
Disease management of atopic dermatitis: a practice parameter

These parameters were developed by the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology*

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INTRODUCTION

Atopic dermatitis is an important manifestation of the atopic diathesis.^{1,2} It not only frequently accompanies allergic respiratory disease but often precedes it as the initial clinical manifestation of allergic disease. The evaluation and management of patients with atopic dermatitis is therefore an integral part of an allergist's practice and training. Since atopic dermatitis

affects more than 10% of children, it is important for the primary care physician/provider to be familiar with the evaluation and management of this common skin condition, and know when to consult a qualified subspecialist, particularly when the diagnosis may not be established (Table 1).

Although the exact role of IgE antibodies in the pathogenesis of atopic dermatitis is not clear, most individuals with atopic dermatitis have elevated serum IgE levels and there is evidence that the eosinophil plays a role in disease pathogenesis, based on elevated tissue and serum levels of eosinophil derived cationic proteins.^{3,4} Research into the pathogenesis of allergic disease continues to suggest a complex inflammatory process involving mast cells, lymphocytes, and infiltrating leukocytes which are orchestrated by a cytokine profile that has been identified with the T Helper Type 2 (TH₂) lymphocyte.⁵

Recent advances in our understanding of the immunopathogenesis of atopic dermatitis are leading to the development of novel forms of therapy that may be helpful in selected patients. The response to topical corticosteroids as the mainstay of treatment for atopic dermatitis is likely to be the result of corticosteroid reduction of cellular immune activation.

CLINICAL CRITERIA FOR DIAGNOSIS

Intense pruritus and cutaneous reactivity associated with a lowered "itch threshold" are hallmarks of atopic dermatitis.^{6,7} Several skin lesions are commonly seen in atopic dermatitis. Acute lesions are characterized by intensely pruritic, erythematous papules and vesicles over erythematous skin. These are frequently associated with extensive excoriations and erosions which are accompanied by a serous exudate. Subacute lesions are characterized by erythema, excoriation, and scaling. Chronic lesions are characterized by thickened plaques of skin, accentuated skin markings (lichenification), and fibrotic papules (prurigo nodularis). In patients with chronic atopic dermatitis, all three skin reaction patterns may coexist in the same individual.

Although atopic dermatitis may present at any age, it often begins between 2 and 6 months of age. The infantile form of atopic dermatitis involves the extensor surfaces of extremities, face, trunk and neck areas early, whereas the flexural aspects of the antecubital fossa and the popliteal fossa become involved in chronic childhood and adult atopic dermatitis. Frequently, atopic dermatitis subsides in severity as the child matures, leaving an adult with skin that is prone to itching and inflammation when exposed to exogenous irritants.⁸ Last, chronic hand eczema may be the primary manifestation of many adults with atopic dermatitis.

The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) have jointly accepted responsibility for establishing atopic dermatitis parameters. Because this document incorporated the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provide an official AAAAI or ACAAI interpretation of these Practice Parameters. Any request for information about or an interpretation of these Practice Parameters by the AAAAI or the ACAAI should be directed to the Executive Offices of the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma and Immunology.

This document has been approved and endorsed by the Allergy & Immunology subsection of the American Academy of Pediatrics.

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Table 1. Differential Diagnosis of Atopic Dermatitis

- Immunodeficiencies
 - Wiskott-Aldrich syndrome
 - DiGeorge syndrome
 - Hyper-IgE syndrome
 - Severe combined immune deficiency
- Metabolic Diseases
 - Phenylketonuria
 - Tyrosinemia
 - Histidinemia
 - Multiple carboxylase deficiency
 - Essential fatty acid deficiency
- Neoplastic Disease
 - Cutaneous T-cell lymphoma
 - Histiocytosis X
 - Sézary syndrome
- Infection and Infestation
 - Candida
 - Herpes simplex
 - Staphylococcus aureus
 - Sarcoptes scabiei*
- Dermatitis
 - Contact
 - Seborrheic
- Psoriasis

The diagnosis of atopic dermatitis is based on clinical criteria. At present, there are no laboratory tests that can definitively establish a diagnosis of atopic dermatitis although many of these patients will have markedly elevated serum IgE levels and peripheral blood eosinophilia. The constellation of features that can be used to establish a diagnosis of atopic dermatitis is listed in Table 2 (modified from ref 6):

EVALUATION OF ATOPIC DERMATITIS

Although there is currently no single laboratory test for the diagnosis of atopic dermatitis, there has been substantial progress in the past decade toward understanding the basis of the immune response in allergic diseases such as atopic dermatitis. Asthma, allergic rhinitis, and atopic dermatitis all have in common the generation of allergen-specific IgE responses and tissue-specific inflammation characterized by the local infiltration of memory T cells, eosinophils, and monocyte/macrophages.² Recent studies have demonstrated that T cells infiltrating the acutely inflamed tissues of patients

with atopic dermatitis, asthma, and allergic rhinitis primarily express IL-4, IL-5, and IL-13.^{9,10} These cytokines are thought to play a critical role in allergic responses with the involvement of IL-4 and IL-13 in immunoglobulin isotype switching to IgE synthesis and vascular endothelial activation, and IL-5 in the enhancement of eosinophil-mediated responses.³

It has also become clear that inflammatory responses in atopic dermatitis are highly complex and represent more than a strictly IgE-dependent immediate hypersensitivity reaction.² In this regard, IgE is thought to play a multifunctional role in allergic diseases beyond just mediating allergen-specific mast cell or basophil degranulation. Several cell types in the atopic skin lesion express IgE on their cell surface.¹¹ These include monocyte/macrophages, Langerhans' cells, mast cells, and basophils. The expression of IgE on Langerhans' cells has been associated with enhanced allergen capture for allergen processing and presentation to T cells.¹² Allergens can also mediate release of proinflammatory cytokines and mediators from IgE-bearing monocyte/macrophages. In addition, monocytes from atopic patients have been demonstrated to have elevated expression of phosphodiesterase as well as increased production of IL-10 and prostaglandin E₂,¹³ which can enhance the development of TH₂-like cells.

Various pathways of immune activation in atopic dermatitis have been used as targets for the development of novel therapies.¹⁴ For the clinician faced with a difficult-to-manage patient, documentation of elevated serum IgE levels and eosinophilia may be useful in confirming the atopic status of the patient. These laboratory studies, however, do not identify the specific trigger of skin inflammation.

