

Atopic Dermatitis

Nancy Wasserbauer, DO, Mark Ballow, MD

Department of Pediatrics, Division of Allergy and Immunology, Women's & Children Hospital of Buffalo, State University of New York at Buffalo, School of Medicine and Biomedical Sciences

Atopic dermatitis (AD), also called eczema, is a chronic inflammatory skin condition that is genetically transmitted and affects 10-20% of the pediatric population and 1-3% of the adult population.¹ Less than 20% of adults with AD have the onset of disease after adolescence.² It is important for the primary care physician to understand how to diagnose and manage this condition as well as when to refer the patient for specialty consultation.

PATHOPHYSIOLOGY

AD is often referred to as “the itch that rashes,” and pruritis is a major diagnostic criteria for diagnosis of the disease.^{2,3} The pathophysiology of the itch is unclear as histamine is not the only mediator for itching. There is both a peripheral and central mechanism to the sensation of pruritis.⁴

Atopic dermatitis results from complex interactions between genetic host factors, environmental and infectious agents, defects in skin barrier function and immunologic inflammatory responses. Eczema occurs in several immune deficiency disorders and in diseases with skin barrier dysfunction (Table 1).

RISK FACTORS IN THE DEVELOPMENT OF AD

Genome-wide screens have identified several regions of the genome linked to AD, and a number of candidate genes have been linked to AD.² Parental atopy, especially AD, is significantly associated with AD in children. Food allergy is associated with infantile and childhood disease but is not a common cause for AD in older children and adults.⁵ Environmental exposures to aeroallergens (eg, dust mites, pol-

lens, and pet dander) increase the risk for AD severity, and are common triggers for exacerbations in adults. Recent studies have implicated certain medications such as calcium channel blockers that may produce an eczematous dermatitis.⁶ Other factors that can lead to persistent or worsening disease include weather conditions or humidity, skin irritants, infections and emotional stress.

CLINICAL APPEARANCE AND DISTRIBUTION

The clinical appearance of AD varies with disease severity (Table 2). Intensely pruritic, erythematous papulovesicles associated with excoriations and serous exudates are seen in the acute phase of AD in infants. As the chronicity increases, there is associated lichenification. At all stages, patients have dry skin. Approximately 40% of childhood AD persists into adulthood.⁴ The presence of pustules within areas of dermatitis suggests a secondary infection, usually *Staphylococcus aureus*. Lesions with a less distinct distribution should prompt a search for an alternative diagnosis.

DIAGNOSIS

There is no specific diagnostic test for AD. A constellation of clinical features defines the disease. Generally, the clinical criteria set forth by Hanifin and Rajka in 1980 are accepted as diagnostic guidelines (Table 3).⁷ The differential diagnosis for AD is shown in Table 4. A search for triggers including irritants, allergens, or bacterial superinfection helps guide therapy. In atypical cases, a skin punch biopsy is often helpful. If a cutaneous lymphoma is suspected, the patient should be referred for further studies.

TREATMENT

The treatment approach is outlined in Figure. The first step is to break the “itch-scratch cycle” that perpetuates the disease. This involves avoidance of triggers, control of exacerbating factors in the environment, restoration of skin barrier function and skin hydration with emollients, and

Funding: None.

Conflict of Interest: the authors have no conflicts of interest with the materials or subject matter discussed in this manuscript.

Authorship: All authors had access to data and had an equal role in writing this manuscript.

Requests for reprints should be addressed to Mark Ballow, MD, Department of Pediatrics, Division of Allergy and Clinical Immunology, Women and Children's Hospital of Buffalo, 219 Bryant St., Buffalo, NY 14222.

E-mail address: ballow@buffalo.edu

Table 1 Immunologic Diseases Associated with Atopic Dermatitis

Wiskott-Aldrich Syndrome
 Hyper-IgE Syndrome
 Immune Deficiency Polyendocrinopathy X-Linked Syndrome
 Spink 5 Deficiency/Netherton's Syndrome
 Fillagrin Deficiency

topical or oral pharmacologics to treat itch and inflammation (Table 5).

Reduce Triggers

Evaluate and remove from the environment any potential triggers such as irritants. Simple measures can be helpful such as wearing loose-fitting cotton clothing, controlling temperature and humidity in the home environment, and the use of mild soaps and detergents. Aeroallergens such as house dust, pet dander, and pollens can cause worsening of the AD.

