

Atopic Dermatitis

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KEYWORDS

- Atopic dermatitis • Eczema • Pruritus • Diagnosis • Complications
- Management recommendations

KEY POINTS

- Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by intense pruritus.
- Patients with AD require periodic physician assessment of disease state, comorbidities, and complications.
- Treatment of AD requires a multimodal approach using intensive patient education, anti-inflammatories, antibacterial intervention, and psychological support.



Video of Pruritus in atopic dermatitis accompanies this article at <http://www.pediatric.theclinics.com/>

OVERVIEW

Atopic dermatitis (AD) is a common chronic inflammatory skin condition characterized by intense pruritus and a waxing and waning course. This condition most often presents in infancy and childhood and can persist, in one form or another, throughout adulthood. The exact cause of AD is unknown, but it likely reflects an interplay between genetic and environmental factors. AD affects up to 20% of children in the United States, and the prevalence may be increasing.¹ Treatment can be very effective in alleviating symptoms but serves only to manage the disease, not cure it. Appropriate therapy can also prevent significant complications, such as infection, sleep disturbance, behavioral problems, and growth impairment.

EPIDEMIOLOGY

Population studies have demonstrated an increasing prevalence of AD throughout the world. In the United States, it affects approximately 10% to 20% of children younger than 18 years, and these numbers are rising. Affected children are more likely to be black, urban, and living in homes with higher education levels.¹ As a chronic disease,

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AD has a significant impact on health care resource utilization, similar to asthma or diabetes. There were an estimated 7.4 million outpatient physician visits for AD during the 7-year-period between 1997 and 2004, amounting to an estimated health care cost of US \$364 million to \$3.8 billion annually.^{2,3}

PATHOPHYSIOLOGY

The exact cause of AD is unknown. However, it is generally agreed that AD results from a combination of genetic and environmental factors. Twin studies support a high rate of concordance; identical twins have a 7-fold increased risk for AD, and fraternal twins have a 3-fold increased risk.⁴

Healthy skin acts as a barrier to both outside influences and transepidermal water loss. Current theory holds that a genetically compromised barrier allows for penetration of environmental factors (irritants, allergens, and bacteria) with resultant immune dysregulation. A mutation in the filaggrin gene, responsible for an important component of the barrier, can be found in up to 10% of people of European ancestry.⁵ Filaggrin is an epidermal protein that acts as waterproof “mortar” between keratinocytes in the outermost layer of the skin. Mutations in this protein cause ichthyosis vulgaris and are positively associated with more severe or persistent AD.⁶

Other prevalent theories of pathogenesis in AD focus on immune dysfunction. One observation in support of the role of immune dysfunction is that many primary immunodeficiency syndromes are characterized by early onset of diffuse eczematous eruptions and are caused by genetic mutations resulting in disruption of various immune functions, such as hyper-immunoglobulin E (IgE) syndrome, severe combined immunodeficiency, Wiskott-Aldrich syndrome, and Omenn syndrome. In the 1980s, a popular theory, termed the “hygiene hypothesis,” emerged in an attempt to explain the fact that atopy tends to affect individuals from developed nations and those in a higher socioeconomic status.⁷ This hypothesis asserts that the lack of childhood exposure to infectious agents results in an immune response favoring atopy, whereas early exposure to infectious agents triggers a T helper 1 (T_H1) response, thus diverting the immune system away from a T helper 2 (T_H2) “atopic” response. There is somewhat conflicting data in support of this hypothesis, and in truth, the interplay between T_H1 and T_H2 is likely more complex than previously thought.^{8,9} More rigorous studies into causation are needed.

PREVENTION AND PROGNOSIS

Many studies have investigated primary prevention strategies and their effect on AD. These studies have examined the effect of early exposure to environmental and dietary factors such as peanuts, eggs, soy, and animal dander or early supplementation of probiotics, breast milk, and vitamin D as related to development of AD.^{10,11} There is currently no convincing evidence that any of these strategies are helpful.

The natural history of AD is variable. Based on population studies, a significant proportion of affected children “outgrow” the disease, as only 1% to 3% of adults are affected.¹² Patients with the most severe disease are more likely to have persistent disease.¹³

PRESENTATION

History

Pruritus, or itch, is defined as an unpleasant sensation that provokes the desire to scratch. A history of pruritus is required to establish the diagnosis of AD. Young

infants, who are not yet capable of coordinating scratching behavior, will exhibit fussiness and poor sleep associated with excessive movement or squirming. Older infants and children will scratch and rub at their skin, often incessantly and particularly at night (Video 1).