Prick skin testing to allergens can be helpful in identifying specific triggers of dermatitis, particularly in young children with moderate to severe atopic dermatitis. Negative allergy skin tests may be useful to exclude

allergic trigger factors. A positive skin test to an allergen, however, does not prove that a particular food or inhalant allergen is clinically significant in atopic dermatitis but only indicates allergen sensitization.¹⁵ With foods, particularly in children, a positive skin test to specific foods can be followed by double-blinded, placebo-controlled food challenges, single-blind challenges, open challenges, and/or controlled nutritionally adequate elimination diets to confirm or exclude clinical sensitivity to a particular food. This is important because the majority of children with food allergy are clinically allergic to three or fewer foods even when they are observed to have multiple positive food skin tests (reviewed in ref 16). Food allergy has been implicated in one-third to one-half of children with atopic dermatitis.¹⁶ In-

Table 2. Diagnostic Criteria of Atopic Dermatitis

Major characteristics
Pruritus
Typical morphology and distribution
Flexural lichenification (thickening of the skin) and linearity in adults
Facial and extensor involvement in infants and young children
Chronic or chronically relapsing dermatitis
Personal or family history of atopy (asthma, allergic rhinoconjunctivitis, atopic dermatitis)
Other characteristics
Xerosis (dry skin)
Ichthyosis/palmar hyperlinearity/keratosis pilaris
Immediate, Type I skin test response
Hand and/or foot dermatitis
Cheilitis
Nipple eczema
Susceptibility to cutaneous infection (especially <i>S. aureus</i> and herpes simplex and other viral infections, warts, molluscum, dermatophytes)
Erythroderma
Early age of onset
Impaired cell-mediated immunity
Recurrent conjunctivitis
Infraorbital fold
Keratoconus
Anterior subcapsular cataracts
Elevated total serum IgE
Peripheral blood eosinophilia

deed, even patients with positive prick skin tests to members of a specific plant or animal family will generally react clinically to only one or two members of that food family.¹⁷ Controlled challenges may be performed to design the most nutritionally complete food allergen-free diet.

With regard to inhalant allergens, seasonal exacerbation of atopic dermatitis in selected patients may correlate with reactions to inhalant allergens, eg, ragweed pollen.¹⁶ Furthermore, allergy skin testing to aeroallergens can be useful in patients with atopic dermatitis and co-existent respiratory allergy (ie, allergic rhinitis and/or asthma). Furthermore, perennial symptoms may occur as the result of exposure to dust mites, mold, or animal dander.^{18,19} It is reasonable to implement dust-mite and mold control procedures in those individuals who are either skin test positive or in vitro test positive to dust mite. Ideally, animals should be removed from the home if animal allergy is found.

In patients with extensive cutaneous involvement due to atopic dermatitis or in patients with marked dermatographism, in vitro tests (eg, RAST, ELISA, etc) to identify serum IgE directed to specific allergens may be used in place of prick skin testing. Such studies, however, must be interpreted carefully because they can result in false positive reactions when sera are obtained from patients with elevated IgE levels. Similar to skin testing, a positive in vitro IgE test has poor predictive value for clinical food allergy. Correlations with history and controlled challenges to the allergens involved are of prime importance.

In patients suspected of having a skin infection, tests for infectious agents—eg, Tzanck smear for viruses such as herpes simplex, potassium hydroxide (KOH) preparation for dermatophytes, and gram stain for bacterial infections—should be considered. These tests can be supplemented with bacterial cultures and antibiotic sensitivity for staphylococcal infections, as well as viral or fungal culture to identify the infectious agent involved. To

distinguish atopic dermatitis from hyperimmunoglobulin E syndrome, an antistaphylococcal IgE level can be helpful, but this test is generally available only through research laboratories. Hyperimmunoglobulin E syndrome, but not atopic dermatitis, is associated with serum IgE directed against the cell wall of *S. aureus*.²⁰

TREATMENT RECOMMENDATIONS

Successful management requires a systematic, multipronged approach that includes skin hydration, emollients, topical corticosteroids, and the identification and possible elimination of exacerbating factors including irritants, allergens, emotional stressors, and infectious agents.¹⁴ Scratching plays an important role in the development of cutaneous lesions in atopic dermatitis. Control of pruritus is therefore an important part of treatment, recognizing that patients may experience both exogenous and endogenous provocation factors. Dry skin in the winter months damages the stratum corneum barrier causing an increased susceptibility to irritants and increased itching, whereas sweating in the warm humid months of the summer may also trigger itching. Patients with atopic dermatitis tend to have an intolerance to wool fiber because of its irritating effect on the skin, but any irritants including soaps and lipid solvents, may provoke pruritus. Patients with atopic dermatitis frequently will experience an accentuation of their itching during times of stress and/or exposure to specific allergens. Clearly, many factors may lead to an intensification of pruritus and treatment plans should be individualized to address trigger factors that are unique to the individual patient. In patients refractory to first line therapy, other anti-inflammatory and immunomodulatory agents may be necessary.

Cutaneous Hydration

Most patients with atopic dermatitis have dry skin contributing to disease morbidity through irritation and by the development of microfissures and cracks in the skin which may serve as

portals of entry for skin pathogens, irritants, and allergens. This problem usually becomes exacerbated during the dry winter months and aggravated in certain work environments. Lukewarm soaking baths for 20 to 30 minutes followed by the application of an occlusive emollient to retain moisture can give the patient excellent symptomatic relief. Addition of substances such as oatmeal or baking soda to the bath water may have a soothing antipruritic effect for certain patients but does nothing to increase water absorption. Emollients make a major contribution to controlling the pruritus of atopic dermatitis while maintaining a soft texture to the skin. They offer a particular advantage when applied immediately after bathing in order to maintain hydration of the epidermis.

Use of an effective emollient combined with hydration therapy will help restore and preserve the stratum corneum barrier and may decrease the need for topical corticosteroids.²¹ Moisturizers are available in the form of lotions, creams, and ointments. Lotions and creams may be irritating due to preservatives, solubilizers, and fragrances. Lotions contain water and may be drying due to an evaporative effect. Lotions containing alcohol may cause a burning sensation upon application to the affected skin. Hydrophilic ointments can be obtained in varying degrees of viscosity. Some patients prefer a thicker preparation than others might require. Occlusive ointments are sometimes not well tolerated because of interference with the function of the eccrine sweat ducts and may induce the development of a sweat retention dermatitis. In these patients, less occlusive agents should be used. Thickened and lichenified plaques of atopic dermatitis and atopic hand dermatitis may, however, respond best to a topical corticosteroid in an ointment base.

Topical Corticosteroid Treatment

Topical corticosteroids, as a result of their anti-inflammatory actions, are the mainstay of treatment for the eczematous lesions, and should be used in conjunction with emollients that help

promote hydration of the epidermis. However, patients should be carefully instructed in their use in order to avoid potential side effects. The potent fluorinated corticosteroids should be avoided on the face, the genitalia and the intertriginous areas. A low potency corticosteroid preparation is generally recommended for these areas. Low potency corticosteroids are generally recommended for infants. The patients should be instructed to apply topical corticosteroids to their skin lesions and to use emollients over uninvolved skin.

There are seven classes of topical corticosteroids ranked according to their potency based on vasoconstrictor assays, and some of those commonly used are listed in Table 3.²² More potent topical corticosteroids may be used for several days in nonfacial, non-skin-fold areas to treat acute skin rashes. Patients should then be instructed to reduce the potency of topical corticosteroids applied to their skin. In Table 3, group I includes the super-potent topical corticosteroids with the greatest potential for side effects, both localized and systemic. Group VII includes the least potent topical corticosteroid and, as a group, has the least potential for side effects.

