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Guidance for the Clinician in Rendering Pediatric Care

CLINICAL REPORT

Atopic Dermatitis: Skin-Directed Management

Megha M. Tollefson, MD, Anna L. Bruckner, MD, FAAP, and SECTION ON DERMATOLOGY

KEY WORDS
atopic dermatitis, eczema, skin care, treatment, topical corticosteroids

ABBREVIATIONS
ACD—allergic contact dermatitis
AD—atopic dermatitis
IgE—immunoglobulin E
MRSA—methicillin-resistant Staphylococcus aureus
NIAID—National Institute of Allergy and Infectious Diseases
QoL—quality of life
TCI—topical calcineurin inhibitor

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abstract

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Atopic dermatitis is a common inflammatory skin condition characterized by relapsing eczematous lesions in a typical distribution. It can be frustrating for pediatric patients, parents, and health care providers alike. The pediatrician will treat the majority of children with atopic dermatitis as many patients will not have access to a pediatric medical subspecialist, such as a pediatric dermatologist or pediatric allergist. This report provides up-to-date information regarding the disease and its impact, pathogenesis, treatment options, and potential complications. The goal of this report is to assist pediatricians with accurate and useful information that will improve the care of patients with atopic dermatitis. *Pediatrics* 2014;134:e1735–e1744

Atopic dermatitis (AD), commonly referred to as eczema, is a chronic, relapsing, and often intensely pruritic inflammatory disorder of the skin. A recent epidemiologic study using national data suggested that the pediatric prevalence is at least 10% in most of the United States.[1] AD primarily affects children, and disease onset occurs before the ages of 1 and 5 years in 65% and 85% of affected children, respectively.[1]

The number of office visits for children with AD is increasing.[2] Up to 80% of children with AD are diagnosed and managed by primary care providers, often pediatricians.[3] Although medical subspecialists, such as pediatric dermatologists and/or pediatric allergists, may be suited to provide more advanced care for children with AD, lack of a sufficient number of such physicians, particularly pediatric dermatologists,[4] likely means the burden of AD care will continue to fall to primary care providers. Although consensus guidelines and practice parameters regarding the management of AD in children have been published,[5–10] considerable variability persists in clinical practice, particularly regarding the roles that bathing, moisturizing, topical medications, and allergies play in management. Inconsistencies in opinion and treatment approach as well as the chronic and relapsing nature of AD can lead to frustration for the patient, family, and primary care providers when managing AD.

STATEMENT OF THE PROBLEM

New data support the theory that AD results from primary abnormalities of the skin barrier,[11] suggesting that skin-directed management of AD is of paramount importance. This clinical report reviews AD and provides an up-to-date approach to skin-directed management that is based on pathogenesis. Effectively using this information to create treatment plans

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and educate families should help pediatric primary care providers manage most children with AD, thereby improving patient satisfaction and clinical outcomes.

CLINICAL FEATURES

The diagnosis of AD is primarily clinical (Table 1). Major clinical features are a pruritic and relapsing eczematous dermatitis in a typical distribution that changes with age.[9] In infancy, the cheeks, scalp, trunk, and extremities are most commonly affected. In early childhood, the flexural areas are characteristic, whereas in adolescents and adults, hands and feet are typically involved. Pruritus is a hallmark of AD, which is often referred to as the "itch that rashes." Other features that support the diagnosis of AD include early age of onset, personal or family history of atopy, ichthyosis vulgaris, and/or xerosis. It is important to exclude other inflammatory skin conditions, such as contact dermatitis, seborrheic dermatitis, and psoriasis. Skin biopsies and laboratory testing are usually unnecessary and not helpful in making the diagnosis of AD, although they may be beneficial when trying to exclude conditions that appear similar to AD (such as those mentioned previously), particularly in patients whose symptoms are not responding to standard skin-directed care.

