

Disease management of atopic dermatitis: an updated practice parameter

Donald Y. M. Leung, MD*; Richard A. Nicklas, MD†; James T. Li, MD‡; I. Leonard Bernstein, MD§; Joann Blessing-Moore, MD¶; Mark Boguniewicz, MD||; Jean A. Chapman, MD**;
David A. Khan, MD††; David Lang, MD‡‡; Rufus E. Lee, MD§§; Jay M. Portnoy, MD¶¶;
Diane E. Schuller, MD|||; Sheldon L. Spector, MD***; and Stephen A. Tilles, MD†††

TABLE OF CONTENTS

I. Preface.....	S1
II. Executive Summary.....	S2
III. Annotations to Figure 1.....	S4
IV. Summary Statements.....	S6
V. Definitions.....	S8
VI. Immunopathology.....	S8
VII. Clinical Diagnosis.....	S8
VIII. First-line Management and Treatment.....	S9
IX. Identification and Elimination of Triggering Factors.....	S13
X. Microbes.....	S14
XI. Emotional Stress.....	S15
XII. Patient Education.....	S15
XIII. Treatment of the Difficult-to-Manage Patient.....	S15
XIV. Acknowledgments.....	S17
XV. References.....	S17

PREFACE

Atopic dermatitis is an important component of the atopic diathesis. It not only frequently accompanies allergic respi-

ratory disease but often is the first manifestation of allergic disease. Most patients with atopic dermatitis will develop allergic rhinitis or asthma. The evaluation and management of atopic dermatitis are, therefore, an integral part of an allergist/immunologist's training and practice. It is also important for the primary care physician to understand the basis for effective evaluation and management of patients with this condition, since atopic dermatitis affects more than 10% of children and can have a significant impact on the patient's quality of life. As discussed in this document, it is also important for the primary care physician to know when to appropriately consult a specialist in atopic dermatitis.

* Division of Pediatric Allergy-Immunology, Department of Pediatrics, National Jewish Medical and Research Center and University of Colorado Health Sciences Center, Denver, Colorado.

† Department of Medicine, Uniformed Services, University of Health Sciences, George Washington University Medical Center, Bethesda, Maryland.

‡ Department of Medicine, Mayo Clinic and Foundation, Rochester, Minnesota.

§ Department of Medicine, Division of Immunology, University of Cincinnati College of Medicine, Cincinnati, Ohio.

¶ Department of Immunology, Stanford University Hospital, Palo Alto, California.

|| Division of Pediatric Allergy-Immunology, Department of Pediatrics, National Jewish Medical and Research Center and University of Colorado School of Medicine, Denver, Colorado

** Retired, Cape Girardeau, Missouri.

†† Department of Internal Medicine, Division of Allergy and Immunology, University of Texas Southwestern Medical Center, Dallas, Texas.

‡‡ Allergy/Immunology Section, Division of Medicine, Cleveland Clinic Foundation, Cleveland, Ohio.

§§ Private practice, Dothan, Alabama.

¶¶ Section of Allergy, Asthma & Immunology, Children's Mercy Hospital, Kansas City, Missouri.

|||Department of Pediatrics, Allergy, Immunology and Pulmonology, Penn State University, Milton S. Hershey Medical College, Hershey, Pennsylvania.

*** Department of Medicine, UCLA School of Medicine, and California Allergy and Asthma Medical Group, Los Angeles, California.

††† Asthma Inc, and Department of Medicine, University of Washington School of Medicine, Seattle, Washington.

This parameter was edited by Dr. Nicklas in his private capacity and not in his capacity as a medical officer with the Food and Drug Administration. No official support or endorsement by the Food and Drug Administration is intended or should be inferred.

Received and accepted for publication January 14, 2004.

Since the initial Parameter on Atopic Dermatitis was published in 1997, there have been remarkable advances in the understanding of the pathophysiology of atopic dermatitis.¹ The pathogenesis of atopic dermatitis involves a complex inflammatory process, our understanding of which is constantly undergoing revision, as more data become available on the role of IgE-bearing Langerhans cells, atopic keratinocytes, monocytes/macrophages, eosinophils, and mast cells and their interaction with interleukin 4 (IL-4), IL-5, and IL-13 producing T_H2 lymphocytes. There is a complicated interaction between these cells and their products and susceptibility genes and the host environment, which leads to the clinical findings that characterize atopic dermatitis.

The major objective of the parameter, *Disease Management of Atopic Dermatitis: An Updated Practice Parameter*, is to improve the care of patients with atopic dermatitis. This should be accomplished by establishing boundaries for the evaluation and management of patients with this condition while reducing unwanted and unnecessary variations in treatment.

This updated Parameter on Atopic Dermatitis was developed by the Joint Task Force on Practice Parameters, which has published 11 practice parameters for the field of allergy/immunology, including the original Parameter on Atopic Dermatitis. The 3 national allergy and immunology societies, the American College of Allergy, Asthma and Immunology (ACAAI), the American Academy of Allergy, Asthma, and Immunology (AAAAI), and the Joint Council of Allergy, Asthma and Immunology (JCAAI), have given the Task Force the responsibility for updating existing parameters. This document builds on the original Parameter on Atopic Dermatitis. It was written and reviewed by subspecialists in allergy and immunology and was funded by the 3 allergy and immunology organizations noted above.

Donald Y. M. Leung, MD, PhD, who chaired the workgroup that developed the original Parameter on Atopic Dermatitis, prepared the initial draft of the updated parameter on this condition. The Joint Task Force revised the initial draft into a working draft of the document, which included a review of the medical literature using a variety of search engines such as PubMed. Published clinical studies were rated by category of evidence and used to establish the strength of a clinical recommendation (Table 1). The working draft of the updated Parameter on Atopic Dermatitis was then reviewed by a number of experts in allergy and immunology and specifically by experts on atopic dermatitis. This document, therefore, represents an evidence-based, broadly accepted consensus opinion.

The updated Parameter on Atopic Dermatitis contains an annotated algorithm that presents the major decision points for the appropriate evaluation and management of atopic dermatitis (Fig 1). Also included in this parameter are summary statements, which represent the key points in the evaluation and management of atopic dermatitis. These summary statements appear again before each section in this document, followed by text that supports the summary statement(s). There are sections on Definitions, Immunopathology, Clinical

Table 1. Classification of Evidence and Recommendations*

Category of evidence	
Ia	Evidence from meta-analysis of randomized controlled trials
Ib	Evidence from at least 1 randomized controlled trial
IIa	Evidence from at least 1 controlled study without randomization
IIb	Evidence from at least 1 other type of quasi-experimental study
III	Evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities or both
LB	Evidence from laboratory-based studies†
Strength of recommendation	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated from category I evidence
C	Directly based on category III evidence or extrapolated from category I or II evidence
D	Directly based on category IV evidence or extrapolated from category I, II, or III evidence
E	Directly based on category LB evidence†
F	Based on consensus of the Joint Task Force on Practice Parameters†

*Data are from Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. *BMJ*. 1999;318:593–596.

† Added by current authors.

Diagnosis, First-line Management and Treatment, Identification and Elimination of Triggering Factors, Microbes, Emotional Stress, Patient Education, and Treatment of the Difficult-to-Manage Patient.

There are a number of legitimate reasons for the development of practice parameters that affect the interaction with managed care and health care providers; education of medical students, interns, residents, and fellows; and the establishment of boundaries and support for the practicing physician. The primary reason for developing practice parameters, however, must always be to improve the quality of care for the patient. If used appropriately, this updated Parameter on Disease Management of Atopic Dermatitis will be another step toward achieving that goal.

EXECUTIVE SUMMARY

Atopic dermatitis is a genetically transmitted, chronic inflammatory skin disease that affects 10% to 20% of children and 1% to 3% of adults.¹ The vast majority of patients develop the disease before the age of 5 years, although it can also present in adulthood.² Atopic dermatitis is the first manifestation of atopy in many patients who later develop allergic rhinitis and/or asthma,³ a pattern that has been referred to epidemiologically as “the atopic march.” Pruritus, scratching, and chronic and/or relapsing eczematous lesions are major hallmarks of the disease. In infants and young children, there is a characteristic pattern of involvement of the face, neck, and extensor skin surfaces. In older children and adults, the skin lesions often involve lichenification and are usually localized to the flexural folds of the extremities. Factors that may

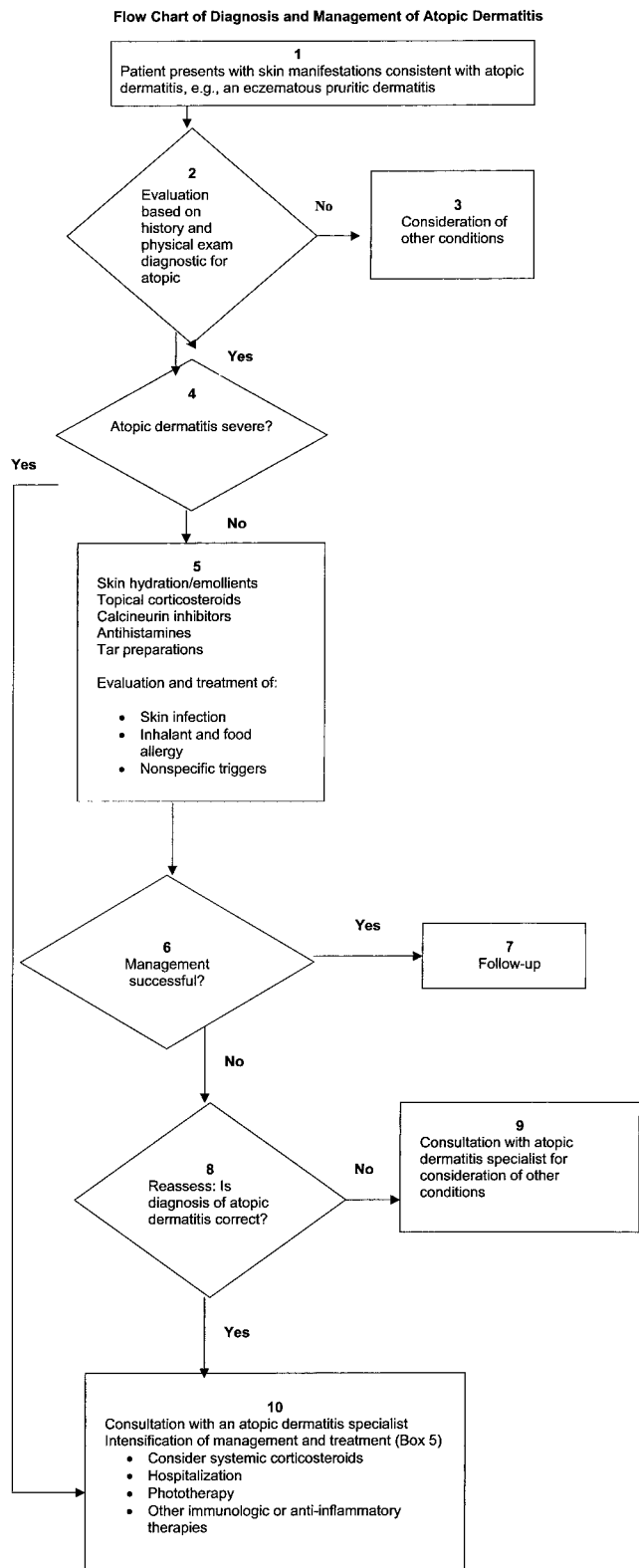


Figure 1. Flow chart of diagnosis and management of atopic dermatitis.

exacerbate symptoms in atopic dermatitis patients include temperature, humidity, irritants, infections, food, inhalant and contact allergens, and emotional stress.⁴ Food allergy has been implicated in approximately one third of children with atopic dermatitis, although specific IgE is often present without clear relevance to the disease process.⁵

The pathogenesis of atopic dermatitis involves a complex interaction between genetic and environmental factors. Xerosis, scratching, and both colonization^{2,6-8} and infection⁹ of the skin by *Staphylococcus aureus* all contribute to the disease process. As with allergic rhinitis and asthma, the inflammatory reaction in atopic dermatitis involves T_H2 lymphocyte activation, resulting in the production of IL-4, IL-5, and IL-13.² Other cells involved in this inflammation include IgE-bearing Langerhans cells, atopic keratinocytes, lymphocytes, monocytes/macrophages, eosinophils, and mast cells.¹⁰⁻¹²

The diagnosis of atopic dermatitis is based on its clinical presentation rather than diagnostic testing.¹³ However, the judicious use of percutaneous skin tests or in vitro testing for the presence of specific IgE to relevant allergens is a sensitive way of identifying potential allergic triggering factors. Double-blind food challenges are sometimes necessary to determine the relevance of specific food ingestion to symptoms.¹⁴

The effective management of atopic dermatitis involves some combination of trigger avoidance,¹⁴⁻¹⁶ measures to restore skin barrier function, and anti-inflammatory medication.⁴ Trigger avoidance should be individualized based on a careful history and the results of specific IgE testing. Barrier function can be improved by careful hydration and emollient application, such as soaking in a lukewarm bath for 20 to 30 minutes followed by the immediate application of an emollient.¹⁷

There are multiple anti-inflammatory medication options available for treating atopic dermatitis. Topical corticosteroids are appropriate for the vast majority of patients, and the potency of the corticosteroid agent chosen should be individualized based on the severity of the dermatitis, the location of the affected skin, the surface area of the affected skin, and the age of the patient.⁴ Clinical exacerbations may require temporarily switching to a more potent topical agent or using a tapering course of a systemic corticosteroid. Tacrolimus and pimecrolimus are anti-inflammatory calcineurin inhibitors and alternatives to corticosteroids that have been recently approved for topical use in adults and children with atopic dermatitis.¹⁸⁻²¹ These agents interrupt activation of lymphocytes and other inflammatory cells,^{18,22} and to date they have been very well tolerated.²³⁻²⁶

There are a variety of other treatment options for patients with severe or refractory atopic dermatitis. These include wet dressings and occlusion,^{27,28} phototherapy,²⁹ systemically administered immunosuppressants such as cyclosporin²⁷ or interferon gamma,³⁰ and antimetabolites.^{31,32} In rare cases, short-term hospitalization is a useful way to temporarily reduce exposure to environmental and emotional triggers while initiating intensive patient education, diagnostic testing

(such as skin testing and food challenges), and aggressive medical treatment.

