divided into so-called dry and wet methods. The preponderance of evidence, as well as widespread clinical experience, supports the superior benefits of the wet method. Nevertheless, some clinicians still consider the dry method to be an acceptable option, and some parents and patients are advised to use it.

The dry method consists of minimization of bathing and is based on the hypothesis that overbathing contributes to exacerbation of skin xerosis. The earliest recommendations for the dry method came from Scholtz, in which bathing or washing was strictly prohibited and the skin was cleansed only with a lipid-free lotion. In 2009, Chiang and colleagues published the results of a crossover study in five pediatric patients with AD (and a parallel group with healthy skin) in whom objective parameters of cutaneous hydration status were assessed following various combinations of bathing and moisturizing regimens. The methods were bathing alone without emollient, bathing and immediate emollient application, bathing and delayed emollient application, and emollient application alone. Emollient alone yielded a significantly greater mean hydration over 90 minutes than did bathing with immediate emollient, bathing and delayed emollient, and bathing alone. Emollient application after...


**Analogy—The Intuitive Story**

Misinformation can be absorbed intellectually and may be transformed into a firmly held belief. Correcting such beliefs by making statements of fact and discussing evidence works for some individuals, but not for all, and with regard to some information, but not all.

The analogy is a story through which a person can understand a concept in terms of another concept that is intuitively understood and accepted. A simple analogy can be an effective tool for education and re-education, particularly if it is clearly presented and accompanied by demonstrations or illustrations.

The following are two “scripts” that one of the authors (AJM) routinely uses in AD education of parents and patients.

**The Diaper Area Analogy: Explaining Why the Wet Method Works**

“Atopic dermatitis likes dry skin, but not moist and hydrated skin. Look at the area covered by your baby’s diaper. Feel how soft and supple it is? And notice that eczema does not occur in this area. By bathing your baby every day and immediately applying the medications and then the moisturizer, we are trying to create the same sort of environment (a moist one) as in the diaper area on the rest of your baby’s skin.”

**The Footprints in the Snow Analogy: Explaining Why Postinflammatory Hypopigmentation Is Not a Medication Side Effect**

“I am walking in the woods on a winter’s day, and I see a scary animal in my path. I chase the animal away, and the only thing left are its footprints. The footprints are temporary, and they will disappear with time.

Atopic dermatitis is like the animal in the snow. We have chased it away with the medication I prescribed. As you can see, the eczema (‘the animal’) is now gone, and the light spots that remain are the ‘footprints in the snow.’ The medication did not cause them, but rather, the atopic dermatitis did. These ‘footprints’ will also disappear over time.”

bathing improved hydration, whereas bathing without emollient application yielded poorer hydration status.

The wet method—also referred to as the “soak and smear” technique—consists of regular daily bathing for short periods of time, followed by the application of topical medications and emollients or barrier repair agents. Hydration for 20 minutes followed by ointment application to wet skin was found to be associated with objective and symptomatic improvement in—and was well accepted by—28 patients referred to a tertiary center for refractory chronic inflammatory dermatoses.

Extensive clinical experience has demonstrated that the wet method is highly useful in the treatment of inflammatory dermatoses, including AD. Bathing provides physical debridement of sloughed cells from, and reduction in superficial microorganisms on, the skin surface, hydration of the stratum corneum, and enhanced penetration of topical agents. It also provides some emotional and social benefits to patients. For example, for infants and toddlers, bath time supports parent-child bonding, particularly when play is incorporated into the event; for older patients, bathing provides a feeling of cleanliness and promotes a sense of well-being. The “diaper area analogy” (see “Analogy—The Intuitive Story” above) frequently used by one of the authors (AJM) may help parents understand why the wet method works (Figure 2).

**Updating Information, Correcting Misinformation**

**Allergen Avoidance**

The nature of AD and the multifactorial aspects involving genetic predisposition and variability in exacerbating factors make trigger identification very challenging. Potential triggers may include climate change, bacterial colonization, environmental irritants, stress, inhalant allergens, and foods.