TABLE 1 Clinical Features in AD[5,6,9]

Major clinical features
Itching/pruritus
Typical dermatitis with a chronic or relapsing history
Patient or family members with atopy
Typical distribution and age-specific patterns
Minor clinical features
Early age of onset
Dry skin/xerosis
Keratosis pilaris
Ichthyosis vulgaris
Lip dermatitis
Hand eczema
Lichenification
Elevated IgE level
Itching on sweating
Recurrent infections
Pityriasis alba
Dermatographism
Eye symptoms: cataracts, keratoconus, inflammation

EFFECTS ON QUALITY OF LIFE

The effects of AD on the quality of life (QoL) of patients and their families cannot be underestimated. Nearly 50% of children with AD report a *severely* negative effect of the disease on QoL.[12] Factors that contribute to poor QoL in AD are fatigue and sleep deprivation (which directly correlate with itch and severity of AD), activity restriction, and depression. Children with severe AD also tend to have fewer friends and participate in fewer group activities than their peers.[13] These children may be at higher risk of depression, anxiety, and other mental health disorders.[14]

AD also has a negative effect on QoL of caregivers and parents of affected children.[15] Parents of children with moderate and severe AD spend up to 3 hours per day caring for their children's skin. The most commonly reported negative effects on parents are lack of sleep (often because of cosleeping), fatigue, absence of privacy (because of cosleeping, disrupted sleep of affected children), treatment-related financial expenditures, and feelings of hopelessness, guilt, and depression. In fact, the depression rate in mothers of children with AD is twice as high as in mothers of children with asthma.[16] Appropriate social and community support resources, such as referral to a counselor, psychologist, or patient support groups, such as the National Eczema Association (www.nationaleczema.org), can be helpful when QoL issues are encountered in patients and families with AD.

PATHOGENESIS

The pathogenesis of AD is complex and multifactorial. Skin barrier dysfunction, environmental factors, genetic predisposition, and immune dysfunction all play a role in its development and are closely intertwined. In the past, emphasis had been placed on T helper cell dysregulation, production of immunoglobulin E (IgE), and mast cell hyperactivity leading to the development of pruritus, inflammation, and the characteristic dermatitis.[11] Recent discoveries, however, have established the key role of skin barrier dysfunction in the development of AD.[17]

The primary function of the skin barrier is to restrict water loss and to prevent entry of irritants, allergens, and skin pathogens. The outermost layer of skin, called the stratum corneum, is critical to the integrity of the skin barrier, with the protein filaggrin being a key player in stratum corneum structure and formation.[18] Loss-of-function mutations (of which more than 40 have been described) in *FLG,* which encodes filaggrin, have been implicated in up to 50% of patients with moderate to severe AD in some demographic populations.[17,19] Mutations in *FLG* are associated with a two- to threefold increased risk of having AD.[20]

There are several proposed mechanisms of how filaggrin defects contribute to the development of AD. Inadequate filaggrin production leads to a reduced ability of keratinocytes to maintain hydration and to restrict transepidermal water loss, which then leads to xerosis, which in turn produces pruritus and, subsequently, AD.[21] An inadequate skin barrier might also allow for the entry of aeroallergens, leading to an inflammatory response, causing AD. Another theory speculates that local pH may be changed with an altered skin barrier, leading to the overgrowth of bacteria, such as *Staphylococcus aureus*, which then may trigger an innate immune response, leading to the development of inflammatory skin lesions. Regardless of the mechanism,

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this new knowledge reinforces the primary role of the skin barrier in the pathogenesis of AD and highlights the need for skin-directed therapy to repair or enhance the function of the skin barrier.

ALLERGIES AND AD

The relationship between AD and food allergy is complex but likely overemphasized. More than 90% of parents incorrectly believe that food allergy is the sole or main cause of their child's skin disease.[22] The resulting focus on food allergy can result in elimination diets; potential nutritional concerns, such as protein or micronutrient malnutrition or deficiencies; and misdirection of treatment away from the skin, thereby leading to undertreatment. Effective treatment of the skin tends to allay parental concern regarding food allergy.[23]

True food-induced AD is rare. The most common cutaneous manifestations of food allergy are often IgE-mediated and consist of acute urticaria, angioedema, contact reactions, or in some cases, an increase in AD symptoms.[24,25] In the case that AD is worsened by exposure to a food allergen, these reactions are not IgE-mediated but rather delayed-type hypersensitivity reactions and usually develop 2 to 6 hours after the exposure to the food.[26]