Most patients manifest symptoms in the first year of life, with the remainder usually presenting before the age of 10 years.¹⁴ Parental or sibling history of atopy supports the diagnosis of AD and is a strong risk factor for the development of the disease.¹⁵

Physical Examination

In infants, involvement of the face, neck, and extensor extremities (elbows, knees) is characteristic. Infantile eczema on the cheeks can appear more acute with a pseudo-vesicular or “weepy” appearance (Fig. 1). This condition is often misdiagnosed as impetigo. Persistent, bright red plaques may develop on the cheeks and chin at the time of teething and introduction of solid food, likely related to chronic irritation from saliva and foods. Infants may also have a more diffuse variant, but often with characteristic sparing of the diaper area. Scalp dermatitis is common and linear excoriations are common at this site, even with minimal skin involvement.

With increasing age, children tend to develop the classic flexural patches and plaques on the antecubital and popliteal fossae (Fig. 2). Hand and foot plantar dermatitis is also quite common (Fig. 3). In more severe cases, thickened plaques are seen on the dorsal hands, feet, and knees, often with a lichenified or leathery appearance, with prominent skin lines (Figs. 4–6). Children with darker skin typically have perifollicular hyperpigmented or hypopigmented rough 1- to 2-mm papules that can coalesce into broad, near-diffuse plaques, most prominent on the extensor surfaces (Fig. 7). This can give the skin a “pebbled” or spotty appearance (Fig. 8). This variant is often termed papular eczema. The nummular variant can be seen on the extremities as coin-shaped crusted or exudative plaques.

The surrounding skin is often dry and flaky, and there may be platelike ichthyosis of the distal extremities, especially in older children. Postinflammatory hyperpigmentation or hypopigmentation representing prior areas of disease activity is common and more obvious in darker-skinned individuals or those with tanned skin. Excoriations and erosions are nearly universal and are often the result of scratching or an indication of bacterial colonization (Fig. 9).

Superinfection is common, especially in children with more severe skin disease. Periauricular erosions and fissures overlying eczematous plaques provide a clue to staphylococcal colonization or infection. Isolated or adjacent pustules can be seen. Thick purulent crust, periocular involvement, or punched out ulcerations are often



Fig. 1. Infantile atopic dermatitis with facial involvement. (Courtesy of Ronald Hansen, MD, Phoenix, AZ.)



Fig. 2. Childhood atopic dermatitis with classical involvement of antecubital fossae.



Fig. 3. Palmar involvement in atopic dermatitis.



Fig. 4. Dorsal foot involvement in atopic dermatitis.



Fig. 5. Lichenification in severe atopic dermatitis.



Fig. 6. Severe atopic dermatitis of the dorsal hands.



Fig. 7. Papular atopic dermatitis.



Fig. 8. Diffuse perifollicular atopic dermatitis.

seen in streptococcal infections.¹⁶ Monomorphic punched out ulcers or vesicopustules within eczematous plaques, with or without fever, can indicate a superimposed herpes simplex viral (HSV) infection, more commonly known as eczema herpeticum (**Fig. 10**).



Fig. 9. Excoriations.



Fig. 10. Eczema herpeticum.

Supporting Features

Other physical examination findings can support the diagnosis of AD. These findings are not specific to AD and can be seen with other atopic disorders or in isolation. One of the most common coexistent conditions is keratosis pilaris, which is common on the upper outer arms and cheeks but can be seen diffusely over the extremities, shoulders, and back ([Fig. 11](#)). Ichthyosis vulgaris, often in association with hyperlinear palms, is present in approximately 25% of patients.¹⁷ Many other skin and eye findings are more commonly seen in patients with AD ([Box 1](#)).

Comorbidities

AD is part of the atopic diathesis accompanied by asthma and seasonal allergies. AD generally precedes the development of asthma and allergic rhinitis and is thought to be the first step of the “atopic march.” Children with eczema have a 2- to 3-fold increased risk of developing asthma and allergic rhinitis later in life.^{18,19}

DIFFERENTIAL DIAGNOSIS

AD is the most common chronic skin condition seen in children. The distribution and appearance are the most distinguishing features. A family or personal history of atopy supports the diagnosis. There are several clues that should alert the clinician to an alternate diagnosis or a complicating feature of preexisting AD ([Table 1](#)).



Fig. 11. Keratosis pilaris.