ANNOTATIONS TO FIGURE 1

Annotation 1: Patient Presents with Skin Manifestations Consistent with Atopic Dermatitis (eg, an Eczematous Pruritic Dermatitis)

There is no objective laboratory test for the diagnosis of atopic dermatitis. Therefore, the diagnosis of atopic dermatitis is based on a constellation of clinical features. These include (1) the essential feature, which is a pruritic dermatitis; (2) typical features, such as facial and extensor eczema in infants and children, flexural eczema in adults, and chronic or relapsing dermatitis; (3) frequently associated features, such as personal or family history of atopic disease, xerosis, cutaneous infections, nonspecific dermatitis of the hands or feet, elevated serum IgE levels, frequent occurrence of nonspecific decrease in cell-mediated immune response (anergy), positive immediate-type allergy skin tests and early age of onset; and (4) other features, such as white dermatographism and delayed blanch response, anterior subcapsular cataracts, keratoconus, Dennie-Morgan infraorbital folds, orbital darkening, facial erythema, or pallor.

Annotation 2: Evaluation Based on History and Physical Examination Diagnostic for Atopic Dermatitis?

Atopic dermatitis often is associated with an early age of onset, with approximately 80% of cases starting before the age of 5 years. It frequently is associated with respiratory allergy and a number of other features, such as Dennie-Morgan infraorbital folds, white dermatographism, and facial pallor.

Acute and subacute lesions of atopic dermatitis are characterized by intensely pruritic, erythematous papulovesicles associated with excoriation and serous exudate. Lesions that do not appear papulovesicular clinically must demonstrate spongiosis histologically. Chronic atopic dermatitis is characterized by lichenification, papules, and excoriations. At all stages of atopic dermatitis, patients usually have dry skin. The distribution and skin reaction pattern vary according to the patient's age and disease activity. The skin distribution pattern in infants and young children generally involves the face, neck, and extensor skin surfaces. In contrast, in older children and adults who have long-standing skin disease, lichenification and localization of the rash to the flexural folds of the extremities usually are found. Chronic hand (and/or foot) eczema may be the primary or sole manifestation of many atopic adults.

Annotation 3: Consideration of Other Conditions

A firm diagnosis of atopic dermatitis depends on the exclusion of other skin conditions with similar symptoms and signs. Failure of any response to "standardized" management of atopic dermatitis is a reason to consider other eczematous conditions. Skin conditions that may mimic atopic dermatitis fall into the following categories: (1) chronic dermatoses,

such as seborrheic and contact dermatitis, nummular eczema, psoriasis, and ichthyoses; (2) infections and infestations such as scabies, human immunodeficiency virus, and dermatophytosis; (3) malignancies, such as cutaneous T-cell lymphoma and Letterer-Siwe disease; (4) immunologic disorders, such as dermatitis herpetiformis, graft-vs-host disease, and dermatomyositis; (5) immunodeficiencies, such as Wiskott-Aldrich, severe combined immunodeficiency disease, hyper-IgE, and DiGeorge syndrome; and (6) metabolic disorders, such as zinc, pyridoxine, or niacin deficiency and phenylketonuria. In situations in which the diagnosis is not obvious, a skin biopsy should be considered. The skin biopsy should be performed by a physician trained and experienced in performing the procedure and should be interpreted by a qualified dermatopathologist.

Annotation 4: Is the Atopic Dermatitis Severe?

Severe atopic dermatitis is characterized by intensely pruritic, widespread skin lesions that often are complicated by persistent bacterial, viral, or fungal infections. The presence of keratoconus, keratoconjunctivitis, anterior cataracts, and eczema vaccinatum suggests that the atopic dermatitis is particularly severe, which may be related to chronicity.

The extent and severity of atopic dermatitis can be determined by careful examination of the patient's skin, grading the extent of affected areas (eg, percentage of involvement of the head, upper limbs, trunk, and lower limbs), and defining the severity of the following signs of eczema: induration, erythema, excoriation, lichenification, scaling, oozing, weeping, and crusting. In general, 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 should be considered for consultation with a specialist. Other patients who should be considered as having severe atopic dermatitis include:

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

Patients not previously receiving appropriate treatment for atopic dermatitis should be started on first-line therapy, and attempts should be made to identify potential triggers.

Annotation 5: Management of Atopic Dermatitis

The treatment of atopic dermatitis 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. 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 atopic dermatitis.

The severity of atopic dermatitis 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.

The initial management of atopic dermatitis may consist of the following categories of treatment: hydration, topical corticosteroids, topical calcineurin inhibitors, tar preparations, and antihistamines.

Tacrolimus, a calcineurin inhibitor, has been shown to be effective and safe for use in atopic dermatitis. Most patients experience a dramatic reduction of pruritus within 3 days of initiating treatment, as well as significant improvement in quality of life. Pimecrolimus also has been shown to be effective and safe for the treatment of atopic dermatitis. When used as long-term maintenance therapy, topical preparations of this drug reduce the number of flares of atopic dermatitis and the requirement for corticosteroid treatment.

There are many factors that may contribute to exacerbations of atopic dermatitis, including food allergens, aeroallergens, infections, temperature, humidity, irritants, and emotional stress.

Skin testing or in vitro testing for IgE antibodies 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 as a cause of atopic dermatitis. Positive skin test results or in vitro test results do not prove that a particular allergen causes clinical symptoms, but they may guide the clinician in considering possible causes. This is particularly true in the case of foods, where controlled food challenges or elimination diets may be needed to confirm or exclude clinical sensitivity to foods.

Skin infections should be treated with short courses of appropriate antimicrobial therapy, with an emphasis on appropriate treatment for staphylococcal infections. Herpetic and dermatophytic infections also need to be considered and treated after appropriate diagnosis has been confirmed.

Annotation 6: Is the Management Successful?

Response to therapy may be classified as a complete response, a partial response, or a treatment failure. Complete response and eradication of the patient's eczema, in the short term, is unusual unless there is a clear-cut trigger (eg, a food allergen that could be eliminated). Atopic dermatitis is a chronic relapsing skin condition, and therefore most patients will have a partial response with reduction in pruritus and the extent of skin disease. These patients will need long-term follow-up for adjustment of medications according to the severity of the illness. Patients who do not respond to treatment should be completely reassessed to be certain of the diagnosis, and alternative treatment should be considered.

Annotation 7: Follow-up

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, and general information about the disease should be provided. Patients should be educated on how to monitor their 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 and/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. Follow-up of patients with atopic dermatitis also should include evaluation for potential triggers of exacerbations (eg, aeroallergens, infection, emotional factors) and cooperative management with the patient and/or parent to prevent such exacerbations.

Annotation 8: Reassess: Is Diagnosis of Atopic Dermatitis Correct?

In patients who do not achieve the goals of atopic dermatitis management, it is important to reassess whether the diagnosis is correct. With the lack of a characteristic skin lesion or a confirmatory laboratory test result, the diagnosis depends on clinical symptoms and the physical examination. Concomitant allergic rhinitis and/or asthma increase the likelihood that the diagnosis of atopic dermatitis is correct. As discussed in annotation 1, many skin conditions may masquerade as atopic dermatitis.

When reassessing patients, it is helpful to consider the following points. Most patients who present with atopic dermatitis are younger than 5 years but are infrequently younger than 6 weeks. Any infant with an eczematous rash presenting earlier than the first month of life should be carefully evaluated for the presence of congenital immunodeficiency, particularly if the course is complicated by recurrent infections and failure to thrive. Atopic dermatitis does not usually affect the diaper area or the nose exclusively. Differentiation of seborrheic dermatitis from atopic dermatitis may be difficult in infants. It is important to consider contact dermatitis and skin infections as complicating factors.

Annotation 9: Consultation with an Atopic Dermatitis Specialist for Consideration of Other Conditions

Patients who are refractory to first-line therapy and who have severe atopic dermatitis with significant dysfunction should have a consultation with an atopic dermatitis specialist, such as an allergist or dermatologist. Such consultation is recommended when the diagnosis of atopic dermatitis is in doubt and for identification of potential allergen triggers, patient education, and implementation of alternative therapies, including potent anti-inflammatory and immunomodulatory agents.

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. Even when an atopic dermatitis specialist is consulted, the primary care physician continues to play an important role in the care of patients with atopic dermatitis by ensuring continuity of care.

Annotation 10: Consultation with an Atopic Dermatitis Specialist: Intensification of Management and Treatment

When atopic dermatitis is either severe or has not responded to appropriate first-line management strategies, specialist consultation should be obtained. This allows both a reevaluation of first-line treatment approaches (eg, hydration, emollients, topical corticosteroids, pimecrolimus, tacrolimus, and tar preparations) and consideration of alternative therapy. Examples of alternative strategies include (1) the application of wet dressings in combination with topical corticosteroids; (2) short-term treatment with systemic corticosteroids with appropriate tapering to avoid rebound; (3) phototherapy with ultraviolet light (UV-B or UV-A [PUVA]); (4) immunomodulatory or immunosuppressive agents; (5) hospitalization to separate the patient from environmental allergens while administering other therapies; and (6) allergen immunotherapy when aeroallergens are clearly implicated in dermatitis flares. In light of potential adverse effects, a careful risk-benefit analysis should be undertaken before initiating any of these alternative therapies. For patients who do not respond to these approaches, investigational treatment can be considered.

SUMMARY STATEMENTS

Definitions

Summary statement 1. Atopic dermatitis is a familial, chronic inflammatory skin disease that commonly presents during early infancy and childhood but can persist or start in adulthood. (C)

Immunopathology

Summary statement 2. Most individuals with atopic dermatitis have elevated serum IgE levels, which are often very high. (C)

Summary statement 3. Pathogenesis of atopic dermatitis involves a complex inflammatory process associated with IgE-bearing Langerhans cells, atopic keratinocytes, lymphocytes, monocytes/macrophages, eosinophils, and mast cells. (C)

Summary statement 4. There is an increased frequency of T_H2 cells producing IL-4, IL-5, and IL-13, but little interferon- γ has been found in the peripheral blood and acute skin lesions of patients with atopic dermatitis. The clinical manifestations of atopic dermatitis result in large part from stimulation of the T_H2 wing of the immunologic pathways. (C)

Summary statement 5. There is a complex interaction among susceptibility genes, the host environment, and multiple immunologic cells, leading to acute and chronic lesions that characterize this skin disease. (B)

Clinical Diagnosis

Summary statement 6. There is no objective diagnostic test for the clinical confirmation of atopic dermatitis. (D)

Summary statement 7. The diagnosis of atopic dermatitis is based on a constellation of clinical features. (D)

Summary statement 8. Pruritus and chronic or relapsing eczematous lesions with typical morphology and distribution in patients with a history of atopy are essential for diagnosis. (F)

Summary statement 9. Acute and subacute skin lesions are most often seen in infants and young children and are characterized by intensely pruritic erythematous papulovesicular lesions associated with excoriation and serous exudate. (D)

Summary statement 10. Chronic atopic dermatitis is characterized by lichenification, papules, and excoriations. (D)

First-line Management and Treatment

Summary statement 11. The intensity of management and treatment of atopic dermatitis is dictated by the severity of illness, which relates to the effect of atopic dermatitis on the quality of life of the patient and his or her family. (A)

Summary statement 12. Successful management requires a systematic, multipronged approach that includes antipruritic therapy, skin hydration, topical anti-inflammatory medications, and the identification and possible elimination of exacerbating factors. (A)

Skin Hydration

Summary statement 13. Atopic dermatitis is characterized by reduced skin barrier function due to loss of vital lipids, which leads to enhanced water loss and dry skin. (E)