The accentuated role of food allergies in AD may stem from the observation that food allergies are prevalent in patients with AD. The prevalence of food allergy in all children in the first 5 years of life is approximately 5%.[24] In children with AD, however, the prevalence of food allergy is approximately 30% to 40%,[25] and up to 80% will have high food-specific IgE concentrations, even in the absence of a true food allergy.[27] In addition, patients who have food allergy often have earlier-onset and more severe AD, and patients with early-onset AD have a higher risk of developing food allergies than those with later-onset AD.[28] However, it is important to stress that this relationship is not causative. Rather, the presence of food allergy predicts a poor prognosis of severe and persistent AD, but food allergy does not necessarily cause AD.

Recent guidelines set forth by the National Institute of Allergy and Infectious Diseases (NIAID) support this position. In these guidelines, the NIAID states: "In some sensitized patients…food allergens can induce urticarial lesions, itching and eczematous flares, all of which may aggravate AD" but do not cause AD. They also state that, in the absence of documented IgE- or non-IgE–mediated food allergy, there is "…little evidence to support the role for food avoidance" in the treatment of AD.[25] Egg allergy may be one exception, as up to half of infants with egg-specific IgE may have improvement in their AD when following an egg-free diet.[29] The NIAID guidelines state that allergy evaluation (specifically to milk, egg, peanut, wheat, and soy) should be considered in children younger than 5 years with severe AD if the child has persistent AD despite optimal management and topical therapy or if the child has a reliable history of an immediate cutaneous reaction after ingestion of a specific food.

The "atopic march" is the concept that AD is the first stop in the progression to other allergic disorders, such as asthma and allergic rhinitis.[30] It has been suggested that early optimal and successful treatment of AD may prevent or attenuate the development of other atopic conditions.[31] The recent findings of the role *FLG* mutations play in causing epidermal barrier defects, thus allowing for the entry of aeroallergens and other allergens into the skin and subsequent epicutaneous sensitization, lends strong support to this possibility and highlights the importance of effective skin-directed treatment of AD.

Allergic contact dermatitis (ACD) is a delayed hypersensitivity reaction to cutaneous allergens that is underestimated in the pediatric population and likely plays a greater role in perpetuating AD than was previously believed. Up to 50% of children with difficult-to-control AD have at least 1 positive patch test reaction to a cutaneous allergen.[32] Not all positive reactions may be relevant, however. Most studies estimate 50% to 70% of all positive reactions to be relevant in patients with suspected ACD. Thus, the possibility of ACD should be considered in children with unusual or difficult-to-control AD.

TREATMENT PRINCIPLES

Skin-directed therapies should be the first approach to management. This approach has 4 main components, each focusing on a specific manifestation of AD: (1) maintenance skin care, designed to repair and maintain a healthy skin barrier; (2) topical antiinflammatory medications, to suppress the inflammatory response; (3) itch control; and (4) managing infectious triggers, recognition and treatment of infection-related flares. Education of patients and families is another critical factor that should not be overlooked. AD is a frustrating disease because of its recurrent nature, even in the face of excellent care plans. When the primary care provider is able to set realistic expectations regarding outcomes, parental compliance is better and frustration is decreased. It can be helpful to discuss the prognosis of AD, because most children will outgrow the symptoms or at least the severity of the disease.[27] Patients whose parents receive comprehensive education regarding AD and its care have better improvement in AD severity than patients whose parents do not receive this education.[33] Written action plans have been shown to improve adherence in children with asthma, and a similar

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model for patients with AD (see Fig 1 for an example), outlining specific indications for different products and medications, is likely to be helpful.[34,35]

Maintenance Skin Care

Maintenance skin care is the foundation of AD management; its goal is to repair and maintain a functional skin barrier. Patients should be instructed to develop these habits and perform them daily. Preliminary evidence supports the role of maintenance skin care in helping to reduce both the frequency and severity of AD flares. The key facets of maintenance care include maintaining skin hydration and avoiding irritants and triggers.