Box 1 Diagnosis of atopic dermatitis in children																			
Major Features Pruritus Typical age-specific distribution and morphology Chronic or relapsing dermatitis Personal or family history of atopy																			
Minor or Associated Features <table> <tr> <td>Xerosis (dry skin)</td><td>Elevated IgE levels</td></tr> <tr> <td>Keratosis pilaris</td><td>Cheilitis</td></tr> <tr> <td>Pityriasis alba</td><td>Eye findings (conjunctivitis, keratoconus, anterior subcapsular cataracts)</td></tr> <tr> <td>Periauricular fissures</td><td>Periorbital darkening</td></tr> <tr> <td>Ichthyosis and palmar hyperlinearity</td><td>Dennie-Morgan lines (infraorbital fold)</td></tr> <tr> <td>Susceptibility to cutaneous infections</td><td></td></tr> <tr> <td>Perifollicular accentuation (dark-skinned patients)</td><td></td></tr> <tr> <td>Hand and foot dermatitis</td><td></td></tr> <tr> <td>Scalp dermatitis</td><td></td></tr> </table>		Xerosis (dry skin)	Elevated IgE levels	Keratosis pilaris	Cheilitis	Pityriasis alba	Eye findings (conjunctivitis, keratoconus, anterior subcapsular cataracts)	Periauricular fissures	Periorbital darkening	Ichthyosis and palmar hyperlinearity	Dennie-Morgan lines (infraorbital fold)	Susceptibility to cutaneous infections		Perifollicular accentuation (dark-skinned patients)		Hand and foot dermatitis		Scalp dermatitis	
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WORKUP/DIAGNOSIS

AD is a clinical diagnosis, based on physical findings and supportive history (see [Box 1](#)).

Histology

Histology of AD is not specific to this condition and resembles most other eczematous eruptions. Therefore, biopsy is not indicated unless other causes remain on the differential diagnosis (eg, psoriasis, pityriasis rubra pilaris, and mycosis fungoides).

Laboratory Studies

There are no specific laboratory studies needed to establish the diagnosis of AD, but certain tests can be helpful in identifying complications and comorbid conditions.

COMPLICATIONS

Infection

The most common complication of AD is secondary infection, occurring as a result of a disrupted epidermal barrier and altered immune response. Children with AD are more frequently colonized with *Staphylococcus aureus* than their healthy counterparts. The rates of colonization vary among studies and regions and range between 40% and 93% of patients with AD, as compared to 24% to 30% of healthy children.^{20–25} Even in the absence of overt superinfection, *Staphylococcus* is thought to serve as a *superantigen*, acting as a significant driver of disease, and thus may be correlated with more severe skin disease.²⁶ True soft tissue infections also occur, affecting 40% to 60% of all patients with AD during their lifetime.^{23,27,28} At least a portion of these infections are caused by drug-resistant organisms, such as methicillin-resistant *Staphylococcus aureus*, although regional variability exists.²¹ Streptococcal superinfection is an emerging problem in AD. This problem is often underrecognized but is associated with higher rates of invasive infection, bacteremia, and need for hospitalization than staphylococcal infections.¹⁶ Eczema herpeticum is a feared complication, and in one

Table 1
Differential diagnosis of atopic dermatitis

Disease	Patient	Physical Examination	Key Features	Diagnosis	Other
Seborrheic dermatitis	Newborns (under 2 mo of age) and teens	Symmetric, <i>well-demarcated</i> , flexural bright red plaques with <i>greasy</i> scale (unlike the dry scale of AD)	Unlike AD, it is usually <i>asymptomatic</i> and can involve the <i>diaper area</i>	Clinical	May overlap with infantile psoriasis, which initially affects the diaper area
Tinea (capitis, faciei, corporis)	Any age	Well-demarcated scaly plaques; may be annular with more scale at the periphery	Usually <i>asymptomatic</i> or mildly pruritic	Fungal scrapings and culture	Can become more widespread with topical steroid use
Allergic contact dermatitis	Any age (although usually school age or older)	Unusually distributed eczematous papules or plaques, usually occurring at sites of exposure	May produce an "id reaction" characterized by widespread pruritic papules far from the site of initial exposure	Clinical, may be confirmed by patch testing	Nickel dermatitis is characterized by periumbilical or periauricular involvement
Scabies	Any age	Polymorphic (papules, vesicles, pustules, nodules); often on intertriginous sites (finger and foot webs, groin)	Spares the face	Clinical. Scabies preparation from linear burrows can confirm presence of the mite	Counsel families that pruritus and eczematous eruption commonly persist for months after successful treatment
Immune deficiencies	Infants and toddlers	Early, severe, and widespread eczematous eruption	Also with growth impairment, frequent skin and systemic infections; may have dysmorphic features	Genetic testing; some role for serologic testing (complete blood cell count and immunoglobulin levels); referral to appropriate specialists	Includes Wiskott-Aldrich syndrome, Omenn syndrome, hyper-IgE syndrome, SCID
Deficiencies (zinc, biotin, essential fatty acids, kwashiorkor)	Premature infants; patients on restrictive diets, TPN, or with malabsorption	Periorificial, acral and perianal scaling, erosions, and desquamation	Associated irritability, alopecia, diarrhea, and infections (especially <i>Candida</i> infections)	Serum zinc, essential fatty acid, and biotin levels; alkaline phosphatase and albumin; genetic testing	Genetic or the result of dietary deficiency; if dietary, must screen for concurrent deficiencies