Bathing and Moisturizers

Bathing can hydrate the skin and can be an effective treatment modality in cleansing the skin and enhancing the penetration of topic medications such as steroids. A daily 20-minute tub bath in warm temperature water is ideal using

Table 2 Clinical Appearance and Distribution of Atopic Dermatitis

Infantile stage (0-2 years old)*
 Face (forehead, cheeks, chin, postauricular)
 Scalp
 Trunk
 Extensor surfaces
 SPARES the nose and diaper area
 Childhood stage (2 years old-puberty)
 Flexural areas (antecubital and popliteal fossa)
 Wrists
 Ankles
 Neck
 Adult stage (After puberty)⁺
 May have similar distribution to childhood form
 Upper arms
 Back
 Wrists
 Dorsa of hands
 Fingers
 Feet
 Toes

*Appearance of infantile and childhood stages range from exudative and weeping areas to lichenified plaques.

⁺Appearance of adult stage can include lichenified plaques along with scaling, erythematous plaques, papules, and prurigo papules.

Table 3 Major Diagnostic Criteria in Atopic Dermatitis*

Pruritic dermatitis
 Typical morphology and distribution based upon age
 Chronic and relapsing course
 Personal and/or family history of atopy
 Supporting Criteria
 Xerosis
 Cutaneous infections
 Non-specific dermatitis of the hands and feet
 Elevated serum IgE (80% of patients)
 Dennie-Morgan infraorbital folds
 Allergic shiners
 Facial erythema or pallor
 Dermatographism and/or delayed blanch response
 Anterior subcapsular cataracts
 Keratoconus

*From reference 7.

a mild soap like Dove. Use of a moisturizer after bathing is key.

Moisturizers/emollients are an extremely important part of the general management of AD. Ointments and creams are suggested over lotions. Patients usually prefer one agent over the other. Application should be as many times during the day as necessary to keep the skin moist and soft (even if no inflammation is present) and/or immediately after patting the skin dry after a bath.⁸

A new class of nonsteroidal skin barrier creams has been introduced (Table 6). They hydrate the skin and help restore the damaged stratum corneum.

Topical Steroids

Topical corticosteroids have been shown to both reduce *S. aureus* colonization of the skin and have anti-inflammatory effects in the treatment of AD.^{2,8,9} They are

Table 4 Differential Diagnosis in Atopic Dermatitis

Other dermatoses	Immunodeficiency syndromes
Contact dermatitis	Wiskott-Aldrich syndrome
Irritant dermatitis	Severe combined
Nummular eczema	immunodeficiency
Seborrheic dermatitis	syndrome with Omen's
Psoriasis ichthyosis	Immune dysregulation,
Infections	polyendocrinopathy,
Dermatophytosis	enteropathy, X-linked
Scabies	Graft vs host disease
Malignancies	Dermatitis herpetiformis
T cell lymphoma/mycosis	Metabolic and nutritional
fungoides	deficiencies
Letterer-Siwe disease	Phenylketonuria
	Zinc deficiency
	Niacin deficiency
	Pyridoxine deficiency