**Figure 2 Diaper Area Spared in AD.** The look and feel of the skin in the area covered by a child’s diaper illustrates the benefit of moisture in mitigating AD-associated dryness and inflammation. Photo courtesy of Anthony J. Mancini, MD.
Many clinicians and parents have been taught (and still believe) that simple allergen avoidance will significantly alter the burden of disease.

The association between AD and other atopic disorders (allergic rhinoconjunctivitis, asthma, and food and environmental allergies) makes it challenging for patients and parents to understand the lack of a consistent or predictable direct cause-and-effect relationship.

The most recent evidence demonstrates that allergen avoidance may alter the clinical course in some patients, but it rarely plays as significant a role as once was believed. Although food allergy may result in a variety of skin reactions, it is only the minority of these reactions that truly exacerbate AD. Food allergy should be defined as clinically significant, immunologically-mediated adverse health effects consistently evident with food consumption. In studies of oral food challenges in patients with AD, the majority of food reactions occurred early after food exposure, usually in the form of urticaria. Delayed reactions, in the form of AD exacerbation, comprise only 5% to 25% of oral food challenge reactions and are not predictable by skin-prick or immunoglobulin E serum testing.11 Parents should be cautioned against extreme restriction diets, which most often are unhelpful and which may lead to serious nutritional deficits.12,13

Recently issued revised Food Allergy Guidelines from the National Institute of Allergy and Infectious Diseases14,15 suggest that food allergy evaluation is warranted in children less than 5 years of age under two circumstances: (1) if they have persistent AD despite optimum management or (2) if they have a reliable history of food reactions. The guidelines recommend evaluating such children for allergies to cow’s milk, eggs, peanuts, and wheat and soy products. Counseling should include information that food allergy tests (specific IgE and skin prick tests) have poor specificity; predictive values are low, around 20% to 25%; only one in four to five positive tests correlates with a clinically significant allergy.11

Anti-inflammatory Therapy

Great strides have been made in recent years in describing and understanding the crucial role of skin barrier defects in patients with AD, and a great deal of attention is being paid—to the importance of maintaining and restoring skin barrier integrity. However, the role of anti-inflammatory medication should not be overshadowed by these emerging discoveries. In patients with AD, controlling inflammation is still a fundamental goal.

Topical corticosteroids remain the cornerstone of first-line treatment strategies. Clinicians must always emphasize that these medications are safe and effective when prescribed and administered appropriately.

Education also is important regarding the role of TCIs; those currently available in the United States are pimecrolimus and tacrolimus. These agents are approved by the US Food and Drug Administration (FDA) for children 2 years of age or older for second-line treatment of moderate to severe AD. The TCIs also are often used as monotherapy for managing mild to moderate flares and as maintenance therapy between flares. In addition, many clinicians prefer TCIs over topical corticosteroids for treating periocular AD, given their superior risk/toxicity profile (compared to topical corticosteroids) for treatment of this area. Topical pimecrolimus has been shown to be effective in preventing AD disease flares and reducing the need for topical corticosteroids in longer-term, intermittent-use trials. Its use has also been associated with improvements in the health-related quality of life in pediatric patients with AD and their parents.16

Concerns expressed in the lay media and the presence of a boxed warning in the prescribing information for TCIs have alarmed some practitioners and parents. However, these concerns should be mitigated by the accumulated body of evidence demonstrating the safety of TCIs. The FDA-mandated patient registries for tacrolimus (APPLES) and pimecrolimus (Pediatric Eczema Elective Registry; PEER) have enrolled more than 12,000 patients to date, and no increased malignancy signal above the Surveillance, Epidemiology, and End Results (SEER) database for the general population has been noted. In addition, at its May 2011 meeting, the FDA Pediatric Advisory Committee reviewed five observational studies published between January 2005 and April 2011, looking at the outcomes of lymphoma, nonmelanoma skin cancer, melanoma, and other cancers.18 In summary, most of the studies reviewed by the FDA committee showed no increased risk for either lymphoma or overall cancer rate. A possible increased risk for T-cell lymphoma was reported with tacrolimus in one study, but the potential confounders discussed included the risks inherent in AD itself, study biases, and “protopathic bias” (that is, misdiagnosis of AD when the patient actually had cutaneous T-cell lymphoma). The FDA committee concluded that the review of the observational literature suggested a possible association between tacrolimus use and increased risk of T-cell lymphoma, but that there were potential biases to explain this observed association. They also noted that the results were not specific to the pediatric population, that the postmarketing safety review did not identify new signals for pediatric malignancies with the TCIs, and that the current labeling and medication guide reflects the safety risk as currently understood.