Abbreviations: IgE, immunoglobulin E; SCID, severe combined immunodeficiency; TPN, total parenteral nutrition.

retrospective study, 57% of affected patients required hospitalization and intravenous antiviral therapy.²⁹ A significant portion of these patients will develop repeat infections. Herpetic keratitis can also occur and cause permanent ocular scarring.

If there is a suspicion for superinfection, skin swabs should be performed to confirm the presence of infection and to direct antimicrobial therapy. For bacterial infection, cultures can be obtained by firmly rubbing the swab tip on moist or eroded areas of the skin. To increase culture yield with dry or crusted areas, the tip can be moistened with culture media or plain water before application. Adherent crusts can be gently dislodged to swab the underlying skin surface. Studies to confirm herpes infection depend on local laboratory availability and include Tzanck smear, HSV polymerase chain reaction, viral culture, and HSV DFA (direct fluorescent antibody). As time is of the essence in eczema herpeticum, often the best test is that which can give a result most quickly. The test is performed by rupturing an intact vesicle or pustule and then scraping the roof *and* the base vigorously. Serologic studies (HSV immunoglobulin G and immunoglobulin M) may be of value in rare cases and are generally not recommended to establish a diagnosis. Periocular involvement should prompt a full evaluation by an ophthalmologist.

Psychosocial Impact

Itch is the most important and debilitating symptom in AD. Consequently, it can have the largest impact on the lives of those with AD. Although itch occurs at all hours of the day, it is often worst at night. Scratching behavior increases as well, and sleep suffers as a result. Studies that have used a combination of polysomnography, parent and patient surveys, actigraphy (measurement of movement), and video monitoring of patients with AD during sleep have repeatedly shown decreased sleep efficiency and total sleep time with increased nighttime awakenings.^{30,31} Patients with AD spend an average of 11 to 84 minutes a night scratching.³² Increased severity of skin disease correlates to increased sleep disruption.

Parental surveys have demonstrated that nearly 60% of children with AD have impairment of their ability to perform daytime activities, particularly in school performance.³³ Neurocognitive testing of children with AD demonstrated deficits in verbal comprehension, perceptual reasoning, and working memory when compared with controls.³⁴ Several recent meta-analyses have established a positive association between AD and attention-deficit/hyperactivity disorder (ADHD) symptoms. Pooled data from several studies suggest a 43% increased risk for a child with AD to display clinical ADHD symptoms when compared with a child without AD.^{35,36} There is some evidence that children with AD *and* sleep disturbance have the highest risk of developing ADHD.³⁷

Caring for a child with AD is more financially and emotionally stressful than caring for a child with insulin-dependent diabetes.³⁸ Parents of children with AD spend an average of 2 to 3 hours per day administering treatment at home and lose an average of 1 to 2 hours of sleep per night. The disease also places considerable financial burdens on families because of prescription medication costs, medical visits, and time off work to care for the child's disease.

THERAPEUTIC RECOMMENDATIONS

A successful treatment plan revolves around parent and patient education about the disease, basic skin care, and methods to reduce the frequency and severity of disease flares. Certain elements of the care plan can be standardized to all patients, whereas other elements should be individualized to account for the patient's severity and extent of disease. It is also important to incorporate patient preference, lifestyle constraints, and specific expectations and phobias into the plan so that these issues can