Summary statement 14. Moisturizers such as lukewarm soaking baths for at least 20 minutes followed by the application of an occlusive emollient to retain moisture can give the patient symptomatic relief. (D)

Summary statement 15. Emollients, available in the form of lotions, creams, and ointments, should be used as first-line therapy. (D)

Topical Corticosteroids

Summary statement 16. Topical corticosteroids, applied to areas of eczema, are effective treatment for atopic dermatitis. (A)

Summary statement 17. Low-potency corticosteroids are recommended for maintenance therapy, whereas intermediate- and high-potency corticosteroids should be used for the treatment of clinical exacerbation and applied to affected areas of skin over short periods of time. (A)

Summary statement 18. Potent fluorinated corticosteroids should be avoided on the face, the eyelids, the genitalia, and the intertriginous areas, as well as in young infants. (D)

Summary statement 19. Ultrahigh-potency corticosteroids should be used only for very short periods of time (several days) and only in areas that are lichenified. (D)

Summary statement 20. 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. (D)

Topical Calcineurin Inhibitors

Tacrolimus

Summary statement 21. Tacrolimus ointment has been shown to be effective and safe in both adults and children for the treatment of mild-to-moderately severe atopic dermatitis, with most patients experiencing a reduction of pruritus within 3 days of initiating therapy. (A)

Summary statement 22. Tacrolimus ointment applied on up to 100% of the body surface in adults and children has demonstrated sustained efficacy with no significant systemic adverse effects. (A)

Summary statement 23. A local burning sensation is the most common adverse effect associated with tacrolimus. This may limit its usefulness in certain patients. (A)

Summary statement 24. Tacrolimus ointment can be used safely for facial and eyelid eczema. (D)

Pimecrolimus

Summary statement 25. Topical pimecrolimus cream is a calcineurin inhibitor that decreases the number of flares of atopic dermatitis, reduces the need for corticosteroids, and controls pruritus. (A)

Tar Preparations

Summary statement 26. Although tar preparations are widely used in the treatment of atopic dermatitis, there are no randomized, controlled studies that have demonstrated their efficacy. (A)

Summary statement 27. Newer coal tar products have been developed that are more cosmetically acceptable, with respect to odor and staining of clothes, than some older products. (B)

Summary statement 28. Tar preparations should not be used on acutely inflamed skin, since this may result in additional skin irritation. (D)

Antihistamines

Summary statement 29. Some patients may benefit from the use of antihistamines for the relief of pruritus associated with atopic dermatitis. (C)

Summary statement 30. Treatment of atopic dermatitis with topical antihistamines is generally not recommended because of potential cutaneous sensitization. (C)

Identification and Elimination of Triggering Factors

Summary statement 31. Avoidance of common irritants (eg, soaps, toiletries, wool, chemicals) that trigger the itch-scratch cycle is recommended. (B)

Summary statement 32. Control of temperature and humidity may be useful for preventing pruritus. (D)

Summary statement 33. Aeroallergens such as house dust mites, animal allergens, and pollens may cause exacerbation, and therefore exposure to them should be minimized. (A)

Summary statement 34. Possible allergenic triggers of atopic dermatitis can be confirmed by skin tests and in vitro tests for specific IgE antibodies and in some cases by patch tests that may produce immediate or delayed reactions to protein allergens. (B)

Summary statement 35. Food allergens trigger atopic dermatitis more commonly in young infants and children than in adults. (D)

Microbes

Summary statement 36. Patients with moderate-to-severe atopic dermatitis have been found to make IgE antibodies against staphylococcal toxins present on their skin. (B)

Summary statement 37. A course of an appropriate systemic antibiotic should be considered in patients who are heavily colonized or infected with staphylococcal *aureus*. Antibiotic treatment may be more difficult if staphylococcal *aureus* is resistant. (D)

Summary statement 38. Atopic dermatitis can be complicated by recurrent viral skin infections, such as herpes simplex, warts, and molluscum contagiosum. (D)

Summary statement 39. Smallpox vaccination or even exposure of patients with atopic dermatitis to recently vaccinated individuals may cause a severe, widespread, potentially fatal dermatitis called *eczema vaccinatum*, which is similar in appearance to *eczema herpeticum*. (C)

Summary statement 40. Dermatophytic infections can complicate atopic dermatitis and may contribute to exacerbation (D) of disease activity. (LB)

Emotional Stress

Summary statement 41. Emotional factors do not cause atopic dermatitis but often cause exacerbation and have been found to induce immune activation as well as increase pruritus and scratching. (D)

Patient Education

Summary statement 42. To achieve effective control of atopic dermatitis, it is important to educate patients and family members about the chronic nature of atopic dermatitis, exacerbating factors, and appropriate treatment options, including patient support organizations to enhance adherence. (B)

Treatment of the Difficult-to-Manage Patient

Wet dressing and occlusion

Summary statement 43. Wet dressings may serve as an effective barrier against persistent scratching, allowing more rapid healing of excoriated lesions. (B)

Summary statement 44. Application of wet-wrap dressings in combination with topical corticosteroids can be efficacious in the treatment of refractory atopic dermatitis. (A)

Allergen immunotherapy

Summary statement 45. Although the effectiveness of allergen immunotherapy in the treatment of atopic dermatitis has not been conclusively demonstrated, there are selected patients with atopic dermatitis who may benefit from such treatment. (F)

Systemic corticosteroids

Summary statement 46. The use of systemic corticosteroids may be required in the treatment of severe, recalcitrant chronic atopic dermatitis. (F)

Summary statement 47. The dramatic clinical improvement that may occur after administration of systemic corticosteroids may be associated with an equally dramatic rebound flaring of atopic dermatitis following discontinuation of systemic corticosteroids. (D)

Phototherapy

Summary statement 48. Natural sunlight can be beneficial for atopic dermatitis, but sunburn and overheating should be avoided. (A)

Summary statement 49. Ultraviolet therapy can be a useful adjunct in the treatment of recalcitrant atopic dermatitis. (D)

Summary statement 50. Phototherapy with PUVA should be restricted to patients with recalcitrant atopic dermatitis. (B)

Systemic immunomodulating agents

Summary statement 51. Immunosuppressive agents such as cyclosporin, interferon gamma, mycophenolate mofetil, and azathioprine have been shown to provide benefit for certain cases of severe refractory atopic dermatitis, but potential benefits should be weighed against their potentially serious adverse effects. (F)

Hospitalization

Summary statement 52. Hospitalization can result in an improvement in atopic dermatitis by removing the patient from environmental allergens and irritants and by providing patient education and improving compliance. (D)

Investigative approaches

Summary statement 53. There are certain investigative treatments that have been proposed for the management of atopic dermatitis. These remain unproven at this time. (D)

Consultation with an atopic dermatitis specialist

Summary statement 54. Patients refractory to first-line therapy should be evaluated by an atopic dermatitis specialist. (F)

DEFINITIONS

Summary statement 1. Atopic dermatitis is a familial, chronic inflammatory skin disease that commonly presents during early infancy and childhood but can persist or start in adulthood. (C)

Atopic dermatitis is a familiarly transmitted, chronic inflammatory skin disease that commonly presents during early infancy and childhood but can persist or start in adulthood.² It often presents as the first step in the atopic march toward respiratory allergy. Recent interest in atopic dermatitis has been sparked by reports of its increasing prevalence and the significant adverse impact it can have on quality of life. Atopic dermatitis is a major public health problem worldwide, with a lifetime prevalence in children of 10% to 20%.¹ The prevalence of atopic dermatitis in adults is approximately 1% to 3%. Wide variations in prevalence have been observed

within countries inhabited by similar ethnic groups, suggesting that environmental factors determine atopic dermatitis expression.³³

IMMUNOPATHOLOGY

Summary statement 2. Most individuals with atopic dermatitis have elevated serum IgE levels, which are sometimes extremely high. (C)

Summary statement 3. Pathogenesis of atopic dermatitis involves a complex inflammatory process associated with IgE-bearing Langerhans cells, atopic keratinocytes, lymphocytes, monocytes/macrophages, eosinophils, and mast cells. (C)

Summary statement 4. There is an increased frequency of T_H2 cells producing IL-4, IL-5, and IL-13, but little interferon- γ has been found in the peripheral blood and acute skin lesions of patients with atopic dermatitis. The clinical manifestations of atopic dermatitis result in large part from stimulation of the T_H2 wing of the immunologic pathways. (C)

Summary statement 5. There is a complex interaction between susceptibility genes, the host environment, and multiple immunologic cells, leading to acute and chronic lesions that characterize this skin disease. (B)

Since the initial Joint Task Force Practice Parameters on Atopic Dermatitis was published,³⁴ there have been remarkable advances in our understanding of the pathophysiology of atopic dermatitis. Nearly 80% of patients with atopic dermatitis develop allergic rhinitis or asthma. In such patients, atopic dermatitis may be considered the skin manifestation of a systemic allergic response.³ An increased frequency of T_H2 cells producing IL-4, IL-5, and IL-13 but little interferon- γ has been found in the peripheral blood and acute skin lesions of patients with atopic dermatitis.¹⁰ This likely contributes to the increased eosinophilia and IgE sensitization to factors in the host environment that characterize most patients with atopic dermatitis. The development of T_H2 cells in atopic dermatitis is related to several factors, including (1) the cytokine microenvironment in which T-cell development takes place; (2) allergic mediators; (3) the costimulatory signals used during T-cell activation; and (4) the antigen-presenting cell.³⁵⁻⁴⁰ There has been considerable interest in the unique features of IgE-bearing Langerhans cells and atopic keratinocytes in promoting the skin lesions of atopic dermatitis.^{11,12}

The picture that has emerged of the pathogenesis of atopic dermatitis involves a complex interaction between susceptibility genes, the host environment, and multiple immunologic cells, resulting in the acute and chronic skin lesions that characterize this skin disease. Effective therapy requires a multipronged approach to reduce environmental triggers and skin inflammation and restore skin barrier function.

CLINICAL DIAGNOSIS

Summary statement 6. There is no objective diagnostic test for the clinical confirmation of atopic dermatitis. (D)

Summary statement 7. The diagnosis of atopic dermatitis is based on a constellation of clinical features. (D)

Summary statement 8. Pruritus and chronic or relapsing eczematous lesions with typical morphology and distribution in patients with a history of atopy are essential for diagnosis. (F)

Summary statement 9. Acute and subacute skin lesions are most often seen in infants and young children and are characterized by intensely pruritic erythematous papulovesicular lesions associated with excoriation and serous exudate. (D)

Summary statement 10. Chronic atopic dermatitis is characterized by lichenification, papules, and excoriations. (D)

At the initial encounter with any patient seeking treatment for atopic dermatitis, particularly if poorly controlled, it is essential to confirm that the correct diagnosis has been made. There is no objective diagnostic test for the clinical confirmation of atopic dermatitis. Therefore, the diagnosis of atopic dermatitis is based on the constellation of clinical features.¹³ Of the major features, pruritus and chronic or relapsing eczematous lesions with typical morphology and distribution are essential for diagnosis. Although pruritus may occur throughout the day, it is usually worse in the early evening and night. Its consequences are scratching followed by the elicitation of eczematous skin lesions.

Acute and subacute skin lesions are characterized by intensely pruritic, erythematous papulovesicles associated with excoriation, and serous exudate. Chronic atopic dermatitis is characterized by lichenification, papules, and excoriations. Patients usually have dry, pale, pasty skin. The distribution and skin reaction pattern vary according to the patient's age, disease activity, and accessibility to scratching. In infants and young children, the rash generally involves the face, neck, and extensor skin surfaces. In older children and adults who have long-standing skin disease, lichenification and localization of the rash to the flexural folds of the extremities are common. Chronic hand eczema may be the primary manifestation in many adults with a history of atopic dermatitis.

Atopic dermatitis is often associated with an early age of onset, with most cases starting before the age of 5 years. Atopic dermatitis can be triggered by IgE-mediated events in many patients, but it can be triggered in some patients by non-IgE-mediated events.^{2,41} Therefore, although respiratory allergy is an important associated condition in patients with atopic dermatitis, it is not essential for diagnosis of this condition. Although a number of other features, such as Dennie-Morgan infraorbital folds, white dermatographism, or facial pallor, can be seen, they are too nonspecific for use in making a diagnosis of atopic dermatitis. A firm diagnosis of atopic dermatitis depends on the exclusion of other skin conditions that share symptoms and signs.

FIRST-LINE MANAGEMENT AND TREATMENT

Summary statement 11. The intensity of management and treatment of atopic dermatitis is dictated by the severity of illness, which relates to the effect of atopic dermatitis on the quality of life of the patient and his or her family. (A)

Summary statement 12. Successful management requires a systematic, multipronged approach that includes antipruritic therapy, skin hydration, topical anti-inflammatory medications, and the identification and possible elimination of exacerbating factors. (A)

The intensity of management and treatment is dictated by the severity of illness and its effect on the patient and immediate family. Successful management requires a systematic, multipronged approach that includes skin hydration, topical anti-inflammatory medications, and the identification and possible elimination of exacerbating factors, including irritants, allergens, emotional stressors, and infectious agents.⁴ 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 be exposed to both exogenous (eg, humidity, allergens) and endogenous (eg, stress) 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 frequently will experience an accentuation of their itching during times of stress and/or exposure to specific allergens. 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.