A meta-analysis of randomized clinical trials of TCIs for the treatment of AD in a combined total of 6,288 pediatric patients who met the inclusion criteria showed that both tacrolimus and pimecrolimus were safe and effective in the treatment of AD, and the incidence of adverse events was similar to that seen with vehicle alone.19

Approaching the Fearful Parent

Effective management necessitates the establishment of good rapport with the patient and caregivers, expression of empathy for their concerns and anxieties, frequent follow-up for reinforcement and emotional support, selection of treatment regimens that are complete yet as simple as feasible, and the
use of ancillary materials (such as written action plans) to encourage treatment adherence.

Clinicians should address safety and correct use of topical agents directly at the time of their recommendation and anticipate (and answer) questions that parents/caregivers may have. Toward this end, practitioners must be thoroughly educated themselves on the appropriate use and safety profiles of the topical regimens they prescribe.

It is important to address with patients and caregivers the distinction between oral and topical corticosteroids and to dispel the notion that different topical corticosteroid agents can be directly compared to each other based on their percentage strengths (for example, 2.5% hydrocortisone is not 25 times stronger than 0.1% mometasone).

Not all topical medications commonly used in infants and young children are specifically indicated by the FDA for patients in these age groups. Clinicians who intend to prescribe use of a medication outside of its approved indications should be up-front with parents about this fact, should explain what “off-label” actually means, and should discuss the fact that off-label therapy is common in treating dermatologic conditions and in pediatric medicine, in general.

The parent education and personal care plan at the end of this article on page S29 was developed by two of the authors (Lawrence F. Eichenfield, MD and Anthony J. Mancini, MD) and is provided as an aid to support clinicians’ efforts in reinforcing important information and instructions. It is organized based on the four areas of treatment that must be addressed in patients with AD: dryness, inflammation, itching, and infection. Understanding these four parameters may be useful to parents to help them stay aware of the range of issues that must be addressed in treating their child with AD. (This two-sided handout may be freely duplicated and distributed, without charge, to patients and parents. Other use, such as inclusion in published materials or presentations, requires proper attribution to the authors and permission from the publisher).

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### Table. Online Resources for Atopic Dermatitis

Online resources include research organizations/consortia, clinical service providers, patient support networks, and educational resources. Some of these are:

- **American Academy of Dermatology**  
  (http://www.aad.org/skin-conditions/dermatology-a-to-z/eczema)
- **The Eczema Center**  
  (http://www.eczemacenter.org)
- **Eczema Support Group**  
  (http://www.mdjunction.com/eczema)
- **National Eczema Association (US)**  
  (http://www.nationaleczema.org)
- **The National Eczema Society (UK)**  
  (http://www.eczema.org)
- **National Jewish Health Pediatric Atopic Dermatitis Program**  
  (http://www.nationaljewish.org/programs/pediatric/atopic-dermatitis/)
- **Talk Eczema**  
  (http://www.talkeczema.com)

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### Education Beyond the Clinic Visit

There are many resources beyond the routine clinic visit that may help patients and families understand the process of AD more completely, hence translating into increased rates of adherence. In some cases, referral to online information and other resources can be helpful (see the Table on this page).

Written action plans have been extensively developed and tested in the setting of pediatric asthma and have been shown to help increase adherence with therapy and improve asthma control. They serve as a communication aid between practitioner and patient/parent and also, when kept in a readily-accessible location in the home, help remind caregivers of the treatment plan. A study on the perceptions of “eczema action plans” for AD found that 100% of the surveyed pediatricians reported that they would be likely to use an eczemas action plan in their clinical practice. Although parallel studies are largely lacking in AD, action plans similar to those used in asthma make intuitive sense and are already used by many practitioners, especially pediatric dermatologists. For an action plan to be successful, it should be personalized for the patient and should be clear, concise, and easy to read. Fleischer noted that written action plans should be quantifiably good and tested.