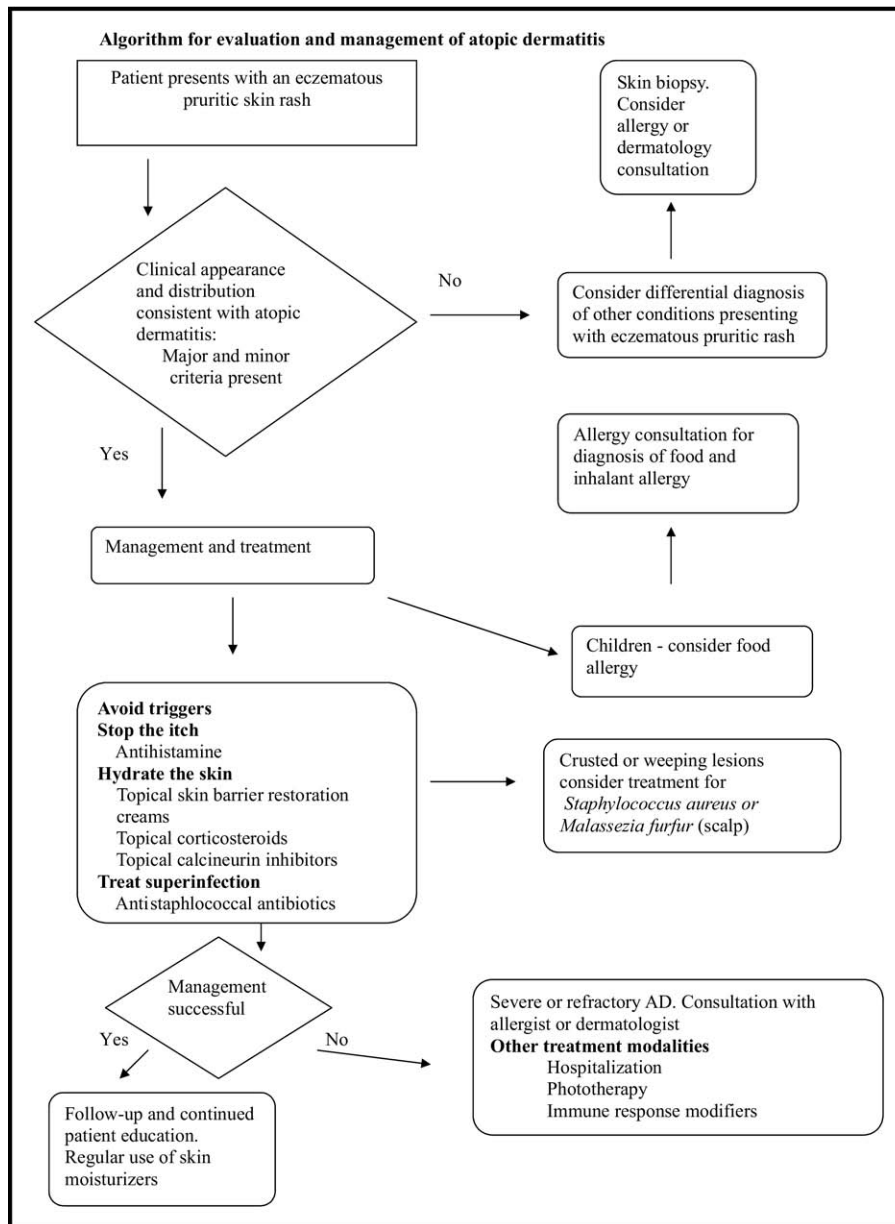


Figure Algorithm for evaluation and management of atopic dermatitis.

recommended as a first line therapy in AD. There is increased absorption of steroids on thin skin such as the eyelids, face, mucous membranes, intertriginous area and genitalia. Class I-V should be avoided in these areas, but the more potent corticosteroids are required on the palms and soles where the epidermal barrier is thicker as well as on lichenified areas, and can be used up to 3 weeks consecutively. The adverse effects of topical corticosteroids should be monitored (Table 7). Instructions for their use are provided in Table 8.

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCI) have anti-inflammatory effects without the side effect profile of topical corticoste-

roids by blocking the T-cell activation pathway.^{10,11} Instructions for their use are given in Table 9.

Antibiotic Therapy

Despite the absence of clinical signs, the skin is often colonized heavily with *S. aureus*. A topical antiseptic has been shown to decrease colonization rates and reduce skin symptoms.² Crusting, weeping or pustulation often indicate infection with *Staphylococcus aureus* and treatment with oral antibiotics is indicated.

AD also can be complicated by recurrent viral skin infections such as herpes simplex, warts, molluscum contagiosum, reflecting local defects in T cell function.^{1,2} Smallpox vaccination or exposure can cause the life-threatening

Table 5 Treatment Approaches in Atopic Dermatitis

Break the itch-scratch cycle
Avoidance of triggers
Irritants, eg, harsh soaps, wool and synthetic fabrics
Finger nails should be cut short to reduce skin abrasion; long nails also harbor bacteria.
Control of exacerbating factors
Avoid exposure to extremely hot water
Avoid alcohol, and hot and spicy foods, especially during flares
Hobbies, frequent hand washing and certain jobs might expose the patient to irritating skin products.
Oral antihistamines
Restore skin barrier function with skin hydration, moisturizers and emollients
Aquaphor, Eucerin, Lac-Hydrin, Keri Lotion and Lubriderm
Nonsteroidal topical skin barrier creams
Restore the damaged stratum corneum
Control inflammation with topical anti-inflammatory agents
Corticosteroids
Calcineurin inhibitors
Treatment bacterial superinfection
The skin is often colonized heavily with <i>Staphylococcus aureus</i>
Topical antiseptic such as triclosan or chlorhexadine
Topical antibiotics, eg, mupirocin can be used at local sites of pustules or weeping lesions, and/or in the nostrils to reduce <i>S. aureus</i> colonization
Systemic antimicrobials for widespread infection
Patient education
Educating patients and caregivers regarding the disease process
Medication side effects and trigger avoidance Improve compliance
Other treatments requiring subspecialty referral
Phototherapy
Immunomodulators