Skin Hydration

Summary statement 13. Atopic dermatitis is characterized by reduced skin barrier function due to loss of vital lipids, which leads to enhanced water loss and dry skin. (E)

Summary statement 14. Moisturizers such as lukewarm soaking baths for at least 20 minutes followed by the application of an occlusive emollient to retain moisture can give the patient symptomatic relief. (D)

Summary statement 15. Emollients, available in the form of lotions, creams, and ointments, should be used as first-line therapy. (D)

Atopic dermatitis is characterized by reduced skin barrier function. This is likely due, at least in part, to high expression of sphingomyelin deacylase, which decreases ceramide levels in atopic dermatitis skin.^{42,43} The loss of vital skin lipids results in enhanced transepidermal water loss and dry skin (xerosis). Application of ceramide-rich lipids may improve skin barrier function and reduce the severity of atopic dermatitis.⁴⁴ Xerosis contributes to the development of epithelial microfissures and cracks, which favor the entry of skin microbes and allergens. This problem usually becomes exacerbated during the dry winter months and aggravated in certain work environments. Lukewarm soaking baths for at least 20 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 pru-

ritus of atopic dermatitis, while maintaining a soft texture to the skin.⁴⁵ They offer a particular advantage when applied immediately after bathing to maintain hydration of the epidermis.

Emollients are available in the form of lotions, creams, and ointments. Lotions and creams may be irritating due to preservatives, solubilizers, and fragrances. Lotions also contain water and may be drying due to an evaporative effect. 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. An increased incidence of peanut allergy has been reported in children in the United Kingdom using emollients with refined peanut oil for atopic dermatitis.⁴⁵

Topical Corticosteroids

Summary statement 16. Topical corticosteroids, applied to areas of eczema, are effective treatment for atopic dermatitis. (A)

Summary statement 17. Low-potency corticosteroids are recommended for maintenance therapy, whereas intermediate- and high-potency corticosteroids should be used for the treatment of clinical exacerbation over short periods of time. (A)

Summary statement 18. Potent fluorinated corticosteroids should be avoided on the face, the eyelids, the genitalia, and the intertriginous areas, as well as in young infants. (D)

Summary statement 19. Ultrahigh-potency corticosteroids should be used only for very short periods (several days) and only in areas that are lichenified. (D)

Summary statement 20. 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, thickness of the skin, the use of occlusive dressing, and the potency of the corticosteroid preparation. (D)

Corticosteroids are effective medications for the treatment of atopic dermatitis.⁴ However, patients should be carefully instructed in their use to avoid potential adverse effects. Certain areas, including the mucous membranes, the genitalia, the eyelids, the face, and intertriginous areas, have increased potential for transepidermal corticosteroid penetration, and for this reason, potent fluorinated corticosteroids should be avoided in these areas. A low-potency corticosteroid preparation is generally recommended for these areas. Patients should be instructed to apply topical corticosteroids to skin lesions and to use emollients over uninvolved skin. There are 7 classes of topical corticosteroids ranked according to their potency based on vasoconstrictor assays. Some of the commonly used ones are listed in Table 2. Group I includes the superpotent topical corticosteroids with the greatest potential for adverse effects, both localized and systemic. Group VII includes the least potent topical corticosteroids and, as a group, has the least potential for adverse effects. More potent topical corticosteroids may be used for

several days in nonfacial, nonskinfold areas to treat acute rashes. Patients should then be instructed to reduce the potency of topical corticosteroids applied to their skin.

Because of their potential adverse effects, the ultrahigh-potency corticosteroids should be used for only very short periods of time and in areas that are lichenified and not on facial or skinfold areas. The high-potency corticosteroids should only be used for short periods of time (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 gel formulations usually contain a propylene glycol base and are irritating to the skin, in addition to promoting dryness, limiting their use to the scalp and beard areas. Compared with topical creams, ointments have enhanced topical potency.

Adverse effects from topical corticosteroids are directly related to the potency ranking of the compound and the duration of use. It is incumbent on the clinician to balance the need for therapeutic potency with the potential for adverse effects. Adverse effects from topical corticosteroids can be divided into local and systemic adverse effects. The latter, which occurs rarely, includes suppression of the hypothalamic-pituitary-adrenal axis. Local adverse effects include the development of striae and atrophy of the skin, perioral dermatitis, rosacea, and allergic contact dermatitis (due to the vehicle in most cases and after use of nonfluorinated corticosteroids). Systemic adverse effects are related to the potency of the topical corticosteroid, 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.^{46,47}

Recent studies with 2 newer topical corticosteroids (fluticasone propionate and mometasone furoate) suggest that they have less systemic absorption and an efficacy profile that allows them to be used once as opposed to twice daily.^{48,49} Furthermore, it has been reported that once control of atopic dermatitis is achieved with a daily regimen of topical corticosteroid, long-term control can be maintained with twice-weekly applications of topical fluticasone propionate to areas that have healed but are prone to developing eczema.⁵⁰

Topical Calcineurin Inhibitors

Topical tacrolimus

Summary statement 21. Tacrolimus ointment has been shown to be effective and safe in both adults and children for the treatment of mild-to-moderately severe atopic dermatitis, with most patients experiencing a reduction of pruritus within 3 days of initiating therapy. (A)

Summary statement 22. Tacrolimus ointment applied on up to 100% of the body surface in adults and children has demonstrated sustained efficacy, with no significant systemic adverse effects. (A)

Table 2. Topical Glucocorticoid Potency Ranking

Group I	Betamethasone dipropionate 0.05% (cream and ointment) Clobetasol propionate 0.05% (cream and ointment) Diflorasone diacetate 0.05% (ointment) Halobetasol propionate 0.05% (cream and ointment)
Group II	Amcinonide 0.1% (ointment) Betamethasone dipropionate 0.05% (cream and ointment) Desoximetasone 0.25% (cream) Desoximetasone 0.05% (gel) Diflorasone diacetate 0.05% (ointment) Fluocinonide 0.05% (cream, gel, ointment, and solution) Halcinonide 0.1% (cream) Mometasone furoate 0.1% (ointment)
Group III	Amcinonide 0.1% (cream and lotion) Betamethasone dipropionate 0.05% (cream) Betamethasone valerate 0.1% (ointment) Desoximetasone 0.05% (cream) Diflorasone diacetate 0.05% (cream) Fluocinonide 0.05% (cream) Fluticasone propionate 0.005% (ointment) Halcinonide 0.1% (ointment and 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) Triamcinolone acetonide 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 and ointment) Betamethasone valerate 0.05% (lotion) Desonide 0.05% (cream) Flucinolone acetonide 0.01% (cream and solution) Triamcinolone acetonide 0.1% (cream)
Group VII	Hydrocortisone hydrochloride 1% (cream and ointment) Hydrocortisone hydrochloride 2.5% (cream, lotion, and ointment) Hydrocortisone acetate 1% (cream and ointment) Hydrocortisone acetate 2.5% (cream, lotion, and ointment) Pramoxine hydrochloride 1.0% (cream, lotion, and ointment) Pramoxine hydrochloride 2.5% (cream, lotion, and ointment)

Summary statement 23. A local burning sensation is the most common adverse effect associated with tacrolimus. This may limit its usefulness in certain patients. (A)

Summary statement 24. Tacrolimus ointment can be used safely for facial and eyelid eczema. (D)

Tacrolimus is a drug that acts by binding with high affinity to a 12-kDa cytoplasmic macrophilin, and the complex inhibits the activity of calcineurin, a calcium-dependent phosphatase. This, in turn, inhibits the translocation of the transcription factor NF-AT into the cell nucleus, blocking the initiation of NF-AT-dependent gene transcription. Tacrolimus inhibits the activation of key cells involved in atopic dermatitis, including T cells, dendritic cells, mast cells, and keratinocytes.¹⁸ Unlike cyclosporin, another well-known calcineurin inhibitor, tacrolimus exhibits activity when applied topically. Multicenter, blinded, vehicle-controlled studies with tacrolimus ointment, 0.03% and 0.1%, in both adults and children have reported topically applied tacrolimus to be effective and safe.^{19,51-53} Local burning sensation is the only common adverse event. Most patients experience a reduction of pruritus within 3 days of initiating therapy. In adults, a dose-response effect was seen between 0.03% and 0.1% tacrolimus, particularly for patients with more severe skin disease. Atopic dermatitis patients treated with topical tacrolimus have been reported to have a significant improvement in quality of life.²⁰

Tacrolimus ointment (Protopic) 0.03% has recently been approved for short-term and intermittent long-term use in moderate-to-severe atopic dermatitis in children 2 to 15 years of age. It has also been approved in the 0.03% as well as 0.1% concentration for adults. Long-term, open-label studies with tacrolimus ointment have been performed in adults and children with sustained efficacy and no significant adverse effects.^{23,24} In addition, unlike topical glucocorticoids, tacrolimus ointment is not atropogenic and has a greater therapeutic margin of safety than medium-strength glucocorticosteroids for facial and eyelid eczema.

Patients with steroid phobia should be started on a topical calcineurin inhibitor to encourage adherence with anti-inflammatory therapy. Furthermore, there is a group of patients with corticosteroid insensitivity who would benefit from early treatment with topical tacrolimus, since corticosteroid-resistant T cells have been found to respond well to tacrolimus.⁵⁴ Furthermore, patients with recalcitrant facial eruptions resistant to topical corticosteroids have reported benefit from use of topical tacrolimus.⁵⁵

A multicenter, randomized, double-blind, parallel-group study comparing 0.03% and 0.1% tacrolimus ointment to a mid-potent topical corticosteroid, hydrocortisone-17-butyrate, ointment was performed in 570 adults with moderate-to-severe atopic dermatitis.⁵⁶ This 3-week study demonstrated that a 0.1% concentration of tacrolimus had a similar efficacy as 0.1% hydrocortisone-17-butyrate. Another randomized, double-blind, parallel-group study compared 0.03% and 0.1% tacrolimus ointment to a low-potency topical corticosteroid, 1% hydrocortisone acetate ointment, in 560 children 2 to 15

years old with moderate-to-severe atopic dermatitis.⁵⁷ Both 0.03% and 0.1% tacrolimus ointment were significantly more effective than 1% hydrocortisone acetate ointment in reducing skin inflammation due to atopic dermatitis. These 2 studies suggest that 0.1% tacrolimus ointment has the strength of a mid-potency topical corticosteroid and should be considered first-line therapy for facial eczema where treatment with corticosteroids is limited to low-potency topical corticosteroids because of safety concerns.

Concern has been raised regarding potential effects of this new class of topical calcineurin inhibitors on prevalence of local viral infections (eg, herpes simplex), so patients should be monitored for this possible complication.⁵⁸ In contrast, the number of staphylococcal *aureus* organisms on atopic dermatitis skin decreases with prolonged use of topical tacrolimus due to its effective control of skin inflammation.⁵⁹

Topical pimecrolimus

Summary statement 25. Topical pimecrolimus cream is a calcineurin inhibitor that decreases the number of flares of atopic dermatitis, reduces the need for corticosteroids, and controls pruritus. (A)

Pimecrolimus is a novel ascomycin macrolactam derivative that binds with high affinity to its cytosolic receptor, macrophilin-12, and thereby inhibits calcineurin using a similar mechanism as tacrolimus. However, studies in experimental animals suggest that structural differences in lipophilicity endow pimecrolimus, compared with tacrolimus, with the ability to preferentially distribute to the skin as opposed to the systemic circulation.⁶⁰ In clinical studies, pimecrolimus blood levels have remained consistently low, with no clinically relevant drug-related systemic adverse events reported.⁶¹ As a consequence of inhibiting calcineurin, pimecrolimus inhibits T-cell proliferation, prevents the gene transcription of T_H1 and T_H2 cytokines, and reduces mediator release from mast cells and basophils.²² Topical application in humans has not been associated with the atrophy observed with topical corticosteroids.²⁵

Short-term, multicenter, blinded, vehicle-controlled studies with pimecrolimus cream 1% patients with atopic dermatitis have shown pimecrolimus to be both effective and safe.²¹ Significant relief of pruritus relative to the vehicle control was observed in the pimecrolimus-treated group at the first efficacy evaluation, 8 days after initial application of the study medication. Pimecrolimus cream 1% (Elidel) has recently been approved for short-term and intermittent long-term use in patients with mild-to-moderate atopic dermatitis who are 2 years and older. When used as long-term maintenance therapy, topical pimecrolimus has been found to reduce the number of exacerbations due to atopic dermatitis and to reduce the need for corticosteroid therapy.^{26,62}

Tar Preparations

Summary statement 26. Although tar preparations are widely used in the treatment of atopic dermatitis, there are no randomized controlled studies that have demonstrated their efficacy. (A)

Summary statement 27. Newer coal tar products have been developed that are more cosmetically acceptable, with respect to odor and staining of clothes, than some older products. (B)

Summary statement 28. Tar preparations should not be used on acutely inflamed skin, since this may result in additional skin irritation. (D)

Crude coal tar extracts were used to reduce skin inflammation before the availability of topical corticosteroids. The anti-inflammatory properties of tars, however, are not well characterized. There are no well-controlled, randomized, vehicle-controlled studies with tar preparations.⁴ Therefore, part of the improvement observed with tar preparations could be due to a placebo effect that can be significant in atopic dermatitis.