Various models of delivery of AD education outside of the traditional clinic visit have been developed. These include nurse-led approaches and group instruction (including “eczema school” or weekly educational seminars). A review of the literature addressing the benefits of nurse-led AD education clinics reviewed 22 relevant publications and supported the efficacy of such clinics in the management of such chronic illnesses. These nurse-led clinics allow for increased time spent with patients, resulting in improved patient education, treatment adherence, and satisfaction with care.

In addition, multidisciplinary clinics for AD are being formed at many centers. These offer the advantages of comprehensive “one-stop” care, intensive education, focused educational curricula, and access to patient support networks.

### Conclusion

Education is the most important promoter of adherence because action without understanding is unlikely to persist long term. However, true education and understanding can be accomplished only when the provider-patient relationship is effective. Such effectiveness is enhanced when the health provider demonstrates an awareness and understanding of psychosocial issues, preconceived notions, anxieties about treatment safety, and psychological comorbidities relevant to the disease being treated (AD) and takes definitive steps to help patients and parents address them. Other proven promoters of education and adherence include simplified treatment regimens, the prescription of treatments and medications in vehicles preferred by the patient and caregivers, and written action plans and referrals for educational resources and patient support networks. Multidisciplinary clinics for
AD, where available, simplify the delivery of comprehensive care and intensive patient education.

References

Treatment Strategies for Atopic Dermatitis: Optimizing the Available Therapeutic Options continued from page 18

Atopic dermatitis (AD) is also called eczema. It is a common skin disease that affects many children worldwide. Its cause is not known for certain. However, we do know that AD tends to run in families. Also, it often occurs with other diseases: asthma, hay fever, and sometimes food allergies.

AD is usually very itchy, and this problem can keep children awake at night. This can cause daytime crankiness and behavioral problems. Also, when your child doesn’t sleep, you don’t sleep.

Your medical team is giving you this personalized care plan to help you work with us to take care of your child’s AD. Our goal is to keep your child—and everyone in your family—comfortable and healthy. To do this, we use the “D plus 3 I” plan.

**Dryness (D)**

An important part of care at home is bathing. Tub bathing and showering are both okay. (If you have been told to use a bleach bath, you will have to put your child in a tub.) The bathing should last for 10 minutes, but no longer. The water should be warm but not hot. Daily bathing is recommended. During a severe flare, your child’s doctor may recommend two baths a day until the AD is improved.

To clean the skin, use a gentle, non-soap cleanser.

After removing your child from the bath or shower, gently pat the skin but do not attempt to completely dry it. It is important for some water to remain on the skin.

Next, apply any medications your clinician has prescribed. Your clinician will also tell you if your child does not need to use a medication at this time.

Put on the recommended moisturizer right after applying medication. Also, remember that moisturizers can be applied throughout the day, as often as needed. During cold weather, dryness tends to get worse, so moisturizing more often is especially important in the winter.

**Inflammation (First I)**

The rash of AD is red and scaly. It is treated with anti-inflammatory medications applied to the skin. These are either topical corticosteroids or topical calcineurin inhibitors (TCIs).

**Itching (Second I)**

Dryness and itching go hand-in-hand, so moisturizing will help with itching. Also, if your child’s itching prevents a good night’s sleep, your clinician may prescribe an antihistamine. Antihistamines may help decrease the itch a bit and, more importantly, they have mild sedative effects that will help your child fall asleep, and break the “itch-scratch” cycle for a while.

**Infection (Third I)**

Bacteria and other microorganisms live on everyone’s skin. This is normal. An important job of the top layers of the skin is to keep these organisms from causing an infection. The skin in patients with AD often does not do such an effective job, and infection is a common problem.

The risk of infection is increased if the skin becomes very inflamed and itchy because it is difficult to keep a child from scratching to relieve the sensation.

Infected skin is usually very red; it will ooze and form crusts and scabs. If your child develops an infection, contact your clinician so that the infection can be treated and cleared.

**Common Questions and Answers**

After I put on the medication, how long do I have to wait before putting on moisturizer?