The optimal frequency of bathing for children with AD has not been well studied and remains controversial. Soaking baths allow the skin to imbibe moisture, and a daily bath can be beneficial in patients with AD as long as a moisturizer is applied afterward.[30,36] The specific frequency of bathing should be titrated to the individual patient and his or her response to bathing. The use of lukewarm water and limiting the duration of the bath can prevent skin dehydration. Cleansing may also remove bacteria from the skin surface. A mild synthetic detergent without fragrance can be used to cleanse soiled areas without fear of exacerbating the skin disease. Additives are not proven to be effective, although dilute bleach can be helpful for patients who are prone to infection and flares (see Managing Infectious Triggers).

A second and extremely important component of maintaining skin hydration is lubrication of the skin, commonly referred to as moisturization. Frequent moisturization alleviates the discomfort associated with xerosis, helps to repair the skin barrier, and reduces the quantity and potency of pharmacologic interventions.[37,38] In a British study evaluating 51 children with AD, parents were educated on the proper use of moisturizers and topical treatments by a nurse specialist. During the study period, the quantity of moisturizer used increased 800% (average use of 426 g per week per patient) while the severity of AD decreased and the percentage of patients having to use moderate or potent topical steroids decreased.[39]

Studies comparing the relative effectiveness of specific moisturizers are lacking, and the plethora of products can make the task of choosing a moisturizer daunting. Simplistically, all moisturizers are mixtures of lipid (liquid or semisolid) and water. Ointments have the highest proportion of lipid (for example, petroleum jelly is 100% lipid) and likewise feel "greasy" when applied to the skin. Creams are emulsions of water in lipid (oil>water) and contain preservatives and stabilizers to keep these ingredients from separating. Although creams can be less greasy than ointments, the added ingredients can sometimes burn or sting atopic skin. Similarly, lotions are also emulsions with a higher proportion of water to lipid than creams. Frequent reapplication of lotions is needed to maintain skin hydration. In general, ointments tend to have the greatest moisturizing effect, followed by creams, and then lotions. The best moisturizers for patients with AD are fragrance free and have the least possible number of preservatives, because these are potential irritants.

An Action Plan to Guide the Care of Your Child's Atopic Dermatitis (Eczema)

1. If your child enjoys a bath, allow him or her to soak daily in lukewarm water for 10 to 15 minutes. If your child does not enjoy a bath or if you feel water irritates his or her skin, bathe every 2 to 3 days. Use a gentle cleanser for dirty areas only at the end of the bath.
2. After the bath, pat the skin dry, leaving it damp to the touch.
3. Prescription medications should be applied to areas of the skin that are red, rough, and itchy. These medications should be applied in a thin layer.
   - Apply _____ to affected areas of the face, neck, armpits, and groin.
   - Apply _____ to affected areas of the body.
4. Apply a moisturizer (preferably a cream or ointment) over the entire face and body. Your child's skin medications and moisturizer should be put on within a few minutes after the bath so the skin does not dry out.
5. Repeat steps 3 and 4 a second time each day if instructed by your doctor.
6. Moisturizer can be applied as often as needed to dry, itchy skin. Prescription skin medications should not be used more than 2 times daily.
7. Continue the prescription skin medications until the red, rough rash is gone. If the flare of the rash has not improved in 2 weeks, talk with your doctor.
8. After the rash has cleared, continue to moisturize all areas of the face and body daily.
9. Restart the prescription skin medications as directed when the rash returns.
10. Antihistamines can help with itching and poor sleep due to eczema.
    - Give _____ 30 minutes before bedtime when your child is itchy.
    - Give _____ in the morning as needed for itching.
11. Oozing, drainage, pus bumps, and yellow crusts can indicate the skin is infected. Talk with your doctor right away if you are concerned about skin infection.

FIGURE 1
An action plan for the management of AD.

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Moisturizers should be applied at least once daily to the entire body, regardless of whether dermatitis is present.

There are a handful of prescription barrier creams marketed for the treatment of AD. These products do not have active pharmacologic ingredients. A small study compared 2 of these products with an over-the-counter ointment and revealed no significant difference in efficacy for patients with mild-to-moderate AD, as defined by investigator global assessment.[40] Although no major adverse effects have been reported with these products, they are considerably more expensive and may, therefore, be less cost effective than standard moisturizers.