Due to their potential side effects, the ultra high potency corticosteroids should be used for only very short periods of time and in areas that are lichenified and not on facial or skin fold areas. The goal of treatment is to use emollients to enhance skin hydration and low potency corticosteroids for maintenance anti-inflammatory therapy. The high potency corticosteroids should only be used for short periods of time (generally up to 3 weeks) for clinical exacerbations. Intermediate potency corticosteroids such as 0.1% triamcinolone can be used for longer periods of time to treat chronic atopic dermatitis involving the trunk and extremities. Corticosteroids in gels are usually in a propylene glycol base and are irritating to the skin in addition to promoting dryness, limiting their use to the scalp and beard areas. Side effects from topical corticosteroids are directly related to the potency ranking

Table 3. Topical Glucocorticoid Potency Ranking

Group I	Betamethasone dipropionate 0.05% (cream & ointment)
	Clobetasol propionate 0.05% (cream & ointment)
	Diflorasone diacetate 0.05% (ointment)
	Halobetasol propionate 0.05% (cream & ointment)
Group II	Amcinonide 0.1% (ointment)
	Betamethasone dipropionate 0.05% (cream & ointment)
	Desoximetasone 0.25% (cream)
	Desoximetasone 0.05% (gel)
	Diflorasone diacetate 0.05% (ointment)
	Fluocinonide 0.05% (cream, gel, ointment & solution)
	Halcinonide 0.1% (cream)
	Mometasone furoate 0.1% (ointment)
Group III	Amcinonide 0.1% (cream & lotion)
	Betamethasone dipropionate 0.05% (cream)
	Betamethasone valerate 0.1% (ointment)
	Desoximetasone 0.05% (cream)
	Diflorasone diacetate 0.05% (cream)
	Fluocinonide 0.05% (cream)
	Halcinonide 0.1% (ointment & solution)
	Triamcinolone acetonide 0.1% (ointment)
Group IV	Hydrocortisone valerate 0.2% (ointment)
	Flurandrenolide 0.05% (ointment)
	Fluocinolone acetonide 0.025% (ointment)
	Mometasone furoate 0.1% (cream)
Group V	Betamethasone dipropionate 0.05% (lotion)
	Betamethasone valerate 0.1% (cream)
	Fluticasone acetonide 0.025% (cream)
	Fluticasone propionate 0.05% (cream)
	Flurandrenolide 0.05% (cream)
	Hydrocortisone valerate 0.2% (cream)
	Prednicarbate 0.1% (cream)
Group VI	Alclometasone dipropionate 0.05% (cream & ointment)
	Betamethasone valerate 0.05% (lotion)
	Desonide 0.05% (cream)
	Fluclonolone acetonide 0.01% (cream & solution)
	Triamcinolone acetonide 0.1% (cream)
Group VII	Hydrocortisone hydrochloride 1% (cream & ointment)
	Hydrocortisone hydrochloride 2.5% (cream, lotion & ointment)
	Hydrocortisone acetate 1% (cream & ointment)
	Hydrocortisone acetate 2.5% (cream, lotion & ointment)
	Pramoxine hydrochloride 1.0% (cream, lotion & ointment)
	Pramoxine hydrochloride 2.5% (cream, lotion & ointment)

of the compound and the length of use, so it is incumbent on the clinician to balance the need for therapeutic potency with the potential for side effects.

In addition, ointments have a greater potential to occlude the epidermis resulting in enhanced systemic absorp-

tion compared with topical creams. Further, certain anatomic areas including mucous membranes, the genitalia, the eyelids, and the face all have increased potential for transepidermal corticosteroid penetration, and for this reason, potent corticosteroids should be avoided in these areas. Side effects

from topical corticosteroids can be divided into local side effects and systemic side effects, the latter including suppression of the hypothalamic-pituitary-adrenal axis. Local side effects include the development of striae and atrophy of the skin, in addition to the development of perioral dermatitis, and rosacea. Systemic side effects are related to the potency of the topical steroid, the site of application, the occlusiveness of the preparation, the percentage of the body covered and the length of use. The potential for prolonged use of potent topical corticosteroids to cause adrenal suppression is greatest in small children and infants.^{23,24}

Identification and Elimination of Triggering Factors

General Considerations

Patients with atopic dermatitis are more vulnerable to irritants than normal individuals.²⁵ It is therefore important to identify and avoid irritants that trigger the itch-scratch cycle. These include soaps, detergents, chemicals, abrasive clothing, extremes of temperature and humidity. Alcohol and astringents found in toiletries are drying. The use of soaps, solvents, and similar compounds should be avoided. When soaps are used, they should have minimal defatting activity and a neutral pH. New clothing should be laundered prior to wearing to decrease levels of formaldehyde and other chemicals added for fabric sizing. Residual laundry detergent in clothing may be irritating. Using a liquid rather than powder detergent and adding a second rinse cycle will facilitate removal of the detergent. Occlusive, tight clothing should be avoided and open-weave, loose-fitting cotton or cotton blend garments worn.

Recommendations regarding environmental living conditions should include temperature and humidity control to avoid problems related to heat, humidity and perspiration. Air conditioning during the summer months tends to help maintain the temperature within the patient's comfort zone while

removing excess humidity, whereas an area humidifier may assist in increasing the relative humidity to prevent excess skin dryness during the winter months. One goal of treatment is for children to be as normally active as possible. Certain sports such as swimming may be better tolerated than other sports involving intense perspiration, physical contact or heavy clothing and equipment, but they must immediately rinse off the chlorine after swimming and lubricate their skin. While ultraviolet light may be beneficial to some patients with atopic dermatitis, sunscreens should be used to prevent sunburn. Since sunscreens can be irritants, care should be used to identify a non-irritating sunscreen. Prolonged sun exposure can lead to evaporative losses or overheating and sweating, both of which can be irritating, as well as photodamage.

Specific Allergens

Foods and aeroallergens such as dust mites, mold, animal danders, and pollens may trigger atopic dermatitis.¹⁶ Potential allergens can be identified by taking a careful history and carrying out selective prick skin tests or in vitro IgE assays.²⁶ Skin tests may be helpful in patients with a history of dermatitis exacerbated by food or environmental allergens. Intradermal skin tests to foods are not recommended as they are overly sensitive and may trigger anaphylactic reactions. Negative skin tests and RAST have a high predictive value for ruling out suspected allergens. Positive skin tests, particularly to foods, do not always correlate well with clinical symptoms and may be confirmed with controlled food challenges and/or elimination diets.¹⁵ In children who have undergone double-blind, placebo-controlled food challenges, milk, egg, peanut, soy, wheat, and fish account for nearly 90% of the foods that exacerbate eczema.²⁷ Avoidance of foods implicated in controlled challenges has been shown to result in clinical improvement.²⁸ Extensive elimination diets, which in some cases can be nutritionally deficient, are rarely required since even with multiple positive skin

tests, the majority of patients will react to three or fewer foods on blinded challenge.²⁷ In dust mite-allergic patients with atopic dermatitis, prolonged avoidance of dust mites has been found to result in improvement of their skin disease.^{29,30} Avoidance measures include use of dust mite-proof encasings on pillows, mattresses, and boxsprings; washing bedding in hot water weekly; removal of bedroom carpeting; and decreasing indoor humidity levels with air conditioning. Since the triggers contributing to the flares of atopic dermatitis are many, attention should be focused on controlling the trigger factors that are important to the individual patient. In general, infants and young children are more likely to have food allergy whereas in older children and adults environmental aeroallergens appear to be important in triggering atopic dermatitis and atopic respiratory disease.