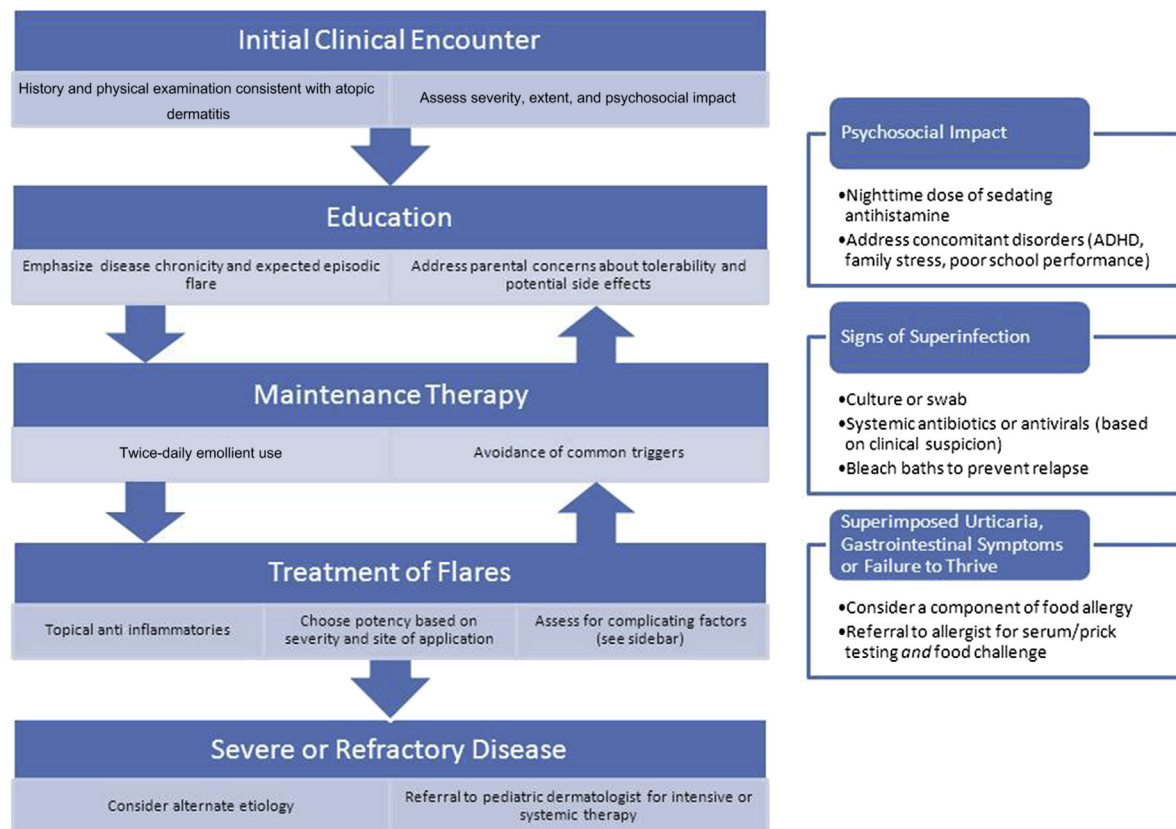


Fig. 12. Treatment algorithm for atopic dermatitis.

be addressed early, thereby increasing patient compliance and adherence to treatment (Fig. 12).

Parent and Patient Counseling

Parent and patient education is essential to the management of AD (Box 2). First and foremost, the physician must prepare the parent for the chronicity of the disease. Families should understand that therapy is directed at controlling, not curing, the disease. The physician must also explain that the disease is characterized by periods of remission and flares and treatment regimens must be adjusted to the stage of the disease. A care plan can be divided into maintenance and flare management strategies, which allows the parent to interpret the stage of the disease and to manage flares at home. This approach has the advantage of limiting the child’s overall exposure to topical corticosteroids (CSs) and helps to overcome parental fears about potential side effects.

Good Skin Care

Daily bathing is important for removing bacteria, gentle exfoliation, and improving hydration of the skin. Parents should be instructed to apply an ointment-based, dye-free, fragrance-free emollient over the child’s entire body immediately after the bath to reduce transepidermal water loss. Parent and patient preference in products should be solicited and reevaluated at each visit. Older children may avoid certain products because they are too greasy, whereas younger children may complain of a stinging or burning sensation with alcohol-containing products, such as diluted lotions. Alternate

Box 2
Patient and parent education

Good Daily Skin Care

- Bath or shower daily in warm (not hot) water for 10 to 15 minutes maximum. Use minimal soap.
- Apply a thick, nonfragranced moisturizer all over twice daily. This can be applied right after the bath after gently patting the skin dry. The best moisturizers come in tubs and are thick and greasy.