Newer coal tar products have been developed that are more cosmetically acceptable with respect to odor and staining of clothes than some older products.⁶³ To increase compliance, tar preparations may be recommended at bedtime. The preparation is then removed by washing in the morning, thus eliminating 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. There is a theoretical risk of tar being a carcinogen based on observational studies of workers using tar components in their occupation. Adverse effects associated with tars include folliculitis and, occasionally, photosensitivity. Tar shampoos (T/Gel, Ionil T) are often beneficial when atopic dermatitis involves the scalp.

Antihistamines

Summary statement 29. Some patients may benefit from the use of antihistamines for the relief of pruritus associated with atopic dermatitis. (C)

Summary statement 30. Treatment of atopic dermatitis with topical antihistamines is generally not recommended because of potential cutaneous sensitization. (C)

Oral antihistamines are commonly prescribed for control of pruritus in atopic dermatitis. However, a recent evidence-based review of 16 controlled studies revealed little objective evidence demonstrating the relief of pruritus when sedating or nonsedating antihistamines were used in the treatment of atopic dermatitis.⁶⁴ Although the majority of these studies were flawed because of small sample size or poor study design, these observations are not surprising, since histamine is only one of many mediators released during the inflammatory response that can induce pruritus. In fact, reduction of skin inflammation with topical glucocorticoids and calcineurin inhibitors will often reduce pruritus.^{19,21,48,51-53}

These observations, however, do not exclude the possibility that there are individual patients with atopic dermatitis who may benefit from use of antihistamines, particularly those patients with concomitant urticaria or allergic rhinitis.⁶⁵ Second-generation antihistamines may be effective in relieving symptoms of atopic dermatitis.⁶⁶⁻⁷⁰ Since pruritus is usually worse at night, sedating antihistamines (eg, hydroxyzine or diphenhydramine) offer an advantage when used at bed-

time. If severe nocturnal pruritus persists, short-term use of a sedative to allow adequate rest may be appropriate.

Treatment of atopic dermatitis with topical antihistamines is generally not recommended because of potential cutaneous sensitization.⁷¹ However, a multicenter, double-blind, vehicle-controlled study of topical 5% doxepin cream demonstrated a significant reduction of pruritus.⁷² In this 1-week study, sensitization was not reported. However, sedation can occur with widespread application, and irritation has also been noted by patients.

IDENTIFICATION AND ELIMINATION OF TRIGGERING FACTORS

Summary statement 31. Avoidance of common irritants (eg, soaps, toiletries, wool, chemicals) that trigger the itch-scratch cycle is recommended. (B)

Summary statement 32. Control of temperature and humidity may be useful for preventing pruritus. (D)

Summary statement 33. Aeroallergens such as house dust mites, animal allergens, and pollens may cause exacerbation, and therefore exposure to them should be minimized. (A)

Summary statement 34. Possible triggers of atopic dermatitis can be confirmed by skin tests and in vitro tests for specific IgE antibodies and in some cases by patch tests, which may produce immediate or delayed reactions to protein allergens. (B)

Summary statement 35. Food allergens trigger atopic dermatitis more commonly in young infants and children than in adults. (D)

There is a lower threshold for irritation of the skin in patients with atopic dermatitis.⁷³ Therefore, it is important to identify and avoid irritants that trigger the itch-scratch cycle (Table 3). These include soaps, detergents, chemicals, abrasive clothing, and extremes of temperature and humidity. Alcohol and astringents found in toiletries are drying. Therefore, 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. Mild soaps include unscented Dove, Basis, Neutrogena, Aveeno, Lowila, Purpose, and Cetaphil. New clothing should be laundered before 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 the patient should be advised to wear open-weave, loose-fitting cotton, or cotton-blend garments.

Recommendations regarding environmental living conditions should include temperature and humidity control to avoid increased pruritus related to heat, humidity, and perspiration. One goal of treatment is for children to be as normally active as possible. Certain sports such as swimming may be better tolerated than sports involving intense perspiration, physical contact, or heavy clothing and equipment, but patients must rinse off the chlorine after swimming immediately and lubricate their skin. Although ultraviolet light may

Table 3. Triggers of Itching in Atopic Dermatitis*

All irritants	Lipid solvents (ie, soaps, detergents) Disinfectants (eg, chlorine in swimming pools) Occupational irritants Household fluids (eg, juices from fresh fruits, meats)
Contact and aeroallergens	Dust mites, contact > aeroallergens Furry animals (cat > dog) Pollens (seasonal) Molds Human dander (dandruff)
Microbial agents	Viral infections (especially upper respiratory tract infections) <i>Staphylococcus aureus</i> (either as a superantigen or pathogen) <i>Pityrosporum ovale</i> yeast <i>Candida</i> (rarely) <i>Dermatophytes</i> (rarely)
Others	Foods (as contact irritants > vasodilators > allergens) Psyche Climate Hormones (eg, menstrual cycle)

* Not all patients with atopic dermatitis will be triggered by every stimulus. There are subsets of patients with atopic dermatitis who will experience exacerbations by some triggers and not by others. Adapted from Beltrani VS. The clinical spectrum of atopic dermatitis. *J Allergy Clin Immunol.* 1999;104:S87-S98.

be beneficial for some patients with atopic dermatitis, sunscreens should be used to avoid sunburn. However, since sunscreens can be irritants, care should be used to identify a nonirritating sunscreen. Prolonged sun exposure can lead to evaporative losses or sweating, both of which can be irritating, as well as produce photodamage.

Foods and aeroallergens, such as dust mites, animal allergens, and pollens, may trigger atopic dermatitis. Potential allergens can be identified by taking a careful history and performing appropriate immediate hypersensitivity skin tests.^{74,75} Intracutaneous skin tests to foods are not recommended, since they are relatively nonspecific, may trigger anaphylactic reactions, and do not provide reliable results in this patient population. Negative skin test or in vitro test results for aeroallergens have a high predictive value for ruling out suspected allergens. On the other hand, positive skin tests, particularly to foods, do not always correlate well with clinical symptoms and may need to be confirmed in the case of foods with a controlled food challenge and/or elimination diet.⁵ Studies indicate that food-specific serum IgE concentrations may be useful for diagnosing symptomatic allergy to certain foods, such as egg, milk, peanut, and fish, and could eliminate the need to perform controlled food challenges in some patients.⁷⁶⁻⁷⁸ However, the amount of food causing a reaction and the severity of the reaction are not predicted by prick skin testing or concentration of food-specific serum IgE.⁷⁹ If the patient has a history suggestive of

food allergy but there is no evidence of food-specific IgE antibodies, it may be necessary to perform an oral food challenge to rule out food sensitivity that is not IgE mediated.⁸⁰

In children who have undergone double-blind, placebo-controlled food challenge, milk, egg, peanut, soy, wheat, and fish account for nearly 90% of the foods that exacerbate atopic dermatitis.¹⁴ Avoidance of foods implicated by controlled food challenge has been shown to result in clinical improvement.^{15,81} Extensive elimination diets, which in some cases can be nutritionally deficient, are rarely required, because, even with multiple positive skin test results, most patients will react to 3 or fewer foods on blinded challenge.

Pruritus and eczematoid skin lesions can develop after intranasal or bronchial inhalation challenge with aeroallergens in sensitized patients with atopic dermatitis who have specific IgE antibodies against the challenge allergen.^{82,83} Epicutaneous application of aeroallergens (eg, house dust mites, weeds, animal danders, molds) by patch testing on uninvolved skin of patients with atopic dermatitis elicits eczematoid reactions in 30% to 50% of patients with atopic dermatitis, although the clinical significance of this finding is unclear.⁸⁴ In contrast, patch test results are usually negative in patients with respiratory allergy and healthy volunteers. Several studies have found that effective reduction in the level of house dust mites is associated with significant improvement in atopic dermatitis.^{16,85-87} Avoidance of house dust mites may include (1) use of dust mite-proof encasings on pillows, mattresses, and box springs; (2) washing bedding in hot water weekly; (3) removal of bedroom carpeting; and (4) decreasing indoor humidity levels with air conditioning.⁸⁸

Since there are many triggers that contribute to flares of atopic dermatitis, attention should be focused on controlling those trigger factors that are important in each patient, for example, infants and young children are more likely to have food allergy, whereas in older children and adults, environmental aeroallergens are more important in causing exacerbation of atopic dermatitis.

MICROBES

Summary statement 36. Patients with moderate-to-severe atopic dermatitis have been found to make IgE antibodies against staphylococcal toxins present on their skin. (B)

Summary statement 37. A course of an appropriate systemic antibiotic should be considered in patients who are heavily colonized or infected with staphylococcal *aureus*. Antibiotic treatment may be more difficult if *S aureus* is resistant. (D)

Summary statement 38. Atopic dermatitis can be complicated by recurrent viral skin infections, such as herpes simplex, warts, and molluscum contagiosum. (B)

Summary statement 39. Smallpox vaccination or even exposure of patients with atopic dermatitis to recently vaccinated individuals may cause a severe, widespread, potentially fatal dermatitis called *eczema vaccinatum*, which is similar in appearance to *eczema herpeticum*. (D)

Summary statement 40. Dermatophytic infections can complicate atopic dermatitis and may contribute to exacerbation of disease activity. (C)

Skin infections, particularly with staphylococcal *aureus*, can be a recurrent problem in atopic dermatitis, requiring specific treatment.² Patients with moderate-to-severe atopic dermatitis have been found to make IgE antibodies against staphylococcal toxins present on their skin.⁶⁻⁸ Therefore, antistaphylococcal antibiotics may be very helpful in the treatment of patients who are heavily colonized or infected with *S aureus*. Erythromycin and the newer macrolide antibiotics (azithromycin and 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. Cephalosporins also offer effective coverage for both staphylococci and streptococci.⁹ In patients with extensive infection, a course of systemic antibiotics is preferred.

Increased binding of *S aureus* to skin is probably related to the underlying inflammation present in atopic dermatitis. This is supported by the observation that treatment with topical glucocorticoids or tacrolimus reduces *S aureus* counts on atopic skin.^{59,89} Recent studies have demonstrated that T_H2 immune responses increase binding of *S aureus* to inflamed skin lesions and reduce local innate immune responses needed to kill *S aureus*.⁹⁰⁻⁹²

Atopic dermatitis can be complicated by recurrent viral skin infections such as herpes simplex, warts, and molluscum contagiosum, which may reflect local defects in T-cell function.⁹³ Herpes simplex, resulting in Kaposi's varicelliform eruption or *eczema herpeticum*, can be a serious infection. The presence of punched-out erosions, vesicles, and/or infected skin lesions that fail to respond to oral antibiotics should initiate a search for herpes simplex. Herpes simplex infection can be diagnosed by a Giemsa-stained Tzanck smear of cells scraped from the vesicle base, commercial immunofluorescence assays, or viral culture. 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.^{94,95} In patients with atopic dermatitis, smallpox vaccination or even exposure to recently vaccinated individuals may cause a severe, widespread, life-threatening dermatitis called *eczema vaccinatum*, which is similar in appearance to *eczema herpeticum*.⁹⁶ In the event of a smallpox bioterrorist attack, patients with atopic dermatitis would be at increased risk for developing this complication.

Dermatophyte infections can complicate atopic dermatitis and may contribute to exacerbation of the disease. There has been particular interest in the role of *Malassezia furfur* (*Pityrosporum ovale*) in patients with atopic dermatitis. *M furfur* is a lipophilic yeast commonly present in the seborrheic areas of the skin and in the scalp. IgE antibodies against *M furfur* are commonly found in patients with atopic dermatitis, most frequently in patients with involvement of the head and

neck.⁹⁷ The potential importance of *M furfur*, as well as other dermatophyte infections, is further supported by a reduction in the severity of atopic dermatitis following treatment with antifungal agents.⁹⁸

EMOTIONAL STRESS

Summary statement 41. Emotional factors do not cause atopic dermatitis but often cause exacerbation (D) and have been found to induce immune activation as well as increase pruritus and scratching. (LB)

Patients with atopic dermatitis can have significant problems with anxiety, anger, and hostility.⁹⁹ Although these emotional factors do not cause atopic dermatitis, they often cause exacerbation and have been found to induce immune activation in patients with this condition.^{100,101} Atopic patients often respond to stress, frustration, embarrassment, or other upsetting events with increased pruritus and scratching.¹⁰² In some patients, scratching is associated with significant secondary gain or simply occurs out of habit. Psychological evaluation and/or counseling should be considered in patients who have difficulty with emotional triggers or who have psychological problems that make it more difficult to manage their disease. Such evaluation and counseling may be especially useful in adolescents and young adults who consider their skin disease disfiguring. Relaxation, behavioral modification, or biofeedback may be helpful, particularly in those patients with habitual scratching.^{103,104}

PATIENT EDUCATION

Summary statement 42. To achieve effective control of atopic dermatitis, it is important to educate patients and family members about the chronic nature of atopic dermatitis, exacerbating factors, and appropriate treatment options, including patient support organizations to enhance adherence. (D)

To achieve effective control of 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 and methods for environmental control, as well as general information about atopic dermatitis, can be helpful. Patients should be educated on how to monitor atopic dermatitis, how to respond to changes in their status, and when to seek additional medical help.