Emotional Stressors

Patients with atopic dermatitis can have significant problems with anxiety, anger, and hostility.³¹ While these emotional factors do not cause atopic dermatitis, they often seem to exacerbate the illness. Atopic patients often respond to stress, frustration, embarrassment, or other upsetting events with increased pruritus and scratching. In some instances, scratching is associated with significant secondary gain or simply occurs out of habit. Psychologic evaluation or counseling should be considered in patients who have difficulty with emotional triggers or psychologic problems contributing to difficulty in managing their disease. It may be especially useful in adolescents and young adults who consider their skin disease disfiguring.³² Relaxation,³³⁻³⁵ behavioral modification, or biofeedback³⁶ may be helpful, particularly in those patients with habitual scratching.

Infectious Agents

Skin infections, particularly with *Staphylococcus aureus*, can be a recurrent problem in atopic dermatitis requiring specific treatment.³⁷ Anti-

staphylococcal antibiotics may be very helpful in the treatment of patients who are heavily colonized with *S. aureus*.³⁸ Erythromycin and the newer macrolide antibiotics (azithromycin & clarithromycin) are usually beneficial and safe for patients who are not colonized with a resistant *S. aureus* strain. In patients with macrolide-resistant *S. aureus*, a penicillinase-resistant penicillin (dicloxacillin, oxacillin, or cloxacillin) may be preferred. First generation cephalosporins also offer effective coverage for both staphylococci and streptococci. All macrolide antibiotics, if administered with either terfenadine or astemizole, have the potential to alter the electrocardiogram and provoke cardiac arrhythmias (torsades des pointes) in patients. Topical mupirocin may offer some utility in the treatment of impetiginized lesions³⁹; however, in patients with extensive superinfection, a course of systemic antibiotics is preferred.

Herpes simplex can occasionally provoke recurrent dermatitis in patients with atopy, and may be misdiagnosed as a staphylococcal infection. When vesiculation is present or when infected skin lesions fail to respond to oral antibiotics, the physician should suspect the possibility of herpes simplex infection. This can be diagnosed by a Giemsa-stained Tzanck smear of cells scraped from the vesicle base or by viral culture. Herpes simplex infections may be localized or become disseminated (Kaposi's varicelliform eruption) in patients with atopic dermatitis. Antiviral treatment for cutaneous herpes simplex infections is of critical importance in the patient with widespread atopic dermatitis since life threatening dissemination has been reported.^{40,41} Acyclovir, 400 mg three times daily for ten days or 200 mg four times daily for ten days by oral administration, is useful in adults with herpes simplex confined to the skin. The dosage should be adjusted according to the weight in children.

Dermatophyte infections can complicate atopic dermatitis and may contribute to exacerbation of disease activity. Elevated serum IgE levels to

both trichophytic antigens and to *Pityrosporum ovale*, a lipophilic yeast, have been reported.⁴²⁻⁴⁴ A pathogenic contribution from dermatophyte⁴⁵ and *P. ovale*⁴⁵ infections is suggested by improvement of atopic dermatitis in infected patients following treatment with antifungal agents. Infestation with scabies should also be considered in the differential diagnosis of flaring atopic dermatitis, and can be diagnosed with skin scrapings examined under the microscope.

Antihistamines

Pruritus is the most common, but often least tolerated symptom of atopic dermatitis. Antihistamines primarily act by blocking the H₁ receptors in the dermis and thereby ameliorate histamine-induced pruritus. Histamine is, however, only one of many mediators that can induce pruritus of the skin. Some antihistamines are mild anxiolytics and may offer symptomatic relief through tranquilizing and sedative effects.⁴⁷ Nonsedating antihistamines have shown variable results in the effectiveness of controlling pruritus in atopic dermatitis.⁴⁸⁻⁵¹ Antihistamine therapy may be useful in some patients for control of pruritus.

Since pruritus is usually worse at night, the sedating antihistamines, eg, hydroxyzine or diphenhydramine, may offer an advantage with their soporific side effects when used at bedtime. Doxepin hydrochloride has both tricyclic antidepressant and H₁- and H₂-histamine receptor blocking effects. It can be used in doses of 10 to 75 mg orally at night or 75 mg to 150 mg in divided doses throughout the day in adult patients. If nocturnal pruritus remains severe, short-term use of a sedative to allow adequate rest may be appropriate. Hydration and topical therapy, including wet dressings, are often quite effective for chronic therapy of nocturnal pruritus as well.

Treatment of atopic dermatitis with topical antihistamines is generally not recommended because of potential cutaneous sensitization.⁵² A multicenter, double-blind, vehicle-controlled study of topical 5% doxepin cream demon-

strated a significant reduction of pruritus.⁵³ In this 1-week study, sensitization was not reported. Sedation, however, is a side effect of widespread application and irritation has been noted by patients.

Tar Preparations

Coal tar preparations may have antipruritic and anti-inflammatory effects on the skin. Crude coal tar extracts were used to reduce skin inflammation before the availability of topical corticosteroids.

Newer coal tar products have been developed that are more acceptable with respect to odor and staining of clothes than some older products. A moisturizer applied over the tar preparation will decrease the drying effect on the skin. Some patients prefer a tar compounded in an ointment or cream base. To increase compliance with use, tar preparations may be recommended at bedtime. The preparation is then removed by washing in the morning, thus eliminating the concern about odor during the day and limiting staining of daytime clothing. Tar preparations should not be used on acutely inflamed skin, since this may result in additional skin irritation. Side effects associated with tars include folliculitis and, occasionally, photosensitivity. Tar shampoos are often beneficial for scalp involvement.

Patient Education

To achieve effective control of a patient's atopic dermatitis, it is important to educate patients and family members about the chronic nature of their disease, exacerbating factors, and appropriate treatment options. This is important to ensure cooperation and compliance with the treatment plan. Written information that includes detailed skin care recommendations, environmental control as well as general disease information can be very helpful. Patients should be educated on how to monitor their skin disease and know how to respond to changes in their status, and when to seek additional medical help.

The treatment plan should be reviewed during follow-up visits and the patient or parent should demonstrate an appropriate level of understanding to ensure a good outcome. Adequate time and teaching materials are necessary to provide effective education. Patient support organizations that provide updates on progress in atopic dermatitis research are important resources for these patients. Educational pamphlets and video may be obtained from the Eczema Association For Science and Education (1221 SW Yamhill, Suite 303, Portland, OR 97205; (503) 228-4430), a national nonprofit, patient-oriented organization.

TREATMENT OF DIFFICULT-TO-MANAGE PATIENTS

Wet Dressings and Occlusion

Hydration, by baths or wet dressings, promotes transepidermal penetration of topical corticosteroid preparations.⁵⁴ Dressings may also serve as an effective barrier against persistent scratching, allowing more rapid healing of excoriated lesions. Wet dressings are recommended for use on severely affected or chronically involved areas of dermatitis refractory to skin care. Overuse of wet dressings may result in chilling or maceration of the skin and may be complicated by secondary infection. Wet dressings or baths also have the potential to promote drying and fissuring of the skin if not followed by topical emollient use. Wet dressing therapy is therefore reserved for poorly controlled atopic dermatitis, and should be closely monitored by a physician.