dermatitis *eczema vaccinatum*. Dermatophyte infections such as *Malassezia furfur* (*Pityrosporum ovale*) are often found in adult AD patients, particularly those with scalp involvement. Treatment with an antifungal is recommended.

Table 6 Nonsteroidal Topical Skin Barrier Creams

Atopiclair™ 2% glycerethinic acid in hydrophilic base (Sinclair Pharmaceuticals, United Kingdom)
MimyX™ N-palmitoyl thanolamine, a natural essential fatty acid with anti-inflammatory properties (Stiefel Laboratories, Coral Gables, FL)
Eletone™ a barrier cream that contains 70% oil in 30% water and acts as an ointment, but feels like a cream (Ferndale Laboratories, Fendale, MI)

Table 7 Selected Side Effects of Topical Steroid Medication to Monitor

Skin atrophy
Telangiectasia
Striae
Perioral dermatitis
Glaucoma
Cataracts

Antihistamines

The major therapeutic value of oral antihistamines is probably their sedative effects. Although oral antihistamines are widely prescribed in the treatment of AD, non-sedating antihistamines appear to have only modest effects in the relief of pruritis in AD.^{1,4,8} Oral antihistamines might still have some benefit, especially in patients with concurrent urticaria and/or allergic rhinitis. If a patient is having considerable sleep difficulty, a sedative sleep aid can be considered rather than a sedating antihistamine to improve quality of life issues. Treatment of AD with topical antihistamines is generally not recommended because it might cause cutaneous sensitization.

Patient Education

An important part of treatment is patient education, and that AD is a chronic disease. Studies report noncompliance to steroid medication because of side effect concerns.^{1,2,8} Time spent educating patients and caregivers has a positive effect on the disease outcome.² Patients should have written instructions on what medicine to use, when to use it and how it should be used (Table 10). The patient should be instructed on a step-up routine if a flare occurs with instructions to be seen by his or her physician.

Table 8 Use of Topical Steroids*

Topical steroids should be applied before the emollients once or twice daily during a flare. A mid-potency steroid is generally effective within 3-7 days. As symptoms resolve, patients should be instructed to gradually decrease use to once daily. Recent studies have supported the application of twice weekly topical steroids (fluticasone) to areas of the skin that are frequently involved in flares.

Topical corticosteroids are supplied as ointments, creams and lotions. Class I steroids are the highest potency and Class VII steroids are the lowest potency. An ointment will better penetrate the upper layer of the epidermis but may be cosmetically less pleasing to the patient. Occlusive dressings can help to increase the absorption of steroids, but also carries an increased risk of side effects and should be monitored carefully. In an acute flare, a short course of oral steroids might be beneficial but may result in a worse flare when discontinued. Long term courses should be avoided.

*This table may be useful as a patient handout.

Table 9 Use of Calcineurin Inhibitors for Atopic Dermatitis*

In the United States, tacrolimus ointment (0.03%) and pimecrolimus cream (1%) are the two calcineurin inhibitors approved for the treatment of patients above the age of 2. Tacrolimus ointment also is supplied as 0.1% concentration and is only approved in the treatment of adults. Tacrolimus can be used safely on facial and eyelid eczema. Studies show that 0.1% tacrolimus ointment has the strength of a mid potency topical corticosteroid and should be considered first line for facial eczema where treatment with corticosteroids is limited to low potency topical corticosteroids secondary to safety concerns.

A transient burning sensation might be noted with the use of TCIs. In studies of children using pimecrolimus 1% vs tacrolimus 0.03%, pimecrolimus achieved better tolerability. There is an unclear association between the risk of developing generalized viral infections such as eczema herpeticum and eczema mollusculatum and the use of TCIs. Although there is no evidence of a causal link between the use of TCIs and cancer, the FDA has placed a black box warning on the TCIs secondary to a lack of long-term safety data.