The treatment plan should be reviewed during each follow-up visit, 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 videos 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, or from the American Academy of Dermatology's Web site Eczemanet.

TREATMENT OF THE DIFFICULT-TO-MANAGE PATIENT

Wet Dressings and Occlusion

Summary statement 43. Wet dressings may serve as an effective barrier against persistent scratching, allowing more rapid healing of excoriated lesions. (B)

Summary statement 44. Application of wet-wrap dressings in combination with topical corticosteroids can be efficacious in the treatment of refractory atopic dermatitis. (A)

Wet dressings can be used on severely affected or chronic lesions refractory to skin care.^{27,28} Dressings may serve as an effective barrier against persistent scratching and encourages healing of excoriated lesions. Application of wet-wrap dressings in combination with topical corticosteroids has been found to be efficacious in the treatment of refractory atopic dermatitis because of better absorption.^{27,105} However, patients should be monitored carefully for secondary microbial infection and adrenal suppression when wet-wrap dressings are used for prolonged periods in combination with potency corticosteroids.

Allergen Immunotherapy

Summary statement 45. Although the effectiveness of allergen immunotherapy in the treatment of atopic dermatitis has not been conclusively demonstrated, there are selected patients with atopic dermatitis who may benefit from such treatment. (A)

Unlike allergic rhinitis and asthma, there is no conclusive evidence that immunotherapy with aeroallergens is effective in the treatment of atopic dermatitis, although there are selected individuals who may benefit from such treatment.¹⁰⁶⁻¹⁰⁹ Expert opinion supports the use of allergen immunotherapy for selected individuals.

Systemic Glucocorticosteroids

Summary statement 46. The use of systemic corticosteroids may be required in the treatment of severe, recalcitrant chronic atopic dermatitis. (F)

Summary statement 47. The dramatic clinical improvement that may occur after administration of systemic corticosteroids may be associated with an equally dramatic rebound flaring of atopic dermatitis following discontinuation of systemic corticosteroids. (F)

The use of systemic corticosteroids, such as oral prednisone, may be required in the treatment of severe chronic atopic dermatitis. However, 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 corticosteroid therapy. 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 corticosteroid taper to suppress rebound flaring of atopic dermatitis. Patients who require more than one course of

oral corticosteroid therapy should be evaluated by an allergist or dermatologist to determine if factors contributing to poorly controlled atopic dermatitis can be identified and eliminated or whether an incorrect diagnosis has been made.

Phototherapy

Summary statement 48. Natural sunlight can be beneficial for atopic dermatitis, but sunburn and overheating should be avoided. (D)

Summary statement 49. Ultraviolet therapy can be a useful adjunct in the treatment of recalcitrant atopic dermatitis. (A)

Summary statement 50. Phototherapy with PUVA should be restricted to patients with recalcitrant atopic dermatitis. (D)

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, exacerbation of atopic dermatitis may occur. Ultraviolet light therapy can be a useful adjunct in the treatment of chronic, recalcitrant atopic dermatitis but should be administered by a health care professional experienced in such treatment. This form of therapy is best performed under the supervision of a dermatologist. Broad-band ultraviolet B, broad-band ultraviolet A, narrow-band ultraviolet B (311 nm), ultraviolet A-1 (340 to 400 nm), and combined ultraviolet AB phototherapy can be useful adjuncts in the treatment of atopic dermatitis.^{29,110,111} Photochemotherapy with PUVA should be restricted to patients with severe, widespread atopic dermatitis, although studies comparing it with other modes of phototherapy are limited. Short-term adverse effects from phototherapy may include erythema, skin pain, pruritus, and pigmentation. Potential long-term adverse effects include premature skin aging and cutaneous malignancies.

Systemic Immunomodulating Agents

Summary statement 51. Immunosuppressive agents such as cyclosporin, interferon gamma, mycophenolate mofetil, and azathioprine have been shown to provide benefit for certain cases of severe refractory atopic dermatitis, but potential benefits should be weighed against their potentially serious adverse effects. (B)

Cyclosporin

Systemic cyclosporin A is a potent immunosuppressive drug that acts primarily on T cells by suppressing cytokine gene transcription. The drug binds to an intracellular protein, cyclophilin, and this complex in turn inhibits calcineurin, a molecule required for initiation of cytokine gene transcription. Several randomized controlled studies have demonstrated that both children and adults with severe atopic dermatitis refractory to conventional treatment can benefit from short-term treatment with oral cyclosporin (5 mg/kg per day) in terms of reduced skin disease and improved quality of life.¹¹²⁻¹¹⁴ However, adverse 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.¹¹⁵

Interferon gamma

Interferon gamma is available as a recombinant molecule for the treatment of chronic granulomatous disease. It is also known to down-regulate T_H2 cell function. Studies of patients with atopic dermatitis have demonstrated that treatment with recombinant interferon gamma results in clinical improvement and decreases total circulating eosinophil counts.^{30,116} In one study, a small subset of patients showed persistent improvement 3 months after treatment was discontinued.¹¹⁷ Reduction in clinical severity of atopic dermatitis correlated with the ability of interferon gamma to decrease blood eosinophilia. In another study in which patients with atopic dermatitis were treated for up to 24 months, total body surface involvement decreased from 62% at baseline to 18.5% after 24 months of treatment.¹¹⁸ Long-term therapy was not associated with any significant laboratory abnormalities or clinical adverse events. However, influenza-like symptoms are commonly observed adverse effects early in the treatment course and limit the use of this therapy.

Mycophenolate mofetil

Mycophenolate mofetil is a purine biosynthesis inhibitor with immunosuppressive activity that has been used for treatment of refractory inflammatory skin disorders.^{31,119} Short-term oral mycophenolate mofetil, 2 g/d, as monotherapy has been reported in open-label studies to clear skin lesions in some adults with atopic dermatitis resistant to other treatment, including topical and oral steroids and PUVA. The drug has generally been well tolerated, with the exception of occasional herpes retinitis and dose-related bone marrow suppression.

Azathioprine

Azathioprine is a purine analog with anti-inflammatory and antiproliferative effects. It has been utilized for severe atopic dermatitis, although no controlled studies have been reported.^{32,120} Myelosuppression is a significant adverse effect, and thiopurinemethyl transferase levels may predict individuals at risk for severe adverse effects from this drug.

Hospitalization

Summary statement 52. Hospitalization can result in an improvement in atopic dermatitis by removing the patient from environmental allergens and irritants and by providing patient education and improving compliance. (F)

Patients with moderately severe, nonresponsive 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 irritants, intense patient education, and assurance of compliance with therapy result in sustained improvement. Clearing of the patient's skin during hospitalization also allows the patient to undergo allergen skin testing and appropriately controlled provocative challenges to correctly identify potential allergens.

Investigative Approaches

Summary statement 53. There are certain investigative treatments that have been proposed for the treatment of atopic dermatitis. These remain unproven at this time. (D)

Chinese herbal therapy. Placebo-controlled clinical studies have suggested that patients with severe atopic dermatitis may benefit from treatment with Chinese herbs.^{121,122} The beneficial response from Chinese herbal therapy, however, is often temporary, and effectiveness may wear off despite continued treatment. The possibility of significant adverse effects associated with long-term use remains a concern.

Leukotriene antagonists. Increased levels of leukotrienes have been measured in patients with atopic dermatitis.^{123,124} Small randomized studies of leukotriene antagonists have suggested beneficial effects in reducing the severity of atopic dermatitis.^{125,126}

Mycobacterium vaccae. Children with moderate-to-severe atopic dermatitis were enrolled in a randomized, double-blind, placebo-controlled study, where they were given either one intradermal injection of killed *Mycobacterium vaccae* or placebo.¹²⁷ Children treated with *M vaccae* showed a significantly greater improvement in severity of skin disease than patients treated with placebo. These observations suggest that down-regulation of the T_H2 response in atopic dermatitis may have potentially beneficial effects.

Consultation

Summary statement 54. Patients refractory to first-line therapy should be evaluated by an atopic dermatitis specialist. (F)

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. The primary care physician plays an important role in the routine care of patients with uncomplicated atopic dermatitis, ensuring continuity of care. Consultation with an allergist or dermatologist is recommended (1) for patients with severe atopic dermatitis who have significant dysfunction as a result of their skin disease; (2) for identification of potential allergen triggers; (3) for patient education; (4) when the diagnosis of atopic dermatitis is in doubt; and (5) for implementation of alternative therapies.

ACKNOWLEDGMENTS

The American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma & Immunology (ACAAI) have jointly accepted responsibility for establishing the *Disease Management of Atopic Dermatitis: An Updated Practice Parameter*. This is a complete and comprehensive document at the current time. The medical environment is a changing environment and not all recommendations will be appropriate for all patients. 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 re-

quest 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 & Immunology (JCAAI). These parameters are not designed for use by pharmaceutical companies in drug promotion. These parameters were developed by the Joint Task Force on Practice Parameters, representing the AAAAI, the ACAAI, and the JCAAI. The Joint Task Force has made an intense effort to appropriately acknowledge all contributors to this parameter. If any contributors are inadvertently excluded, the Task Force will ensure that appropriate recognition of such contributions is subsequently made.

The following served as reviewers for this Practice Parameter: Vincent S. Beltrani, MD, Department of Dermatology, College of Physicians & Surgeons, Columbia University, New York, NY, and Department of Medicine, Division of Allergy, University of Medicine & Dentistry of New Jersey, Newark, NJ; Ernest N. Charlesworth, MD, Department of Allergy & Dermatology, Shannon Clinic, San Angelo, TX, and Departments of Allergy and Dermatology, University of Texas Medical School at Houston, Houston, TX; Hugh A. Sampson, MD, Jaffe Food Allergy Institute, Mount Sinai School of Medicine, New York, NY; and Lynda C. Schneider, MD, Allergy Program and Atopic Dermatitis Center, Children's Hospital, and Department of Pediatrics, Harvard Medical School, Boston, MA.

REFERENCES

1. Schultz-Larsen F, Hanifin JM. Epidemiology of atopic dermatitis. *Immunol Allergy Clin North Am.* 2002;22:1-24. (IV)
2. Bieber T, Leung DY, editors. *Atopic Dermatitis*. New York, NY: Marcel Dekker Inc; 2002. (IV)
3. Beck LA, Leung DY. Allergen sensitization through the skin induces systemic allergic responses. *J Allergy Clin Immunol.* 2000;106:S258-S263. (IV)
4. Hoare C, Li Wan Po A, Williams H. Systematic review of treatments for atopic eczema. *Health Technol Assess.* 2000;4: 1-191. (Ia)
5. Sampson HA, Albergo R. Comparison of results of skin tests, RAST, and double-blind, placebo-controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol.* 1984;74:26-33. (IIb)
6. Leung DY, Harbeck R, Bina P, et al. Presence of IgE antibodies to staphylococcal exotoxins on the skin of patients with atopic dermatitis: evidence for a new group of allergens. *J Clin Invest.* 1993;92:1374-1380. (LB)
7. Nomura I, Tanaka K, Tomita H, et al. Evaluation of the staphylococcal exotoxins and their specific IgE in childhood atopic dermatitis. *J Allergy Clin Immunol.* 1999;104:441-446. (III)
8. Bunikowski R, Mielke ME, Skarabis H, et al. Evidence for a disease-promoting effect of *Staphylococcus aureus*-derived exotoxins in atopic dermatitis. *J Allergy Clin Immunol.* 2000; 105:814-819. (III)
9. Boguniewicz M, Sampson H, Leung SB, Harbeck R, Leung DY. Effects of cefuroxime axetil on *Staphylococcus aureus* colonization and superantigen production in atopic dermatitis. *J Allergy Clin Immunol.* 2001;108:651-652. (III)