Systemic Corticosteroids

The use of systemic corticosteroids, such as oral prednisone, may be required in the treatment of severe chronic atopic dermatitis. The dramatic clinical improvement that may occur with systemic corticosteroids may be associated with an equally dramatic rebound flaring of atopic dermatitis following the discontinuation of systemic corticosteroids. If a short course of oral corticosteroid therapy is

given for a patient with severe atopic dermatitis, it is important to taper the dosage as it is discontinued. Intensified skin care, particularly with topical corticosteroids and frequent bathing followed by application of emollients, should also be instituted during the taper to suppress rebound flaring of atopic dermatitis. Patients requiring more than one course of oral corticosteroid therapy should consult an allergist/immunologist or dermatologist to determine whether factors contributing to poorly controlled atopic dermatitis can be identified and eliminated, or whether an incorrect diagnosis has been made.

Ultraviolet Light

Natural sunlight frequently is beneficial to patients with atopic dermatitis although sunburn should be avoided. If the sunlight occurs in the setting of high heat or humidity which triggers sweating and pruritus, it may be unacceptable to patients. Ultraviolet (UV) light therapy can be a useful adjunct in the treatment of chronic recalcitrant atopic dermatitis.⁵³ This form of therapy is best done under supervision by a dermatologist. Short-wave ultraviolet B light (UVB) is commonly available in dermatology offices.⁵⁶ Addition of longer wavelength UVA to UVB, may provide an additional therapeutic response⁵⁷; however, high-intensity ultraviolet B and A irradiation lamps are not currently available in the United States. More recently, high intensity UVA irradiation has been found to be a fast acting and effective phototherapeutic approach to the treatment of patients with acute exacerbations of atopic dermatitis.⁵⁸ Of interest, investigation of the photoimmunologic mechanisms responsible for the therapeutic effectiveness of this modality indicates that eosinophils and epidermal Langerhans' cells may be targets for high intensity UVA.⁵⁹

Photochemotherapy with oral methoxypsoralen therapy followed by UVA (PUVA) may be indicated in patients with severe, widespread atopic dermatitis, especially with failure of topical steroid therapy or significant

corticosteroid side effects.⁶⁰ This form of therapy should only be undertaken in dermatologic facilities experienced with its use. Short-term adverse effects may include erythema, pruritus, and pigmentation.⁶¹ Long-term adverse effects include premature skin aging and cutaneous malignancies.⁶² Maintenance therapy is an important part of successful outcome with PUVA.

Hospitalization

Patients with atopic dermatitis who appear erythrodermic, or have widespread severe skin disease resistant to outpatient therapy may require hospitalization. In many cases, removing the patient from environmental allergens or emotional stressors, intense patient education, and assurance of compliance with therapy results in a sustained improvement in their atopic dermatitis. Clearing of the patient's skin during hospitalization also allows the patient to undergo subsequent allergen skin testing, and appropriately controlled provocative challenges to correctly identify potential allergens.

Allergen Immunotherapy

Available evidence of the effectiveness of immunotherapy with aeroallergens in the treatment of atopic dermatitis is mixed.⁶³⁻⁶⁶ Well controlled studies are still required to determine the future role for immunotherapy with this disease.

A novel approach to specific allergen desensitization in atopic dermatitis using allergen-antibody complexes has been proposed.⁶⁷ The rationale for this approach is based on the observation that under certain conditions, immune complexes can suppress the immune response to the antigen they contain.⁶⁸ In several studies, patients with atopic dermatitis and *D. pteronyssinus* hypersensitivity were treated with complexes of *D. pteronyssinus* and autologous antibodies specific to that allergen^{69,70} and patients showed sustained improvement in their atopic dermatitis. These intriguing results require confirmation by other investigators.

Interferons

Interferon-gamma is available as a recombinant molecule for the treatment of chronic granulomatous disease. This cytokine is also known to suppress IgE responses⁷¹ and downregulate TH₂ cell proliferation and function.⁷² Several studies of patients with atopic dermatitis, including a multicenter, double-blinded, placebo-controlled trial, have demonstrated that treatment with recombinant interferon-gamma results in clinical improvement in atopic dermatitis and decreases in total circulating eosinophil counts.^{73,74} In one study, a small subset of patients showed persistent improvement 3 months after treatment was discontinued.⁷⁵ The exact role and long-term safety remain to be defined and a large multicenter clinical trial is underway.

Recombinant interferon-alpha has also been used to treat patients with atopic dermatitis in several small, uncontrolled trials. Although a few reports suggest some clinical benefit using this immunomodulator^{76,77}; other studies have not confirmed this finding, although a significant decrease in circulating eosinophils has been noted.^{78,79} A single study of two patients with atopic dermatitis suggests improvement in their atopic dermatitis when recombinant interferon-gamma and interferon-alpha were used sequentially.⁸⁰ Further controlled studies are required before any firm conclusion can be made regarding the role of interferon therapy in atopic dermatitis.

Cyclosporin and FK-506

Cyclosporin A is a potent immunosuppressive drug that acts primarily on T cells by suppressing cytokine transcription.^{81,82} The drug binds to cyclophilin, an intracellular protein, and this complex in turn inhibits calcineurin, a molecule required for initiation of cytokine gene transcription. Several short-term studies have demonstrated that patients with severe atopic dermatitis, refractory to treatment with topical corticosteroids, can benefit from treatment with oral cyclosporin (5 mg/kg per day). Treatment with cyclo-

sporin was associated with reduced skin disease and improved quality of life.⁸³⁻⁸⁶ Side effects (nausea, abdominal discomfort, hypertrichosis, paresthesias, hypertension, hyperbilirubinemia, and renal impairment) dictate caution in the use of this drug. Furthermore, discontinuation of treatment frequently results in rapid relapse of skin disease.

Due to concerns over systemic side effects from oral cyclosporin, the efficacy of topically administered cyclosporin has been investigated in atopic dermatitis with mixed results.^{87,88} Recent studies using topically applied FK-506, an immunosuppressive agent with a spectrum of activity similar to cyclosporin, has resulted in more promising results.⁸⁹ Preliminary data using FK-506 in ointment form (tacrolimus) suggest that atopic dermatitis patients receiving this form of therapy have markedly diminished pruritus within three days of initiating therapy.⁹⁰ Skin biopsy results after treatment revealed markedly diminished T-cell and eosinophilic infiltrates. Short-term studies have not uncovered any systemic side effects with topical FK-506 application. Further trials are currently in progress to confirm these encouraging preliminary studies.