Avoidance of Triggers

- Eczema is usually worsened by cold and dry weather, harsh detergents, and fragrances.
- Avoid products that have added fragrances or additives (this includes lotions, detergents, fabric softeners, perfumes) and look for products that are labeled fragrance free.
- It can be very difficult to pinpoint specific environmental triggers (eg, dust, pet dander, pollen, food) in most patients with eczema. Try to avoid those that seem to clearly cause flares of skin disease.

Treatment of Eczema Flares

- Treat the red, itchy, and rough areas with the topical medicines until they are smooth and itch free.
- Always apply medicines to the areas that need them before applying a moisturizer all over.
- Prescription topical medications are tailored to match the severity of the eczema and the part of the body they are used on, so use as prescribed.

When to Call the Doctor

- Call the doctor if there are areas of crusting, scabbing, or oozing or sores that do not heal. The presence of such areas can be a sign of infection.
- If using the topical medications as prescribed and the eczema has not improved.

products should be suggested to improve patient compliance. It should be stressed that moisturizers only work in preventing severity of flares when they are applied regularly.

Avoidance of Triggers

Harsh detergents, dry weather, and fragrances are known to exacerbate disease in most patients with AD and should be avoided. Aeroallergens, such as animal dander, pollens, and dust mites, may worsen AD in a subset of patients, particularly those with asthma or rhinitis. It is difficult for most patients to completely avoid environmental triggers, and doing so may not resolve or improve the underlying disease.³⁹

Specific foods may act as triggers for a limited number of patients with AD. The most common skin manifestations of food allergy are IgE mediated and include acute urticaria and angioedema. Mixed IgE- and cell-mediated food allergies may play a role in some patients with AD, manifesting as what is commonly known as *late eczematous reactions* or worsening of existing eczema.⁴⁰ One study by Breuer and colleagues⁴¹ found that although 45% of patients with AD developed late eczematous reactions with food challenge, only 12% of these positive reactions were seen in isolation. Most of these late eczematous reactions were accompanied by an immediate-type reaction, such as urticaria. In this study, food-specific IgE levels had only a 64% positive predictive value of clinically observed food reaction.

Many patients with AD have elevated baseline IgE levels, and nearly 80% will have positive food-specific IgE titers.⁴² The clinical relevance of a positive test result must be explored before dietary restrictions are recommended. Confirming the presence and clinical impact of food allergens is difficult, but should include a good patient history (including relevant food exposures), specific allergen testing of implicated foods, and confirmatory food challenge testing. An estimated 35% to 40% of patients with AD will have a relevant food allergy with food challenge, most commonly to egg, milk, and/or peanut.⁴³ A 2008 Cochrane review⁴⁴ showed no benefit of typical elimination diets, however, in *unselected* participants with AD. Therefore, a switch to elemental formulas or avoidance of eggs or milk is not recommended unless confirmatory testing is performed. Clinicians and parents should be cautioned against extreme elimination diets because these have resulted in severe malnutrition in several patients with AD, most notably in infants.^{45,46}

Topical CSs

Emollients and trigger avoidance alone are rarely sufficient in controlling flares of AD. Topical CSs have been the mainstay in treatment of AD since they were first synthesized in 1951. CSs have been proven to be effective in decreasing inflammation and thereby reducing the severity and duration of flares, reducing bacterial colonization, and improving sleep.

The choice of topical CS depends on several factors, including age of the patient, site of application, and distribution and severity of the disease. Topical CSs are divided into 7 classes based on their vasoconstrictive properties. Class I CSs represent the strongest potency; class 7, the lowest potency. The difference in potency between classes is dramatic and not linear (**Box 3**). For example, clobetasol propionate, a class 1 CS, is 1800 times more potent than hydrocortisone, a class 7 CS.⁴⁷ A common misperception among patients is that the percentage on the CS label following the drug name corresponds to the strength or potency of the medication. To increase patient understanding, it may be helpful for the physician to visually list prescribed medications on a ladder of potency, so that families understand, for example, that triamcinolone acetonide 0.1% is much stronger than hydrocortisone 1%. This may also help to explain why certain CSs are used on certain parts of the body and avoided on other sites.