You can put on moisturizer right after you put on medication. The moisturizer your clinician recommends should be put on the whole body, including the areas affected by AD.

Will my child need treatment forever?

AD is a chronic disease, so many children need treatment over a long period of time. However, there will be times when your child’s skin improves—the skin will be smooth to the touch and will no longer look dry. Your clinician will tell you what medications you can stop using during times when the skin is improved. If a flare of AD occurs, these medications will be needed again.

My child’s skin has changed color. Is that from the treatment?

AD can cause light spots to occur on the skin. None of the treatments is responsible. These areas of discoloration will eventually fade, although it may take weeks or months for this to happen. If there is no redness or scaling, the discolored areas do not need to be treated with medication.

Where can I read more about AD online?

A Google search of “atopic dermatitis” on the Internet will show many hundreds of hits. Some of these sites have good information, and some are either not particularly useful or contain misinformation.

**Your clinician recommends the following online resources:**

- American Academy of Dermatology (www.aad.org/skin-conditions/dermatology-a-to-z/eczema)
- National Eczema Association (www.nationaleczema.org)
- National Eczema Society (UK) (www.eczema.org)
- Eczema Support Group (www.mdjunction.com)
- Talk Eczema (www.talkeczema.com)
- The Eczema Center (www.eczemacenter.org)
- National Jewish Pediatric Atopic Dermatitis Program (www.nationaljewish.org/programs/pediatric/atopic-dermatitis)
Specific Recommendations for Your Child

Areas of Dermatitis

A careful physical examination shows that your child has atopic dermatitis on the following areas of the body:

- Scalp
- Face
- Right Arm/Hand
- Right Leg/Foot
- Left Arm/Hand
- Left Leg/Foot
- Trunk

**Dryness**

1. Bathe your child _____ × per □ day □ week
2. Bathe in □ regular tap water □ a bleach solution
3. Your clinician recommends the following cleanser:
   __________________________________________
4. Apply moisturizer after bathing and _____ other times during the day.
5. Your clinician recommends the following moisturizers:
   __________________________________________

**Itching**

- □ No treatment is needed at this time.
- □ Treatment is needed at this time.

1. Name of antihistamine: ___________________________
   Administer: _____ × every day
2. Name of antihistamine: ___________________________
   Administer: _____ × every day

**Infection**

- □ No treatment is needed at this time.
- □ No treatment is needed at this time.

1. Name of medication: ___________________________
   Apply to affected areas: _____ × every day until improved
   □ Face □ Trunk □ Arms □ Legs
2. Name of medication: ___________________________
   Apply to affected areas: _____ × every day until improved
   □ Face □ Trunk □ Arms □ Legs
3. Name of medication: ___________________________
   Apply to affected areas: _____ × every day until improved
   □ Face □ Trunk □ Arms □ Legs
4. Name of medication: ___________________________
   Apply to affected areas: _____ × every day until improved
   □ Face □ Trunk □ Arms □ Legs

**AD of the Scalp**

- □ No treatment is needed at this time.
- □ Treatment is needed at this time.

Name of medication: ___________________________
Apply to affected areas: _____ × every day
Type of formula: □ Foam □ Lotion □ Oil □ Solution

To wash your child's hair, your clinician recommends using:
__________________________________________________
__________________________________________________

**One more thing… Sun Protection**

Sunscreens are important for everyone, even children being treated for AD.
Your clinician recommends the following product(s) for your child: ___________________________
__________________________________________________
The most common side effects seen with topical corticosteroids in patients with atopic dermatitis are skin atrophy and irritation. The concept of rotational therapy in managing patients with atopic dermatitis involves: changing from a higher- to a lower-potency topical corticosteroid agent when the flare is under control. Initially using a medium-potency topical corticosteroid to control a flare, then switching to a topical calcineurin inhibitor when the flare is under control. Initially using a topical calcineurin inhibitor to bring the flare under control, then using low-dose topical corticosteroids as long-term maintenance therapy. Using systemic agents to control flares, then switching to a topical corticosteroid for long-term maintenance.