Phosphodiesterase Inhibitors

Leukocytes from patients with atopic dermatitis have increased cyclic AMP-phosphodiesterase (PDE) enzyme activity.^{91,92} This abnormality is most pronounced in monocytes of atopic individuals which have a unique, highly active PDE isoenzyme.⁹³ Monocytes from patients with atopic dermatitis produce elevated levels of prostaglandin PGE₂ and IL-10, which both inhibit interferon-gamma production.^{13,94,95} Phosphodiesterase inhibitors such as Ro 20-1724 have been found to reduce IL-10 and PGE₂ secretion by monocytes of atopic individuals.⁹⁶ Importantly, preliminary clinical studies using topical application of high potency PDE inhibitors have demonstrated clinical benefit in atopic dermatitis.⁹⁷

Other Therapeutic Possibilities

Essential Fatty Acids (EFA)

Disturbances in the metabolism of EFA, involved in the generation of inflammatory mediators, has been suggested in patients with atopic dermatitis.^{98,99} Consequently, clinical trials with either fish oil as a source of n-3 series EFA, or oil extracted from the seeds of *Oenothera biennis*, evening primrose, as a source of n-6 series EFA have been conducted. Conflicting results were reported in earlier studies; however, recently better controlled studies failed to demonstrate clinical benefit with either primrose oil or fish oil.^{100,102}

Chinese herbal therapy

Several placebo-controlled clinical trials have suggested that patients with severe atopic dermatitis benefit from treatment with Chinese herbs.^{103,104} Patients receiving Chinese herbal therapy, as compared with placebo, had significantly reduced skin disease, reduced pruritus, and improved sleep. The beneficial response of Chinese herbal therapy, however, is often temporary and effectiveness may wear off despite continued treatment.¹⁰⁵ The possibility of toxicity, particularly hepatic or cardiac side effects, associated with long-term use or idiosyncratic reactions remains a concern. The specific ingredients of the herbs that result in clinical improvement remain to be elucidated.¹⁰⁶ At present, Chinese herbal therapy for atopic dermatitis is considered investigational.

Atopic dermatitis is an illness associated with immunoregulatory abnormalities. As a result, future directions in therapy are likely to focus on a number of different immunologic targets in this illness.

CONSULTATION WITH A SPECIALIST IN ATOPIC DERMATITIS

The therapeutic goals of atopic dermatitis care are to control the skin disease and produce a better quality of life for the patient with minimal complications. Cooperation between the patient

and/or the patient's guardian(s), the primary care physician and the allergist/immunologist or dermatologist is important to implement strategies necessary for the care of patients with chronic atopic dermatitis and ultimately fulfill the goals set forth in the treatment of atopic dermatitis. It is important that the primary physician recognize the contributions that can be made by the allergist/immunologist or dermatologist in the management of this chronic skin disease. This includes the ability to identify trigger factors, identify allergens, and to educate patients about how to manage their disease and how to manage allergenic triggers.

Similarly, the specialist in atopic dermatitis, should recognize the role of primary care physicians in ensuring continuity of care for patients with atopic dermatitis and their important involvement in ultimately securing a successful outcome for the patient's long-term prognosis. Communication between specialist and primary care physicians is therefore important in the management of patients with poorly controlled atopic dermatitis. Consultation with a specialist is recommended for:

- severe or persistent atopic dermatitis (ie, 20% general skin involvement or 10% skin involvement affecting eyelids, hands, intertriginous areas, and not responsive to first line therapy)
- erythroderma, or extensive exfoliation
- patients requiring more than one course of systemic corticosteroids
- patients requiring hospital treatment of atopic dermatitis
- identification of triggers and allergens
- intensive education, including control of allergenic triggers
- co-existing asthma, rhinitis
- impaired quality of life (lost work days, lost school days, sleep disturbance, and poorly controlled pruritus)
- infectious complications
- ocular complications
- psychosocial complications

- when the diagnosis of atopic dermatitis is in doubt

SUMMARY STATEMENTS AND CONCLUSIONS

The guidelines offered are not intended to define the standard of care for each individual patient with atopic dermatitis but rather to provide practice parameters for the diagnosis and management of atopic dermatitis. These practice parameters should not be considered inclusive of all proper methods of management or exclusive of other methods that are reasonably directed toward achievement of successful outcomes. The specific decisions regarding the treatment of atopic dermatitis must be made by the physician and patient in consideration of all the circumstances presented by the individual patient.

Diagnosis and Evaluation

1. Atopic dermatitis is a chronic cutaneous condition that presents with acute, subacute and/or chronic lesions always associated with pruritus and a lowered "itch threshold" which predisposes the patient to secondary lesions from rubbing, scratching, and infection.
2. Atopic dermatitis may present at any age (but often begins in the first 6 months of life) and the clinical presentation may differ with age.
3. Patients with infantile atopic dermatitis initially have involvement of the neck, trunk, and face (with sparing of the nasolabial skin).
4. Older children and adults with atopic dermatitis have involvement primarily of the antecubital fossa and the popliteal fossa, hands, feet, and face.
5. There are many factors that may contribute to exacerbations of atopic dermatitis including food allergens, aeroallergens, infections, temperature, humidity, irritants, and emotional stress.
6. Skin testing or in vitro IgE testing can be useful in the identification of potential allergens. In particular, negative skin tests or in vitro

tests can be used to exclude allergic trigger factors. Positive skin tests or in vitro tests do not prove a particular allergen causes clinical symptoms. In the case of foods, controlled food challenges or elimination diets may be needed to confirm or exclude clinical sensitivity.

Pathophysiology

7. Most individuals with atopic dermatitis have elevated serum IgE levels, as well as elevated tissue and serum levels of eosinophil-derived cationic protein.
8. Pathogenesis of this skin disease involves a complex inflammatory process associated with the local activation of lymphocytes, monocytes/macrophages, eosinophils, and mast cells.

Management

9. Control of pruritus involves characterization and elimination of as many endogenous and exogenous provocative factors as possible.
10. Emollients and topical corticosteroids, applied to the eczema, are the mainstay of treatment.
11. Potent fluorinated corticosteroids should be avoided on the face, the genitalia, and the intertriginous areas as well as in young infants. The ultra-high potency corticosteroids should be used only for very short periods (several days) of time and only in areas that are lichenified.
12. Emollients and low potency corticosteroids are recommended for maintenance therapy, and intermediate and high potency corticosteroids for short periods of time to treat clinical exacerbations.
13. The degree of corticosteroid absorption through the skin, and hence the potential for systemic adverse effects is directly dependent on the surface area of the skin involved, the use of occlusive dressing, and the potency of the corticosteroid preparation.