Box 3 Topical corticosteroid potency classes^a
Class 1: Superpotent • Clobetasol ointment 0.05% • Halobetasol propionate 0.05%
Class 2: Potent • Fluocinonide 0.05% • Desoximetasone 0.25%
Class 3: Upper Midstrength • Fluticasone propionate 0.005% • Mometasone furoate 0.1%
Class 4: Midstrength • Fluocinolone acetonide 0.025% • Triamcinolone acetonide 0.1%
Class 5: Lower Midstrength • Desonide 0.05% • Triamcinolone acetonide 0.025%
Class 6: Low Potency • Alclometasone dipropionate 0.05%
Class 7: Least Potent • Hydrocortisone 2.5% • Hydrocortisone 1%
^a Ointment formulation.

Physicians should be comfortable with the use of at least one CS in the major potency classes (mild, moderate, moderate-high, and high potency) for prescribing. As a general rule, the clinician should choose the least potent CS that is effective at quickly decreasing the severity of disease flare. Potency should be tailored to site of application and severity of disease (Table 2). General guidelines for patients and families should include the following: (1) medications should be applied twice daily to the red, rough, and itchy areas of the skin; (2) topical medications should be applied before application of a bland emollient; and (3) treatment with topical medications should continue until the affected skin is smooth, no longer red, and itch free.

Various strategies exist to control disease flares (designated as disease maintenance).⁴⁸ Some advocate more prolonged use of lower potency preparations, with occasional medication “holidays.” Others recommend intermittent or rotational strategies, such as twice-weekly application of low- to medium-potency preparations to disease-prone areas. Others prescribe a “topical steroid burst” for severe flares, with the use of a higher-potency medication for a few days followed by a medium-potency steroid for a week followed by a lower-potency medication, as needed only for maintenance. With any prescribed strategy, parent education about goals of therapy is tantamount to success, and follow-up is needed to monitor response and potential side effects of therapy.

Table 2
Pharmacologic treatment of atopic dermatitis

	Examples	Suggested Use	Key Points
Antiinflammatories			
Topical corticosteroids	Low potency (hydrocortisone 2.5%)	Face and folds (groin, axillae)	Ointment formulation preferred
	Midpotency (triamcinolone 0.1%)	Body involvement	Instruct patient to use medication on rough, raised, itchy areas until smooth and itch free
	Potent (fluocinonide) Superpotent (clobetasol)	Lichenified and thickened areas on hands and feet	Typically do <i>not</i> need to set time limits for duration of use, unless using a “topical steroid burst” therapy model
Topical calcineurin inhibitors	Pimecrolimus and tacrolimus	Practical for maintenance therapy or mild flares on the face and folds, to minimize risk of steroid atrophy	
Oral Corticosteroids	Rarely necessary and known to cause rebound symptoms after cessation		
Adjunctive Therapies			
Oral Antihistamines	Hydroxyzine, diphenhydramine, doxepin	Sedating antihistamines are given at bedtime to promote good sleep	
Oral Antibiotics	Cephalexin, clindamycin, doxycycline	For active infection or with severe flares of AD and signs of significant colonization	Always perform culture of site to direct therapy
Topical Antibacterials	Mupirocin	Rarely effective as monotherapy (because of widespread colonization) but may be used intranasally in conjunction with bleach baths for MRSA eradication	
Bleach Baths	Dilute sodium hypochlorite (regular bleach) 0.005%	One-eighth to one-fourth cup in a half tub of water (half cup in full tub), soak neck down for 10–15 min, repeat 2–3 times weekly	Chlorhexidine wash is an alternative for children or teens who prefer showering

Abbreviation: MRSA, methicillin-resistant *Streptococcus aureus*.

There are few long-term, well-designed studies that examine the true incidence of side effects with topical CS use. When used appropriately, the risk of local and systemic effects of topical CS is thought to be quite low. Risk of skin atrophy (characterized by striae, telangiectasia, and epidermal thinning) increases with excessive use. Excessive use is characterized by prolonged duration of therapy, high-potency preparations, and use on thin-skinned areas (face or intertriginous sites) or under occlusion. Excessive use of topical CS periorcularly is thought to cause glaucoma

and cataracts. Risk of systemic side effects, namely, adrenal suppression, is quite low but increases in younger children and infants.⁴⁹ For this reason, the use of class 1 corticosteroids is typically avoided in very young children.⁵⁰

It is important to address parental concerns about the potential risks of topical CS use and place the true risk of adverse reactions into perspective. CS phobia can lead to poor patient compliance and lack of response to treatment. A recent multicenter survey of patients with AD and parents of children with AD revealed that more than 80% of responders expressed fears about using topical CSs and 36% of responders admitted to nonadherence to treatment.⁵¹

Even in the absence of CS phobia, adherence to topical regimens in AD is low. One small study of 26 children with AD used electronic stealth monitoring of medication use and found an overall adherence rate of only 32% to recommended topical therapy. Better adherence was associated with a greater decrease in disease severity. Adherence rates doubled around the time of office visits, but decreased rapidly thereafter.⁵²

It is therefore important to address parental and patient (when age-appropriate) concerns about side effects at each visit, establish close follow-up appointments to increase compliance and adherence to therapy, and continue to explore and address reasons for treatment failure.