Atopic dermatitis persists into adulthood in 15% to 45% of those diagnosed in childhood. The most recent evidence on food allergy shows that allergen avoidance may alter the clinical course in some patients. Delayed reactions commonly take the form of urticaria. Food allergy is a large factor in exacerbation of atopic dermatitis. Severe restriction diets are helpful in most patients with atopic dermatitis and food allergy.

CME Questions Instructions: For each question or incomplete statement, choose the answer or completion that is correct. Circle the most appropriate.

1. The most common side effects seen with topical corticosteroids in patients with atopic dermatitis are skin atrophy and irritation. The concept of rotational therapy in managing patients with atopic dermatitis involves: changing from a higher- to a lower-potency topical corticosteroid agent when the flare is under control. Initially using a medium-potency topical corticosteroid to control a flare, then switching to a topical calcineurin inhibitor when the flare is under control. Initially using a topical calcineurin inhibitor to bring the flare under control, then using low-dose topical corticosteroids as long-term maintenance therapy. Using systemic agents to control flares, then switching to a topical corticosteroid for long-term maintenance.

3. The classic study by Richards and colleagues showed that medications prescribed for chronic conditions are not taken as prescribed an estimated 10% to 20% of the time. The most recent evidence on food allergy shows that allergen avoidance may alter the clinical course in some patients. Delayed reactions commonly take the form of urticaria. Food allergy is a large factor in exacerbation of atopic dermatitis. Severe restriction diets are helpful in most patients with atopic dermatitis and food allergy.

5. Atopic dermatitis persists into adulthood in 15% to 45% of those diagnosed in childhood. The most recent evidence on food allergy shows that allergen avoidance may alter the clinical course in some patients. Delayed reactions commonly take the form of urticaria. Food allergy is a large factor in exacerbation of atopic dermatitis. Severe restriction diets are helpful in most patients with atopic dermatitis and food allergy.

8. A recent population-based study of children with atopic dermatitis in the US found that the severity of skin disease correlates with: age of onset of symptoms, asthma comorbidity, early exposure to food allergens, and severity of asthma.

9. Recent advances in understanding AD pathogenesis occurred following the identification of: cytokines in the epidermis, immunoglobulin E lgE, inflammatory pathways, and mutations in the filaggrin gene.

10. With respect to infectious microbes in patients with atopic dermatitis, recent studies have demonstrated that: methicillin-resistant Staphylococcus aureus infections are significantly higher in patients with AD than in nonatopic patients. Methicillin-resistant Staphylococcus aureus infections are relatively equal in patients with AD and nonatopic patients. Methicillin-sensitive staphylococcal infections are rarely seen in patients with AD. Patients with AD more commonly have methicillin-sensitive staphylococcal infections than they do methicillin-resistant.

EVALUATION FORM: We would appreciate your answering the following questions in order to help us plan for other activities of this type. Please print.

Name: __________________________ Specialty: __________________________

Degree: MD DO PharmD RPPh NP RN BS PA Other

Affiliation: __________________________

Address: __________________________ City: __________________________ State: __________ Zip: __________

Telephone: __________________________ Fax: __________________________ E-mail: __________________________

Signature: __________________________ (All information is confidential.)

CME Credit Verification I verify that I have spent ________ hour(s)/ ________ minutes of actual time working on this CME activity. No more than 2.0 CME credit(s) will be issued for this activity.

COURSE EVALUATION: GAPS

This activity was created to address the professional practice gaps listed below. Please respond regarding how much you agree or disagree that the following gaps were met:

- Differentiating atopic dermatitis (AD) from skin disease with similar skin manifestations so that treatment can be initiated at earlier stages
- Designing the best treatment strategies for AD
- Identifying all possible treatment selections, as well as safety and efficacy profiles
- Preparing medication regimens to reduce the risk for flares and to manage flares when they do occur
- Appropriately selecting medications with the understanding of how to use the available medication classes—including topical corticosteroids and calcineurin inhibitors—within this conceptual framework of flare prevention and management
- Recognizing the far-reaching implications of a child’s AD for an entire family

Please provide any additional comments you may have about this journal.

The University of Louisville thanks you for your participation in this CME activity. All information provided improves the scope and purpose of our programs and your patients’ care. Copyright © 2012 Global Academy of Medical Education, Inc.