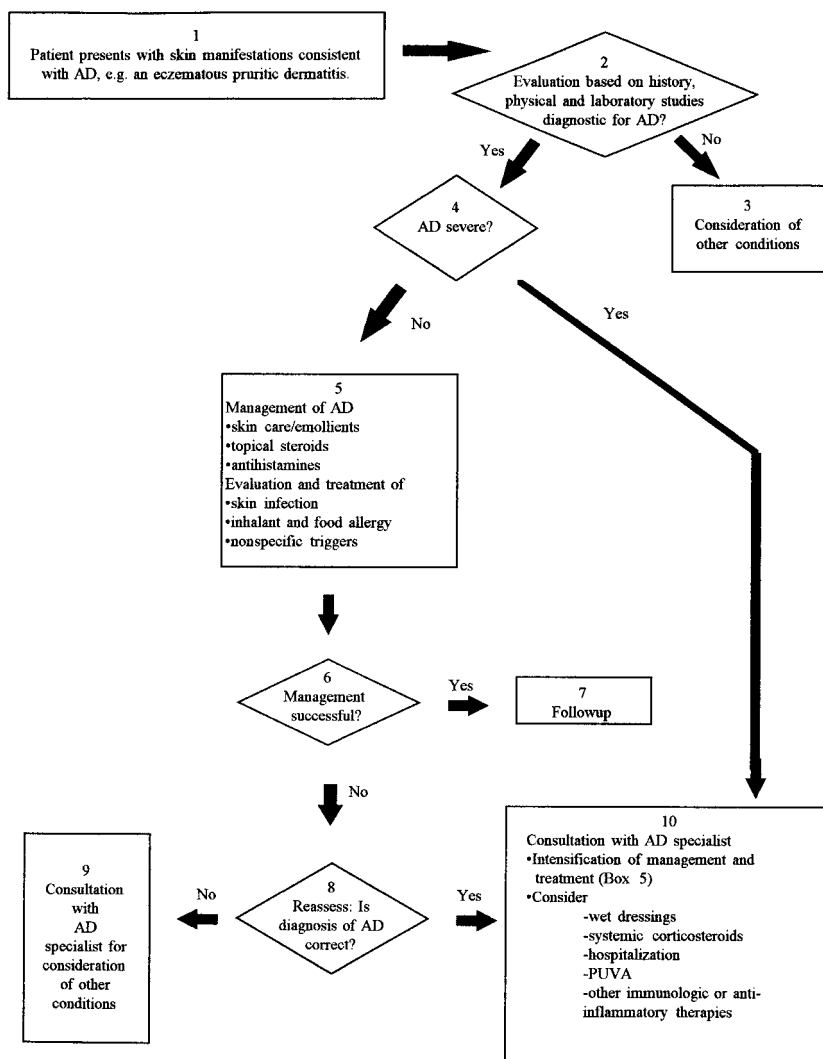


Figure 1. Flow chart for diagnosis and management of atopic dermatitis (See “Algorithm Annotations”).

14. Antihistamines may be useful in controlling the pruritus of atopic dermatitis.
15. Hydration of the skin with the proper use of emollients or topical hydrating agents is important since dry skin contributes to disease morbidity.
16. Skin infections should be treated early with short courses of anti-staphylococcal antibiotics. Herpes and dermatophyte infections should be considered if the patient does not respond to antibiotics.

Consultation with the Specialist

17. Cooperation between the patient and/or the patient’s guardian(s), the primary care physician, and the allergist or dermatologist is important in the implementation of strategies necessary for the care of patients with chronic atopic dermatitis.
18. The primary care physician plays an important role in the routine care of patients with uncomplicated atopic dermatitis and in ensuring continuity of care.

19. Consultation with an allergist/immunologist or dermatologist is recommended for patients with severe atopic dermatitis who have significant dysfunction as a result of their skin disease, for identification of potential allergen triggers, for patient education and when the diagnosis of atopic dermatitis is in doubt.

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ALGORITHM ANNOTATIONS FOR THE DIAGNOSIS AND MANAGEMENT OF ATOPIC DERMATITIS (Figure 1)

1. Patient Presents with “Eczema”

Although the terms “eczema” and “atopic dermatitis” are frequently used interchangeably, the term eczema refers to a pruritic dermatitis that includes a long list of differential diagnoses (refer to annotation #2 and #3) that is not restricted to atopic dermatitis (AD). The major features of AD are pruritus, a chronic or chronically relapsing dermatitis found in a typical distribution [ie, flexural lichenification (thickening of the skin) and linearity in adults, a facial and extensor involvement in infants and young children] and a personal or family history of atopy (asthma, allergic rhinoconjunctivitis, atopic dermatitis). Patients with AD should have all the major features. In patients who do not have an atopic history (possibly because the patient is young and has not yet developed respiratory allergy), three or more of the following “minor” or associated features may be substituted: xerosis (dry

skin), ichthyosis, early age of onset, palmar hyperlinearity, susceptibility to cutaneous infection (especially *S. aureus* and herpes simplex), infraorbital fold, impaired cell-mediated immunity, nipple eczema, cheilitis, immediate, Type I skin test response, keratoconus, and anterior subcapsular cataracts.

2. Clinical Evaluation Diagnostic for AD?

A number of conditions can share the symptom and signs of AD (annotation #3). The medical history of the patient with atopic dermatitis should include an assessment of the pruritic nature of the skin rash, age of onset, duration of illness, triggers including nocturnal exacerbation, problems with infection, foods, irritants or aeroallergens, seasonal variation, eye complications, environmental exposures, chronicity, and distribution of the skin rash. The physical examination of the patient with atopic dermatitis should include an evaluation of the morphology and distribution of the atopic skin lesions as well as potential complications from chronic corticosteroid therapy including striae or skin atrophy. Important skin findings in atopic dermatitis include diffuse xerosis (dryness of the skin), erythema, excoriation, papulation, crusting/oozing/pustules of skin lesions indicative of infection, scaling, and lichenification. Associated features include conjunctivitis, nipple eczema, allergic shiners, Dennie-Morgan infraorbital fold, keratoconus, anterior subcapsular cataracts, pityriasis alba, anterior neck folds, and ichthyosis.

Laboratory testing that may be helpful in patients with atopic dermatitis includes skin testing or in vitro testing for specific allergens. The majority of patients have elevated serum IgE and eosinophilia; however these findings are not useful in guiding clinical decisions. In patients suspected of infection, culture for *S. aureus*, herpes simplex, or dermatophytes may be useful. More than 90% of patients with chronic atopic dermatitis are colonized with *S. aureus*. Establishing the antibiotic sensitivity of the *S. aureus* in pa-

tients who fail to respond to antibiotic treatment may be useful. In patients with suspected herpes simplex infection, diagnosis can also be made rapidly with a Giemsa-stained Tzanck smear of cells scraped from the vesicle base.

The diagnosis of atopic dermatitis cannot be made solely on the basis of laboratory testing. A diagnosis of AD should be made based on the criteria described in annotation #1.

3. Consideration of Other Conditions

Patients not fulfilling the diagnostic criteria for AD (see Box #2) should be evaluated for an alternative condition and treated accordingly. The differential diagnosis of AD includes

- other forms of eczema including seborrheic dermatitis, contact dermatitis, nummular eczema, dyshidrotic eczema, and irritant dermatitis;
- immunodeficiencies associated with eczematoid rashes including Wiskott-Aldrich syndrome, DiGeorge syndrome, severe combined immune deficiency, ataxia telangiectasia, or hyperimmunoglobulinemia E syndrome;
- infectious diseases and infestations including dermatophytosis, scabies, recurrent *Staphylococcus aureus* and herpes simplex infections, and HIV disease;
- metabolic diseases such as phenylketonuria, tyrosinemia, and histidinemia;
- neoplastic disease including cutaneous T-cell lymphoma, histiocytosis X, or Sézary syndrome; and
- other chronic inflammatory skin conditions including psoriasis.