Multiple patient-specific factors, commonly referred to as triggers, may exacerbate AD. Triggers may be unavoidable, but minimizing exposure to them can be helpful. Common triggers may include aeroallergens or environmental allergens, infections (particularly viral illnesses), harsh soaps and detergents, fragrances, rough or nonbreathable clothing fabrics, sweat, excess saliva, and psychosocial stress.

Topical Antiinflammatory Medications

The eczematous dermatitis seen in AD is the manifestation of an inflammatory immune response in the skin. Flares of dermatitis are unlikely to respond to moisturization alone, and during these times, treatment is focused on suppressing the inflammatory response. Topical steroids are the first-line, most commonly used medications to treat active AD and have been used for the last 40 to 50 years.[30] When used appropriately, they are effective and safe.[41] However, when used inappropriately, there are potential risks of cutaneous atrophy, striae, telangiectasia, and systemic absorption with resulting adrenal suppression. There are also other potential local effects when used around the eyes (intraocular hypertension, cataracts) or mouth (periorificial dermatitis). Because of these potential risks, there is a real phenomenon of "steroid phobia" on the part of both parents and health care providers. Although this phobia does not correlate with AD severity, it does lead to undertreatment of the skin disease.[42,43]

Topical steroids are classified according to their potency, ranging from class VII (low potency) to class I (super potent; Table 2). Class I medications are 1800 times more potent than the least potent class VII medications. Risk of adverse effects directly correlates with potency, with high-potency and superpotent topical steroids carrying the greatest risk. When treating most cases of AD, high-potency medications are generally not needed. Patients treated with higher-potency topical steroids are at risk for developing the aforementioned adverse effects, making close follow-up necessary. Choosing an appropriate topical steroid can be difficult, given the number of different medications, and health care providers are advised to rely on 2 or 3 medications from the low- (classes VI and VII) and moderate-potency groups (classes III, IV, and V) as "go-to" medications for everyday practice. These choices may be based on regional prescribing practices and insurance coverage or cost. Inexpensive low- and moderate-potency generic topical steroids are hydrocortisone and triamcinolone, respectively. Acceptable "limits" of topical steroid potency in a primary care practice are low-potency topical steroids for the face, neck, and skin folds and moderate-potency topical steroids for the trunk and extremities.

For acute flares and moderate to severe cases, wet wrap therapy (also called wet dressings) can be used in conjunction with topical steroids to quickly control the dermatitis.[44] Wet dressings increase penetration of topical steroids into the skin, decrease

TABLE 2 Topical Steroid Medications by Class

Class I: Superpotent
Clobetasol propionate 0.05% ointment, cream, solution, and foam
Diflorasone diacetate 0.05% ointment
Fluocinonide 0.1% cream
Halobetasol propionate 0.05% ointment and cream
Class II: High potency
Betamethasone dipropionate 0.05% ointment and cream
Budesonide 0.025% cream
Desoximetasone 0.25% ointment and cream
Diflorasone diacetate 0.05% cream
Fluocinonide 0.05% ointment, cream, and gel
Halcinonide 0.1% cream and ointment
Mometasone furoate 0.1% ointment
Class III: Moderate potency
Betamethasone valerate 0.1% ointment, foam
Desoximetasone 0.05% cream
Diflorasone diacetate 0.05% cream
Fluticasone propionate 0.005% ointment
Triamcinolone acetonide 0.1% ointment
Triamcinolone acetonide 0.5% cream
Class IV: Moderate potency
Betamethasone valerate 0.12% foam
Clocortolone pivalate 0.1% cream
Flurandrenolide 0.05% ointment
Fluocinolone acetonide 0.025% ointment
Halcinonide 0.025% cream
Hydrocortisone valerate 0.2% ointment
Mometasone furoate 0.1% cream and lotion
Triamcinolone acetonide 0.1% cream
Class V: Moderate potency
Betamethasone valerate 0.1% cream
Clocortolone pivalate 0.1% cream
Flurandrenolide 0.025% ointment
Flurandrenolide 0.05% cream
Fluocinolone acetonide 0.01% cream
Fluocinolone acetonide 0.025% cream
Hydrocortisone butyrate 0.1% ointment, cream, and lotion
Hydrocortisone probutate 0.1% cream
Hydrocortisone valerate 0.2% cream
Prednicarbate 0.1% cream
Triamcinolone 0.025% ointment
Class VI: Low potency
Alclometasone dipropionate 0.05% ointment and cream
Desonide 0.05% ointment, cream, lotion, hydrogel, and foam
Fluocinolone acetonide 0.01% oil
Flurandrenolide 0.025% cream
Triamcinolone acetonide 0.025% cream
Class VII: Low potency
Hydrocortisone 0.5% and 1% ointment and cream (over the counter)
Hydrocortisone 2.5% ointment, cream, and lotion