10. Leung DY. Atopic dermatitis: new insights and opportunities for therapeutic intervention. *J Allergy Clin Immunol.* 2000; 105:860–876. (IV)
11. von Bubnoff D, Geiger E, Bieber T. Antigen-presenting cells in allergy. *J Allergy Clin Immunol.* 2001;108:329–339. (LB)
12. Giustizieri ML, Mascia F, Frezzolini A, et al. Keratinocytes from patients with atopic dermatitis and psoriasis show a distinct chemokine production profile in response to T cell-derived cytokines. *J Allergy Clin Immunol.* 2001;107: 871–877. (LB)
13. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol.* 1980;92:44–47. (IV)
14. Lever R, MacDonald C, Waugh P, Aitchison T. Randomized controlled trial of advice on an egg exclusion diet in young children with atopic eczema and sensitivity to eggs. *Pediatr Allergy Immunol.* 1998;9:13–19. (Ib)
15. Woodmansee DP, Christiansen SC. Improvement in atopic dermatitis in infants with the introduction of an elemental formula. *J Allergy Clin Immunol.* 2001;108:309. (IIb)
16. Gutgesell C, Heise S, Seubert S, et al. Double-blind placebo-controlled house dust mite control measures in adult patients with atopic dermatitis. *Br J Dermatol.* 2001;145:70–74. (Ib)
17. Andersson AC, Lindberg M, Loden M. The effect of two urea-containing creams on dry eczematous skin in atopic patients, I: expert, patient and instrumental evaluation. *J Dermatol Treat.* 1999;10:165:169. (IV)
18. Wollenberg A, Sharma S, von Bubnoff D, Geiger E, Heberstok J, Bieber T. Topical tacrolimus (FK506) leads to profound phenotypic and functional alterations of epidermal antigen-presenting dendritic cells in atopic dermatitis. *J Allergy Clin Immunol.* 2001;107:519–525. (LB)
19. Boguniewicz M, Fiedler VC, Raimer S, Lawrence ID, Leung DY, Hanifin JM; Pediatric Tacrolimus Study Group. A randomized, vehicle-controlled trial of tacrolimus ointment for treatment of atopic dermatitis in children. *J Allergy Clin Immunol.* 1998;102:637–644. (Ia)
20. Drake L, Prendergast M, Maher R, et al. The impact of tacrolimus ointment on health-related quality of life of adult and pediatric patients with atopic dermatitis. *J Am Acad Dermatol.* 2001;44(Suppl):S65–S72. (Ia)
21. Eichenfield LF, Lucky AW, Boguniewicz M, et al. Safety and efficacy of pimecrolimus (ASM 981) cream 1% in the treatment of mild and moderate atopic dermatitis in children and adolescents. *J Am Acad Dermatol.* 2002;46:495–504. (Ia)
22. Zuberbier T, Chong SU, Grunow K, et al. The ascomycin macrolactam pimecrolimus (Elidel, SDZ ASM 981) is a potent inhibitor of mediator release from human dermal mast cells and peripheral blood basophils. *J Allergy Clin Immunol.* 2001; 108:275–280. (LB)
23. Kang S, Lucky AW, Pariser D, Lawrence I, Hanifin JM. Long-term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. *J Am Acad Dermatol.* 2001;44(Suppl):S58–S64. (IIb)
24. Reitamo S, Wollenberg A, Schopf E, et al, The European Tacrolimus Ointment Study Group. Safety and efficacy of 1 year of tacrolimus ointment monotherapy in adults with atopic dermatitis. *Arch Dermatol.* 2000;136:999–1006. (IIb)
25. Queille-Roussel C, Paul C, Duteil L, et al. The new topical ascomycin derivative SDZ ASM 981 does not induce skin atrophy when applied to normal skin for 4 weeks: a randomized, double-blind controlled study. *Br J Dermatol.* 2001;144: 507–513. (IIb)
26. Wahn U, Bos JD, Goodfield M, et al. Efficacy and safety of pimecrolimus cream in the long-term management of atopic dermatitis in children. *Pediatrics.* 2002;110:e2. (Ib)
27. Schnopp C, Holtmann C, Stock S, et al. Topical steroids under wet-wrap dressings in atopic dermatitis—a vehicle-controlled trial. *Dermatology.* 2002;204:56–59. (IIa)
28. Devillers AC, de Waard-van der Spek FB, Mulder PG, Oranje AP. Treatment of refractory atopic dermatitis using 'wet-wrap' dressings and diluted corticosteroids: results of standardized treatment in both children and adults. *Dermatology.* 2002;204:50–55. (III)
29. Krutmann J, Diepgen TL, Luger TA, et al. High dose UVAq therapy for atopic dermatitis: results of a multicenter trial. *J Am Acad Dermatol.* 1998;38:589–593. (Ib)
30. Hanifin JM, Schneider LC, Leung DY, et al. Recombinant interferon γ therapy for atopic dermatitis. *J Am Acad Dermatol.* 1993;28:189–197. (Ib)
31. Benez A, Fierlbeck G. Successful long-term treatment of severe atopic dermatitis with mycophenolate mofetil. *Br J Dermatol.* 2001;144:638–639. (III)
32. Kuanprasert N, Herbert O, Barnetson RS. Clinical improvement and significant reduction of total serum IgE in patients suffering from severe atopic dermatitis treated with oral azathioprine. *Aust J Dermatol.* 2002;43:125–127. (III)
33. Williams H, Robertson C, Stewart A, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol.* 1999;103:125–138. (III)
34. Leung DY, Hanifin JM, Charlesworth EN, et al. Disease management of atopic dermatitis: a practice parameter. 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. Work Group on Atopic Dermatitis. *Ann Allergy Asthma Immunol.* 1997;79:197–211. (IV)
35. Romagnani S. The role of lymphocytes in allergic disease. *J Allergy Clin Immunol.* 2000;105:399–408. (III)
36. Higashi N, Gesser B, Kawana S, Thestrup-Pedersen K. Expression of IL-18 mRNA and secretion of IL-18 are reduced in monocytes from patients with atopic dermatitis. *J Allergy Clin Immunol.* 2001;108:607–614. (II)
37. Hanifin JM, Chan SC, Cheng JB, et al. Type 4 phosphodiesterase inhibitors have clinical and in vitro anti-inflammatory effects in atopic dermatitis. *J Invest Dermatol.* 1996;107: 51–56. (LB)
38. Soumelis V, Reche PA, Kanzler H, et al. Human epithelial cells trigger dendritic cell mediated allergic inflammation by producing TSLP. *Nat Immunol.* 2002;3:673–680. (LB)
39. Jirapongsananuruk O, Hofer MF, Trumble AE, Norris DA, Leung DY. Enhanced expression of B7.2 (CD86) in patients with atopic dermatitis: a potential role in the modulation of IgE synthesis. *J Immunol.* 1998;160:4622–4627. (LB)
40. Langeveld-Wildschut EG, Bruijnzeel PL, Mudde GC, et al. Clinical and immunologic variables in skin of patients with atopic eczema and either positive or negative atopy patch test reactions. *J Allergy Clin Immunol.* 2000;105:1008–1016. (II)
41. Wuthrich B, Schmid-Grendelmeier P. The atopic eczema/dermatitis syndrome: epidemiology, natural course, and immunology of the IgE-associated (“extrinsic”) and non-allergic (“intrinsic”) AEDS. *J Investig Allergol Clin Immunol.* 2003;

- 13:1–5. (IV)
42. Imokawa G. Lipid abnormalities in atopic dermatitis. *J Am Acad Dermatol.* 2001;45(Suppl):S29–S32. (LB)
 43. Hara J, Higuchi K, Okamoto R, Kawashima M, Imokawa G. High-expression of sphingomyelin deacylase is an important determinant of ceramide deficiency leading to barrier disruption in atopic dermatitis. *J Invest Dermatol.* 2000;115:406–413. (LB)
 44. Chamlin SL, Frieden IJ, Fowler A, et al. Ceramide-dominant, barrier-repair lipids improve childhood atopic dermatitis. *Arch Dermatol.* 2001;137:1110–1112. (IIb)
 45. Lack G, Fox D, Northstone K, Golding J. Factors associated with the development of peanut allergy in childhood. *N Engl J Med.* 2003;348:977–985. (III)
 46. Cornell RC, Stoughton RB. Six-month controlled study of effect of desoximetasone and betamethasone 17-valerate on the pituitary-adrenal axis. *Br J Dermatol.* 1981;105:91–95. (Ib)
 47. Fritz KA, Weston WL. Topical glucocorticosteroids. *Ann Allergy.* 1983;50:68–76. (IV)
 48. Wolkerstorfer A, Strobos MA, Glazenburg EJ, Mulder PG, Oranje AP. Fluticasone propionate 0.05% cream once daily versus clobetasone butyrate 0.05% cream twice daily in children with atopic dermatitis. *J Am Acad Dermatol.* 1998;39:226–231. (II)
 49. Lagos BR, Maibach HI. Frequency of application of topical corticosteroids: an overview. *Br J Dermatol.* 1998;139:763–766. (IV)
 50. Van Der Meer JB, Glazenburg EJ, Mulder PG, Eggink HF, Coenraads PJ. The management of moderate to severe atopic dermatitis in adults with topical fluticasone propionate. The Netherlands Adult Atopic Dermatitis Study Group. *Br J Dermatol.* 1999;140:1114–1121. (Ib)
 51. Ruzicka T, Bieber T, Schopf E, et al. A short-term trial of tacrolimus ointment for atopic dermatitis. European Tacrolimus Multicenter Atopic Dermatitis Study Group. *N Engl J Med.* 1997;337:816–821. (Ib)
 52. Paller A, Eichenfield LF, Leung DY, Stewart D, Appell M. A 12-week study of tacrolimus ointment for the treatment of atopic dermatitis in pediatric patients. *J Am Acad Dermatol.* 2001;44(Suppl):S47–S57. (Ib)
 53. Hanifin JM, Ling MR, Langley R, Breneman D, Rafal E. Tacrolimus ointment for the treatment of atopic dermatitis in adult patients: part I, efficacy. *J Am Acad Dermatol.* 2001;44(Suppl):S28–S38. (Ib)
 54. Hauk PJ, Leung DY. Tacrolimus (FK506): new treatment approach in superantigen-associated diseases like atopic dermatitis? *J Allergy Clin Immunol.* 2001;107:391–392. (IV)
 55. Sugiura H, Uehara M, Hoshino N, Yamaji A. Long-term efficacy of tacrolimus ointment for recalcitrant facial erythema resistant to topical corticosteroids in adult patients with atopic dermatitis. *Arch Dermatol.* 2000;136:1062–1063. (IIb)
 56. Reitamo S, Van Leent EJ, Ho V, et al. Efficacy and safety of tacrolimus ointment compared with that of hydrocortisone acetate ointment in children with atopic dermatitis. *J Allergy Clin Immunol.* 2002;109:539–546. (Ib)
 57. Reitamo S, Rustin M, Ruzicka T, et al. Efficacy and safety of tacrolimus ointment compared with that of hydrocortisone butyrate ointment in adult patients with atopic dermatitis. *J Allergy Clin Immunol.* 2002;109:547–555. (Ib)
 58. Lubbe J, Pournaras CC, Saurat JH. Eczema herpeticum during treatment of atopic dermatitis with 0.1% tacrolimus ointment. *Dermatology.* 2000;201:249–251. (IV)
 59. Remitz A, Kyllonen H, Granlund H, Reitamo S. Tacrolimus ointment reduces staphylococcal colonization of atopic dermatitis lesions. *J Allergy Clin Immunol.* 2001;107:196–197. (IV)
 60. Stuetz A, Grassberger M, Meingassner JG. Pimecrolimus (Elidel, SDZ ASM 981)—preclinical pharmacologic profile and skin selectivity. *Semin Cutan Med Surg.* 2001;20:233–241. (IV)
 61. Van Leent EJ, Ebelin ME, Burtin P, Dorobek B, Spuls PI, Bos JD. Low systemic exposure after repeated topical application of pimecrolimus (Elidel), SD Z ASM 981 in patients with atopic dermatitis. *Dermatology.* 2002;204:63–68. (IIb)
 62. Kapp A, Papp K, Bingham A, et al. Long-term management of atopic dermatitis in infants with topical pimecrolimus, a non-steroid anti-inflammatory drug. *J Allergy Clin Immunol.* 2002;110:277–284. (Ib)
 63. Niordson AM, Stahl D. Treatment of psoriasis with Clinitar cream: a controlled clinical trial. *Br J Clin Pract.* 1985;39:67–68, 72. (IIa)
 64. Klein PA, Clark RA. An evidence-based review of the efficacy of antihistamines in relieving pruritus in atopic dermatitis. *Arch Dermatol.* 1999;135:1522–1525. (Ia)
 65. Simons FE. Prevention of acute urticaria in young children with atopic dermatitis. *J Allergy Clin Immunol.* 2001;107:703–706. (Ib)
 66. Diepgen TL. Long-term treatment with cetirizine of infants with atopic dermatitis: a multi-country, double-blind, randomized, placebo-controlled trial (the ETAC trial) over 18 months. *Pediatr Allergy Immunol.* 2002;13:278–286. (Ib)
 67. Hrachovec J. Publication bias with cetirizine in atopic dermatitis: safe but ineffective [letter to the editor]? *J Allergy Clin Immunol.* 2002;110:818. (IV)
 68. La Rosa M, Ranno C, Musarra I, Guglielmo F, Corrias A, Bellanti JA. Double-blind study of cetirizine in atopic eczema in children. *Ann Allergy.* 1994;73:117–122. (Ib)
 69. Langeland T, Fagertun HE, Larsen S. Therapeutic effect of loratadine on pruritus in patients with atopic dermatitis: a multi-crossover study. *Allergy.* 1994;49:22–26. (Ib)
 70. Hannuksela M, Kalimo K, Lammintausta K, et al. Dose ranging study: cetirizine in the treatment of atopic dermatitis. *Ann Allergy.* 1993;70:127–133. (Ib)
 71. Shelley WB, Shelley ED, Talanin NY. Self-potentiating allergic contact dermatitis caused by doxepin hydrochloride cream. *J Am Acad Dermatol.* 1996;34:143–144. (IV)
 72. Drake LA, Fallon JD, Sober A. Relief of pruritus in patients with atopic dermatitis after treatment with topical doxepin cream. The Doxepin Study Group. *J Am Acad Dermatol.* 1994;31:613–616. (Ib)
 73. Nassif A, Chan SC, Storrs FJ, Hanifin JM. Abnormal skin irritancy in atopic dermatitis and in atopy without dermatitis. *Arch Dermatol.* 1994;130:1402–1407. (IIb)
 74. Bernstein IL, Storms WW. Practice parameters for allergy diagnostic testing. Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma. The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol.* 1995;75:543–625. (IV)
 75. Sampson HA. Food allergy, part 1: immunopathogenesis and clinical disorders. *J Allergy Clin Immunol.* 1999;103:717–728. (IV)
 76. Yunginger JW, Ahlstedt S, Eggleston PA, et al. Quantitative IgE antibody assays in allergic diseases. *J Allergy Clin Immunol.* 2000;105:1077–1084. (LB)

77. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol.* 2001;107:891–896. (LB)
78. Rance F, Abbal M, Lauwers-Cances V. Improved screening for peanut allergy by the combined use of skin prick tests and specific IgE assays. *J Allergy Clin Immunol.* 2002;109:1027–1033. (IIb)
79. Sicherer SH, Morrow EH, Sampson HA. Dose-response in double-blind, placebo-controlled oral food challenges in children with atopic dermatitis. *J Allergy Clin Immunol.* 2000;105:582–586. (IIb)
80. Niggemann B, Reibel S, Roehr CC, et al. Predictors of positive food challenge outcome in non-IgE-mediated reactions to food in children with atopic dermatitis. *J Allergy Clin Immunol.* 2001;108:1053–1058. (IIb)
81. Tupker RA, De Monchy JG, Coenraads PJ, Homan A, van der Meer JB. Induction of atopic dermatitis by inhalation of house dust mite. *J Allergy Clin Immunol.* 1996;97:1064–1070. (Ib)
82. Huang JL, Chen CC, Kuo ML, Hsieh KH. Exposure to a high concentration of mite allergen in early infancy is a risk factor for developing atopic dermatitis: a 3-year follow-up study. *Pediatr Allergy Immunol.* 2001;12:11–16. (IIb)
83. Wheatley LM, Platts-Mills TA. In: Leung DY, Greaves MW, editors. *Allergic Skin Disease: A Multidisciplinary Approach.* New York, NY: Marcel Dekker; 2000:423. (IV)
84. Palmer RA, Friedmann PS. Effect of house dust mite avoidance measures in children with atopic dermatitis. *Br J Dermatol.* 2001;144:912–913. (IIb)
85. Ricci G, Patrizi A, Specchia F, et al. Effect of house dust mite avoidance measures in children with atopic dermatitis. *Br J Dermatol.* 2000;143:379–384. (Ib)
86. Tan BB, Weald D, Strickland I, Friedmann PS. Double-blind controlled trial of effect of housedust-mite allergen avoidance on atopic dermatitis. *Lancet.* 1996;347:15–18. (Ib)
87. Holm L, Bengtsson A, van Hage-Hamsten M, Ohman S, Scheynius A. Effectiveness of occlusive bedding in the treatment of atopic dermatitis—a placebo-controlled trial of 12 months' duration. *Allergy.* 2001;56:152–158. (Ib)
88. Arlian LG, Platts-Mills TA. The biology of dust mites and the remediation of mite allergens in allergic disease. *J Allergy Clin Immunol.* 2001;107(Suppl):S406–S413. (IV)
89. Nilsson EJ, Henning CG, Magnusson J. Topical corticosteroids and *Staphylococcus aureus* in atopic dermatitis. *J Am Acad Dermatol.* 1992;27:29–34. (III)
90. Cho SH, Strickland I, Tomkinson A, Fehringer AP, Gelfand EW, Leung DY. Preferential binding of *Staphylococcus aureus* to skin sites of Th2-mediated inflammation in a murine model. *J Invest Dermatol.* 2001;116:658–663. (LB)
91. Cho SH, Strickland I, Boguniewicz M, Leung DY. Fibronectin and fibrinogen contribute to the enhanced binding of *Staphylococcus aureus* to atopic skin. *J Allergy Clin Immunol.* 2001;108:269–274. (III)
92. Ong PY, Ohtake T, Brandt C, et al. Endogenous antimicrobial peptides and skin infections in atopic dermatitis. *N Engl J Med.* 2002;347:1151–1160. (IIa)
93. Ambach A, Bonnekoh B, Gollnick H. Perforin hyperreleasability and depletion in cytotoxic T cells from patients with exacerbated atopic dermatitis and asymptomatic rhinoconjunctivitis allergica. *J Allergy Clin Immunol.* 2001;107:878–886. (IIa)
94. Novelli VM, Atherton DJ, Marshall WC. Eczema herpeticum: clinical and laboratory features. *Clin Pediatr (Phila).* 1988;27:231–233. (III)
95. Bork K, Brauning W. Increasing incidence of eczema herpeticum: analysis of seventy-five cases. *J Am Acad Dermatol.* 1988;19:1024–1029. (III)
96. Engler RJ, Kenner J, Leung DY. Smallpox vaccination: risk considerations for patients with atopic dermatitis. *J Allergy Clin Immunol.* 2002;110:357–365. (IV)
97. Zargari A, Eshaghi H, Back O, Johansson S, Scheynius A. Serum IgE reactivity to *Malassezia furfur* extract and recombinant *M. furfur* allergens in patients with atopic dermatitis. *Acta Derm Venereol.* 2001;81:418–422. (III)
98. Lintu P, Savolainen J, Kortekangas-Savolainen O, Kalimo K. Systemic ketoconazole is an effective treatment of atopic dermatitis with IgE-mediated hypersensitivity to yeasts. *Allergy.* 2001;56:512–517. (Ib)
99. Bender BG. Psychological dysfunction associated with atopic dermatitis. *Immunol Allergy Clin North Am.* 2002;22:43–53. (IV)
100. Schmid-Ott G, Jaeger B, Meyer S, Stephan E, Kapp A, Werfel T. Different expression of cytokine and membrane molecules by circulating lymphocytes on acute mental stress in patients with atopic dermatitis in comparison with healthy controls. *J Allergy Clin Immunol.* 2001;108:455–462. (LB)
101. Schmid-Ott G, Jaeger B, Adamek C, et al. Levels of circulating CD8⁺ T lymphocytes, natural killer cells, and eosinophils increase upon acute psychosocial stress in patients with atopic dermatitis. *J Allergy Clin Immunol.* 2001;107:171–177. (LB)
102. Kodama A, Horikawa T, Suzuki T, et al. Effect of stress on atopic dermatitis: investigation in patients after the great hanshin earthquake. *J Allergy Clin Immunol.* 1999;104:173–176. (IIb)
103. Melin L, Frederiksen T, Noren P, Swebilius BG. Behavioural treatment of scratching in patients with atopic dermatitis. *Br J Dermatol.* 1986;115:467–474. (Ib)
104. Haynes SN, Wilson CC, Jaffe PG, Britton BT. Biofeedback treatment of atopic dermatitis: controlled case studies of eight cases. *Biofeedback Self Regul.* 1979;4:195–209. (IIb)
105. Pei AY, Chan HH, Ho KM. The effectiveness of wet wrap dressings using 0.1% mometasone furoate and 0.005% fluticasone propionate ointments in the treatment of moderate to severe atopic dermatitis in children. *Pediatr Dermatol.* 2001;18:343–348. (Ib)
106. Di Prisco DE, Fuenmayor MC, Champion RH. Specific hyposensitization in atopic dermatitis. *Br J Dermatol.* 1979;101:697–700. (IV)
107. Glover MT, Atherton DJ. A double-blind controlled trial of hyposensitization to *Dermatophagoides pteronyssinus* in children with atopic eczema. *Clin Exp Allergy.* 1992;22:440–446. (Ib)
108. Kaufman HS, Roth HL. Hyposensitization with alum precipitated extracts in atopic dermatitis: a placebo-controlled study. *Ann Allergy.* 1974;32:321–330. (Ib)
109. Zachariae H, Cramers M, Herlin T, et al. Non-specific immunotherapy and specific hyposensitization in severe atopic dermatitis. *Acta Derm Venereol Suppl (Stockh).* 1985;114:48–54. (IIb)
110. Krutmann J, Czech W, Diepgen T, Niedner R, Kapp A, Schopf E. High-dose UVA1 therapy in the treatment of patients with atopic dermatitis. *J Am Acad Dermatol.* 1992;26:225–230. (Ib)
111. Abeck D, Schmidt T, Fesq H, et al. Long-term efficacy of medium-dose UVA1 phototherapy in atopic dermatitis. *J Am*

-
- Acad Dermatol.* 2000;42:254–257. (IIb)
112. Sowden JM, Berth-Jones J, Ross JS, et al. Double-blind, controlled, crossover study of cyclosporin in adults with severe refractory atopic dermatitis. *Lancet.* 1991;338:137–140. (Ib)
113. Salek MS, Finlay AY, Luscombe DK, et al. Cyclosporin greatly improves the quality of life of adults with severe atopic dermatitis: a randomized, double-blind, placebo-controlled trial. *Br J Dermatol.* 1993;129:422–430. (Ib)
114. van Joost T, Heule F, Korstanje M, van den Broek MJ, Stenvald HJ, van Vloten WA. Cyclosporin in atopic dermatitis: a multicentre placebo-controlled study. *Br J Dermatol.* 1994;130:634–640. (Ib)
115. Harper JI, Berth-Jones J, Camp RD, et al. Cyclosporin for atopic dermatitis in children. *Dermatology.* 2001;203:3–6. (IV)
116. Boguniewicz M, Jaffe HS, Izu A, et al. Recombinant γ interferon in treatment of patients with atopic dermatitis and elevated IgE levels. *Am J Med.* 1990;88:365–370. (IIb)
117. Ellis CN, Stevens SR, Blok BK, Taylor RS, Cooper KD. Interferon- γ therapy reduces blood leukocyte levels in patients with atopic dermatitis: correlation with clinical improvement. *Clin Immunol.* 1999;92:49–55. (IIa)
118. Schneider LC, Baz Z, Zarcone C, Zurakowski D. Long-term therapy with recombinant interferon- γ (rIFN- γ) for atopic dermatitis. *Ann Allergy Asthma Immunol.* 1998;80:263–268. (III)
119. Grundmann-Kollmann M, Podda M, Ochsendorf F, et al. Meprobamate is effective in the treatment of atopic dermatitis. *Arch Dermatol.* 2001;137:870–873. (III)
120. Meggitt SJ, Reynolds NJ. Azathioprine for atopic dermatitis. *Clin Exp Dermatol.* 2001;26:369–375. (III)
121. Koo J, Arain S. Traditional Chinese medicine for the treatment of dermatologic disorders. *Arch Dermatol.* 1998;134:1388–1393. (II)
122. Harper J. Traditional Chinese medicine for eczema. *BMJ.* 1994;308:489–490. (IV)
123. Koro O, Furutani K, Hide M, Yamada S, Yamamoto S. Chemical mediators in atopic dermatitis: involvement of leukotriene B₄ released by a type I allergic reaction in the pathogenesis of atopic dermatitis. *J Allergy Clin Immunol.* 1999;103:663–670. (II)
124. Hishinuma T, Suzuki N, Aiba S, Tagami H, Mizugaki M. Increased urinary leukotriene E₄ excretion in patients with atopic dermatitis. *Br J Dermatol.* 2001;144:19–23. (II)
125. Capella GL, Grigerio E, Altomare G. A randomized trial of leukotriene receptor antagonist montelukast in moderate-to-severe atopic dermatitis of adults. *Eur J Dermatol.* 2001;11:209–213. (Ib)
126. Yanase DJ, David-Bajar K. The leukotriene antagonist montelukast as a therapeutic agent for atopic dermatitis. *J Am Acad Dermatol.* 2001;44:89–93. (Ib)
127. Arkwright PD, David TJ. Intradermal administration of a killed *Mycobacterium vaccae* suspension (SRL 172) is associated with improvement in atopic dermatitis in children with moderate-to-severe disease. *J Allergy Clin Immunol.* 2001;107:531–534. (Ib)

Requests for reprints should be addressed to:
Joint Council of Allergy, Asthma and Immunology
50 N Brockway St
#3-3
Palatine, IL 60067