4. AD Severe?

The extent and severity of AD can be determined by careful examination of the patient's skin, grading the extent of affected areas, eg, percent involvement of the head, upper limbs, trunk and lower limbs, and defining the severity of the following signs of eczema: induration/edema/papulation, erythema, excoriation, lichenification, scaling, and oozing/weeping/crusting. In gen-

eral, patients who have more than 20% skin involvement (or 10% of skin involvement if affected areas include the eyelids, hands, or intertriginous areas) that has not been responsive to first line treatment (see annotation #5) should be considered for consultation with a specialist. Other patients who should be considered as having severe AD include

- patients with extensive skin involvement who are erythrodermic and at risk for exfoliation;
- patients requiring ongoing or frequent treatment with high potency topical glucocorticoids or systemic glucocorticoids;
- patients requiring hospitalization for severe eczema or skin infections related to the AD;
- patients with ocular or infectious complications, and
- patients who have significant disruption of their quality of life eg, sleepless nights, school or work days lost, etc.

Patients not previously receiving appropriate treatment for AD should be started on first line therapy and attempts should be made for identification of potential triggers as described in annotation #5.

5. Management of AD

The treatment of AD is directed at symptom relief and reduction of cutaneous inflammation. Characterization of each patient's skin disease severity and the reduction of exacerbating factors are critical for effective management. As described above, all patients require skin hydration in combination with an effective emollient. Potential trigger factors should be identified and eliminated. These include irritants, allergens, and emotional stresses. Therapy must be individualized and is dependent on whether the patient is experiencing an acute flare or dealing with the management of chronic AD.

The severity of AD is based on the extent of skin involvement, the intensity of pruritus, the presence of complications, the effect on quality of life and the amount of medication required for control. For patients with milder

atopic dermatitis, 1% or 2.5% hydrocortisone should be applied to areas of mild eczema preferably after baths, and no more than twice a day. Patients with moderate atopic dermatitis may require a low potency topical corticosteroid, such as 2.5% hydrocortisone ointment, to affected areas on the face and intertriginous areas. A medium potency topical corticosteroid, such as 0.1% triamcinolone ointment, can be applied to the moderately affected areas on the body. In more severe atopic dermatitis, frequent bathing up to three times a day may be required followed by the application of 2.5% hydrocortisone ointment to affected areas on the face and intertriginous areas and 0.1% triamcinolone ointment to affected areas on the trunk and extremities. In some cases, more potent topical corticosteroids may be used under close supervision and not for more than 1 week. Wet dressings may also be required in these individuals to enhance hydration, penetration of topical corticosteroids, and reduce pruritus. In some patients, antihistamines may offer some relief from severe pruritus, particularly with the use of high doses of sedating antihistamines at bedtime.

Systemic antimicrobial therapy (such as macrolide antibiotics, cephalosporins, and penicillinase-resistant penicillins) is often necessary to control infection and/or overgrowth with *S. aureus*. In patients with herpes simplex infection or dermatophyte infections, anti-viral or antifungal therapy may be indicated. In the poorly controlled patient with AD, foods and aeroallergens such as dust mites or animal danders may be a problem. Potential allergens can be identified by taking a careful history and carrying out selective prick skin tests or in vitro testing for specific IgE to allergens. Patients with significant food or aeroallergen allergy may benefit from diagnostic challenge and testing, dietary modification, and environmental control measures.

6. Management Successful?

Response to therapy may be classified as complete response, partial response,

or treatment failure. Complete response and eradication of the patient's eczema, over the short term, would be unusual unless there was a clear cut trigger, eg, a food allergen, that could be eliminated. Atopic dermatitis is a chronic relapsing skin condition; therefore, most patients will have a partial response with reduction in pruritus and extent of skin disease. These patients will need long-term follow-up for adjustment of their medications according to the severity of their illness (see annotations #5 & 7). Patients who fail to respond to treatment should be completely reassessed to be certain of the diagnosis and consider alternative treatment approaches (see annotation #8).

7. Follow-up

Follow-up should be established to monitor the patient's response to therapy and adjust medications and skin care according to severity of illness (see annotation #5 for treatment of mild, moderate, and severe AD). A plan should be established to step-up medications for flare-ups and to step-down on medications when the illness is under control.

8. Reassess Diagnosis of AD?

In any patient who fails to respond to treatment, it is important to reassess the diagnosis to be certain the patient simply has severe AD (refer to annotations #2, #3 and #10). The following may be helpful in the differential diagnosis:

- Most patients present with AD below the age of 5 years. Any patient presenting above the age of 16 years with eczema should be evaluated for contact dermatitis, initially with a careful history, and using patch testing to confirm possible allergens when appropriate. In patients presenting as adults, it is important to consider cutaneous T cell lymphoma;
- AD uncommonly presents under the age of 6 weeks. Any patient presenting with an eczematoid skin rash dating from the first month of life should be carefully followed for the

possibility of an immunodeficiency disorder particularly if the clinical course becomes complicated by recurrent infection and failure to thrive;

- AD does not exclusively affect the diaper area. In patients with diaper dermatitis, other causes of skin rash including infection or contact dermatitis must be considered;
- differentiating seborrheic dermatitis from AD may be difficult in an infant. Involvement of the top of the scalp (cradle cap), axilla, and diaper area makes it more likely the patient has seborrheic dermatitis whereas excoriated dermatitis involving the extensor surfaces, face, and trunk favor AD;
- consider the possibility of contact dermatitis to the topical therapy including allergy to a corticosteroid or a preservative in patients with well established AD who become resistant to therapy;
- Aside from *S. aureus* infections, it is important to consider other skin infections that may complicate AD. These include herpes simplex and dermatophyte infections. Appropriate cultures and skin scrapings may be helpful.

9. Further Evaluation and Consideration of Consultation

Consultation with an AD specialist is appropriate if the diagnosis of AD is in doubt (refer to annotation #2, #3, and #10).

10. Consultation with AD Specialist/Intensive Treatment of AD

The patient who does not respond to first line therapy (see annotation #5) is highly challenging and requires a multidisciplinary approach that may exceed the resources of the primary care physician. For these patients, consultation with an AD specialist who is skilled in the management of patients with severe atopic dermatitis can be beneficial. The management of severe AD is detailed in the preceding sections.

Wet dressings are recommended for use on severely affected or chronically involved areas of dermatitis refractory to skin care. A short course of oral corticosteroid therapy can be given to gain control of deteriorating severe acute AD. In such patients, it is important to limit the course of therapy, to taper the dosage as it is discontinued, and to intensify local skin care to avoid rebound. Ultraviolet light (UVB or PUVA) therapy may be a useful adjunctive modality in the treatment of chronic recalcitrant AD. Hospitalization should be carried out before considering other anti-inflammatory or immunologic therapies. In many cases, removing the patient from environmental allergens or emotional stressors, intense patient education, and assurance of compliance with therapy results in a sustained improvement in their skin disease. Clearing of their skin during hospitalization also allows the patient to undergo subsequent allergen skin testing, and controlled provocative challenges to correctly identify potential allergens.

For patients who are resistant to these approaches, investigational treatment should be considered. Evolving treatments include the use of interferon-gamma, systemic cyclosporin, topical FK-506, and phosphodiesterase inhibitors.

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