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itch, and serve as an effective deterrent to scratching. The technique is straightforward: after a soaking bath, topical steroid is applied to affected areas followed by application of moisturizer to the rest of the skin; moist gauze or cotton clothing that has been dampened with warm water is then applied; the wet layer is covered with dry cotton clothing. Blankets and a warm room keep the child comfortable. The dressings can be left in place for 3 to 8 hours before being changed. Wet dressings can be used continuously for 24 to 72 hours or overnight for up to 1 week at a time.

Another consideration when prescribing topical steroids is the vehicle or form of product by which the active ingredient is delivered. Ointments are less likely to produce a burning or stinging sensation and are better tolerated by infants and younger children. When comparing the same active ingredient and concentration, ointments are more effective than creams or lotions, because their occlusive effect results in a higher relative potency. Topical steroids should be applied as a thin layer once or twice daily to affected areas until these areas are smooth to touch and no longer red or itchy. Traditionally, topical steroids are held when dermatitis is quiescent and restarted when the eruption recurs. Placing an absolute limit on the duration of topical steroid use can be confusing for families, leads to unsatisfactory outcomes, and conflicts with the relapsing nature of the disease itself. However, if AD is not responding after 1 to 2 weeks of treatment, reevaluation to consider other diagnoses or treatment plans is indicated. When these general guidelines are followed, the risk of adverse effects from the use of topical steroids is extremely low.

Topical calcineurin inhibitors (TCIs) are a newer treatment of AD. These medications are topical immunosuppressive agents that inhibit T-cell function. There are currently 2 forms: tacrolimus ointment (available in 0.03% and 0.1%) and pimecrolimus 1% cream. Both are approved as second-line therapy for moderate-to-severe AD. A recent meta-analysis in pediatric patients with AD demonstrated that both tacrolimus and pimecrolimus are effective; tacrolimus is more effective than pimecrolimus, but both reduce the inflammation and pruritus associated with AD.[45]

TCIs have a different adverse effect profile than topical steroids and do not cause atrophy, striae, telangiectasia, and adrenal suppression. Thus, they are highly beneficial to treat AD in patients for whom concerns for adverse effects from long-term use of topical steroids are highest (eg, face, eyelids). The negatives, however, are a higher relative cost and the potential adverse effects of burning and stinging (tacrolimus>pimecrolimus). In addition, the Food and Drug Administration has issued a so-called "black box" or boxed warning for TCIs, citing a potential cancer risk with the medication, on the basis of the observation that laboratory animals exposed to high doses of systemic calcineurin inhibitors developed malignancies more frequently and on rare case reports of adult patients using TCIs who developed lymphoma and skin cancers.[46] However, the cause-and-effect relationship between TCI use and malignancy in these case reports is unclear. Reassuringly, TCIs have been used in children for more than 15 years, there have been no reports of malignancy in children, and there is little to no concern for systemic absorption or systemic immunosuppression.[47] Indeed, in 1 adult study, there was a lower rate of nonmelanoma skin cancer in patients with AD who used TCIs to treat their inflammatory disease.[48]

Proactive Treatment

Although traditional AD management consists of treating active disease and flares with topical steroids and/or TCIs, emerging data suggest that use of these medications when a patient is not having active disease may be helpful as well. In 1 study, patients used twice-daily antiinflammatory medications to treat active AD and were then randomly assigned to receive "proactive" twice-weekly treatment with topical tacrolimus or placebo. Patients who received topical tacrolimus had significantly less AD flares and increased time to new flare development when compared with those who received placebo.[49] A similar effect may also be true with topical steroids (fluticasone propionate and methylprednisolone aceponate have been studied),[50] although none of these studies have evaluated the long-term safety of this treatment regimen. The choice of medication used for flare prevention may depend on patient age, location of involvement, and cost.