*This may be used as a patient handout.

WHEN TO REFER

Patients who do not display the common diagnostic characteristics of AD should be referred to an allergist or dermatologist specialist. Patients who have recalcitrant disease, not responding to first line environmental controls and medications also should be referred. Other therapies may be considered, but carry potentially serious side effect profiles and require close monitoring (Table 11).

SUMMARY

Atopic dermatitis is pervasive, chronic and relapsing disease. An understanding of the disease epidemiology

Table 10 A Sample Topical Drug Regimen for Severe Atopic Dermatitis

Layer 1*	If erythematous, indurated or pustular: Topical (mupirocin) or oral antistaphylococcal penicillin for 14-21 days.
Layer 2	If erythematous: Topical corticosteroids: 0.1% triamcinalone (medium potency) or 0.05% fluocinonide (high potency). Apply 2-3 times per day.
Layer 3	Moisturizer: Aquaphor ⁺ . Apply 2-3 times per day.
Layer 4	Skin barrier: Eucerin, skin barrier creams (Table 6). Apply 2-3 times a day.

*If itching is severe: add an oral sedative antihistamine (diphenhydramine).

⁺0.1% triamcinalone may be mixed with either Aquaphor or Eucerin in equal parts for combination anti-inflammatory and moisturizer therapy as a step down therapy for improving atopic dermatitis. The amount of topical agent to be applied should be demonstrated to the patient in the office.

Table 11 Therapies for Atopic Dermatitis Requiring Specialty Referral

Cyclosporin A
Azathioprine
Interferon γ
Mycophenolate mofetil
Phototherapy

and pathophysiology will aid in the rational approach to its treatment. Environmental controls for potential triggers and pharmacotherapy are first line treatments. Patient education is essential for successful disease management. Subspecialty referral is required for recalcitrant disease, requiring therapies with higher side effect profiles and closer monitoring. If concerns regarding accuracy of diagnosis or specific allergic triggers or complicating disease processes affect a particular patient, subspecialty referral is recommended.

References

1. Leung DYM, Nicklas RA, Li JT, et al. Disease management of atopic dermatitis: an updated practice parameter. *Ann Allergy Asthma Immunol.* 2004;93:S1-S21.
2. Akdis CA, Akdis M, Bieber T, et al. Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL Consensus Report. *J Allergy Clin Immunol.* 2006;118:152-169.
3. Koblenzer C. Itching and the atopic skin. *J Allergy Clin Immunol.* 1999;104(Suppl 3, Pt 2):S109-S113.
4. Beltrani VS. The clinical spectrum of atopic dermatitis. *J Allergy Clin Immunol.* 1999;104(Suppl 2):S87-S98.
5. Sicherer S, Sampson H. Food hypersensitivity and atopic dermatitis; pathophysiology, epidemiology and management. *J Allergy Clin Immunol.* 1999;104(Suppl, Pt 2):S114-122.
6. Joly P, Benoit-Corven C, Baricault S, et al. Chronic eczematous eruptions of the elderly are associated with chronic exposure to calcium channel blockers: results from a case-control study. *J Invest Dermatol.* 2007;127:2766-2771.
7. Hanifin J, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol.* 1980;92(suppl):44-7.
8. Hanifin J, Cooper K, Ho V, et al. Guidelines of care for atopic dermatitis: Outcomes Task Force. *J Amer Acad Dermatol.* 2004;50:391-404.
9. Berth-Jones J, Damstra R, Golsch S, et al. Twice weekly fluticasone propionate added to emollient maintenance treatment to reduce risk of relapse in atopic dermatitis: randomised, double-blind, parallel group study. *Br Med J.* 2003;326:1367-1373.
10. Ashcroft DM, Dimmock P, Garside R, et al. Efficacy and tolerability of topical pimecrolimus and tacrolimus in the treatment of atopic dermatitis: meta-analysis of randomized controlled trials. *Br Med J.* 2005;333:516-525.
11. Nghiem P, Pearson G, Langley R. Tacrolimus and pimecrolimus: From clever prokaryotes to inhibiting calcineurin and treating atopic dermatitis. *J Amer Acad Dermatol.* 2002;46:228-241.