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCIs) have been used to treat AD for over a decade, and have been studied extensively in children. TCIs, which include tacrolimus (Protopic[®]) and pimecrolimus (Elidel[®]), function via local inhibition of immune cells at the site of application. TCIs have been proved to be effective in multiple randomized controlled trials in the treatment of AD in children and are approved for use as second-line therapy for intermittent use in children older than 2 years.⁵³ One advantage of TCIs over topical CSs is that they do not cause atrophy or ocular complications, making them particularly useful for chronic or recurrent facial or intertriginous AD involvement.⁵⁰ The most commonly observed side effect is a localized burning sensation, which usually resolves with continued use.⁴⁸ In 2006, the US Food and Drug Administration placed a black box warning on the label based on a theoretical risk of increased skin malignancy and lymphoma. Although long-term studies are lacking, there is currently no data in support of this theory.^{50,53,54} The role of TCIs in the management of AD is still evolving.

Adjuvant Therapy

Many patients may benefit from treatment of bacterial colonization.⁵⁰ “Bleach baths” have recently become the standard of care for managing recurrent infections in many dermatology practices (see [Table 2](#)). Huang and colleagues⁵⁵ studied a series of 31 patients with moderate to severe AD and signs of bacterial infection. All patients were treated with a course of cephalexin and then randomized to receive bleach baths with intranasal mupirocin or placebo, and eczema severity scores were assessed for 3 months. Although posttreatment *Staphylococcus* cultures gave positive results for all patients, patients in the treatment arm demonstrated improvement of their eczema in areas of the body that were submerged.

Wet wraps are a form of adjuvant therapy that have been in use for many decades and tend to be particularly helpful for children with moderate to severe AD experiencing a severe or diffuse flare.⁵⁶ This treatment can be performed in several ways but typically involves stepwise wetting of the skin, application of a topical CS (often triamcinolone acetonide 0.1% ointment or cream), and application of a “wet” layer (eg, tight-fitting damp pajamas) followed by a “dry” layer (eg, loose pajamas). Ideally the wet layer is rewetted every 2 to 3 hours, or the process is repeated twice a day.

These treatments can be administered in the hospital, or at home, and can be continued safely for up to a week or two at a time. A retrospective study from Mayo clinic demonstrated an improvement in all 218 hospitalized children receiving wet wrap treatment at their institution.⁵⁷

Although helpful for comorbidities, such as allergic rhinoconjunctivitis, there is little role for oral antihistamine therapy in AD. Daily nonsedating antihistamines do not reduce pruritus or disease flares in children with AD. Longer-acting, sedating oral antihistamines given before bedtime are helpful to promote sleep and thus prevent the nighttime scratch-wake cycle.⁵⁰ Topical antihistamines should be avoided because these can cause allergic or irritant contact dermatitis.

Referral to Specialists

The first step in managing patients with recalcitrant disease is to rule out other causes, such as immunodeficiency, and to assess for complicating factors, such as allergic contact dermatitis. Patients with true persistent chronic disease, severe flares, or other complicating factors (eg, frequent superinfection or significant psychosocial distress) may benefit from suppressive immunotherapy. Therapies used in these cases include phototherapy, cyclosporine, azathioprine, mycophenolate mofetil, and methotrexate. Referral to a specialist with experience with systemic treatments for pediatric patients with AD should ensue so that these options can be discussed with the family, because these therapies are not without risks and require safety monitoring and follow-up visits. Professional psychological evaluation with subsequent support and treatment may be necessary for some children or families. Referral to internet resources such as www.nationaleczema.org may be helpful for some older children and families.

SUMMARY

AD is a chronic inflammatory skin condition characterized by pruritus and a waxing and waning course. It is common in childhood, but can persist into adulthood. Treatment can be very effective at alleviating symptoms and is essential in preventing complications, including infection, sleep disturbance, behavioral complications, and psychosocial stress. Topical treatment is the mainstay of therapy, with systemic therapy often reserved for severe cases. Parent and patient education is essential in managing this chronic disease.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.pcl.2013.11.002>.

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