Itch Control

Pruritus is another important component of AD. AD is commonly referred to as the itch that rashes; the associated pruritus may be significant, even in the absence of significant rash. Often, parents may be unaware of how much their child scratches, because itching is generally worse at night. The pathophysiology behind pruritus is complex, and both peripheral and central factors are involved.[51] Examples of peripheral factors are irritant entry through a defective epidermal barrier, transepidermal water loss, and protease activity in the skin.[52] Centrally, there is a complex interplay of multiple different mediators, although histamine seems to have a limited role, if any.[52,53] Clinical factors can also promote itch, including scratching (the "itch-scratch" cycle), xerosis, psychological stress, sweat, and contact with irritants such as wool and aeroallergens.

It is often challenging to remove itch, even when a patient's skin is improving. Management of itch initially focuses on

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minimizing triggers and continuing the skin-directed treatments of restoring the skin barrier and suppressing inflammation. Adjunctive systemic therapy can be added to help manage itch. Oral antihistamines do not have a direct effect on the dermatitis, but can help reduce the sensation of itching and, thus, decrease scratching and trauma to the skin in patients with AD flares.[54] Sedating antihistamines (such as diphenhydramine or hydroxyzine) should be used with caution in infants, who may be more prone to adverse effects of these agents. In addition, paradoxical effects of agitation instead of sedation may occur in some children. Nonsedating antihistamines (such as cetirizine and loratadine) are less effective on pruritus but can be helpful for patients who have environmental allergic triggers.[54] Topical antihistamines are not effective in the treatment of AD-associated pruritus and contain potential irritants and allergens that may worsen dermatitis.

Managing Infectious Triggers

Both bacterial and viral skin infections are associated with flares in children with AD. Affected patients, particularly those with poorly controlled AD, have a higher risk of cutaneous infections. The skin of patients with AD has an abnormal expression of antimicrobial peptides responsible for responding to bacteria or skin barrier compromise, toll-like receptor defects, and immune dysregulation in the form of diminished immune cell recruitment.[55] This combination of factors puts patients with AD at higher risk of skin infection.

Ninety percent of patients with AD are colonized with *S aureus*.[56] Pruritus may occur even in patients who are colonized but not actively infected. Many patients with AD have sudden exacerbations of their disease that can be attributed to active infection with bacteria, most commonly *S aureus*, and active treatment of the infection subsequently improves the skin.[56] Clinical signs of infection, such as pustules, oozing and honey-colored crusts, and less commonly fever and cellulitis, may lead the primary care provider to prescribe antibacterial treatment. Secondary infection of AD is a clinical diagnosis and is often associated with flare of the underlying AD. Obtaining skin cultures, particularly of pustules and draining lesions, before treatment can be helpful in determining the causative pathogen but is not always necessary. The rate of methicillin-resistant *S aureus* (MRSA) colonization in patients with AD varies depending on the community in which the patient resides.[57] Streptococcal infections may also occur in patients with AD. Signs of streptococcal infection include pustules, painful erosions, and fever. In addition, patients may have facial or periorbital involvement and invasive infections.[58]

There are multiple synergistic components involved in treating active *S aureus* and streptococcal infection in AD. Topical, oral, or intravenous antibiotic therapy may be needed depending on the extent and severity of infection. The specific medication used should be directed at *S aureus* and *Streptococcus*. Topical mupirocin can be used for limited skin lesions. Cephalexin is a common first-choice when oral antibiotics are needed and MRSA is not suspected. Repair of the skin barrier is continued simultaneously: bathing, moisturization, and topical anti-inflammatory therapies are all usually indicated. MRSA or other etiologies may be considered in patients who remain refractory to treatment.

Dilute bleach baths may have a useful role in the management of patients with AD, particularly those prone to recurrent infection and AD flares. A recent placebo-controlled, blinded study examined the effects of 0.005% bleach baths plus intranasal mupirocin versus placebo in children with moderate to severe AD. Patients bathed for 5 to 10 minutes twice weekly with the intervention. Those in the treatment group had significant improvement in their AD severity scores versus those in the placebo group.[56] Areas of the body that were not submerged in the bleach-containing water, specifically the head and the neck, revealed no difference in AD severity scores between the 2 groups. The treatment was well tolerated, without any adverse effect, and without any increase in resistant strains of *S aureus*. Although a relatively small study, the results provide support for the practice of using dilute bleach baths as one modality in the treatment of patients with AD. A concentration of 0.005% bleach is made by adding 120 mL (1/2 cup) of 6% household bleach to a full bathtub (estimated to be 40 gallons) of water. The amount of bleach should be adjusted based on the size of the bathtub and the amount of water in the tub.

Patients with AD are also at greater risk of viral skin infections. These include molluscum contagiosum, eczema herpeticum, the recently described atypical enteroviral infection attributable to Coxsackie virus A6 (the so-called "eczema coxsackieum"),[59] and vaccinia virus (the virus used in smallpox vaccine). Patients with eczema herpeticum present with shallow, "punched-out" erosions in areas of skin affected with or prone to AD. Similarly, the lesions seen with hand, foot, and mouth disease caused by Coxsackie virus A6 tend to localize to AD skin. In cases in which the diagnosis is not clear, viral studies are indicated.

Eczema herpeticum can be potentially life threatening and requires systemic treatment with acyclovir. In addition, adequate analgesia, skin care, and topical antiinflammatory medications are used. Secondary bacterial infection

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often coexists with eczema herpeticum and should be treated appropriately as well. Herpetic keratitis is associated with periocular eczema herpeticum.[60]

Smallpox vaccine uses a live vaccinia virus, and its use was resumed by the military in 2002. Although it is contraindicated for those with AD and in those who have a close contact with AD, rare cases of eczema vaccinatum have been reported. Eczema vaccinatum manifests as a rapidly developing papular, pustular, or vesicular eruption with a predilection for areas of AD, following inadvertent transmission of vaccinia virus from the unhealed inoculation site of the immunized person to a close contact with AD. Systemic dissemination may follow, and case fatality rates range from 5% to 40%. If eczema vaccinatum is suspected, infectious disease experts should be consulted, because treatment with cidofovir may be necessary.[61]

Final Points

Using this information, the pediatric primary care provider should be well equipped to treat most children with AD. If patients with suspected AD do not respond to these treatments, referral to a pediatric medical subspecialist, such as a pediatric dermatologist, may be useful. Other reasons for referral include poorly controlled or generalized AD with consideration for systemic immunosuppressive therapy, recurrent infections (viral or bacterial) in the setting of AD, suspected ACD, and the presence of atypical features or physical examination findings. In cases of persistent, refractory, and/or generalized AD, systemic treatment, such as phototherapy or immunosuppressive medications, may be indicated. Oral steroids are generally not indicated because of their adverse side effect profile and a high likelihood of rebound dermatitis, making ongoing management difficult.

SUMMARY

AD can be a challenging and frustrating chronic disease for pediatric patients, parents, and primary care providers. Although the pathogenesis of AD is complex, recent research advances support the role of an abnormal skin barrier. The clinical corollary to these discoveries is a greater focus on skin-directed therapies as the first-line treatment of children with AD. This includes maintenance skin care and the use of topical steroids for active disease. Low- and moderate-potency topical steroids are safe and effective for children when used appropriately. Early recognition and treatment of infectious complications can lead to improved patient outcomes. Patient and family education and counseling by the health care provider regarding the pathogenesis, specific treatment, and prognosis of the disease play an extremely important role in the management of AD.

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Atopic Dermatitis: Skin-Directed Management

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