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# GUIDELINES OF CARE FOR THE MANAGEMENT OF ATOPIC DERMATITIS:

## Part 1: Diagnosis and Assessment of Atopic Dermatitis

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**DISCLAIMER**

Adherence to these guidelines will not ensure successful treatment in every situation. Furthermore, these guidelines should not be interpreted as setting a standard of care, or be deemed inclusive of all proper methods of care nor exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient, and the known variability and biological behavior of the disease. This guideline reflects the best available data at the time the guideline was prepared. The results of future studies may require revisions to the recommendations in this guideline to reflect new data.

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## Abstract

Atopic dermatitis (AD) is a chronic, pruritic inflammatory dermatosis that affects up to 25% of children and 2–3% of adults. This guideline addresses important clinical questions that arise in AD management and care, providing updated and expanded recommendations based on the available evidence. In this first of four sections, methods for diagnosis and monitoring of disease, outcomes measures for assessment and common clinical associations that affect patients with AD are discussed. Known risk factors for the development of disease are also reviewed.

### Keywords

atopic dermatitis; diagnosis; criteria; biomarkers; risk factors; assessment scales; clinical associations

## METHOD

A work group of recognized AD experts was convened to determine the audience and scope of the guideline, and to identify important clinical questions in the diagnosis and assessment of atopic dermatitis (Table I). Work group members completed a disclosure of interests which was updated and reviewed for potential relevant conflicts of interest throughout guideline development. If a potential conflict was noted, the work group member recused him or herself from discussion and drafting of recommendations pertinent to the topic area of the disclosed interest.

An evidence-based model was used and evidence was obtained using a systematic search of PubMed, the Cochrane Library, and the Global Resources for Eczema Trials (GREAT)[1] databases from November 2003 through November 2012 for clinical questions addressed in the previous version of this guideline published in 2004, and 1964–2012 for all newly identified clinical questions as determined by the work group to be of importance to clinical care. Searches were prospectively limited to publications in the English language. MeSH terms used in various combinations in the literature search included: atopic dermatitis, atopic eczema, diagnosis, diagnostic, severity course, assessment, biomarkers, outcomes measures, morbidity, quality-of-life, appearance, comorbidity, food allergy, allergic rhinitis, asthma, cancer, sleep, growth effects, developmental effects, behavioral, psychological, attention deficit hyperactivity disorder (ADHD), treatment, and outcome. A total of 1,417 abstracts were initially assessed for possible inclusion. After removal of duplicate data, 292 were retained for final review based on relevancy and the highest level of available evidence for the outlined clinical questions. Evidence tables were generated for these studies and utilized by the work group in developing recommendations. The Academy's prior published guidelines on AD were also evaluated, as were other current published guidelines on atopic dermatitis.[2–5]

The available evidence was evaluated using a unified system called the Strength of Recommendation Taxonomy (SORT) developed by editors of the U.S. family medicine and primary care journals (i.e. *American Family Physician*, *Family Medicine*, *Journal of Family Practice*, and *BMJ USA*).[6] Evidence was graded using a 3-point scale based on the quality of study methodology (*e.g*. randomized control trial, case-control, prospective/retrospective cohort, case series, etc.), and the overall focus of the study (*i.e*. diagnosis, treatment/prevention/screening, or prognosis) as follows:

- **I.** Good-quality patient-oriented evidence (*i.e*. evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life).
- **II.** Limited-quality patient-oriented evidence.
- **III.** Other evidence including consensus guidelines, opinion, case studies, or disease-oriented evidence (*i.e*. evidence measuring intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes).

Clinical recommendations were developed based on the best available evidence tabled in the guideline. These are ranked as follows:

- **A.** Recommendation based on consistent and good-quality patient-oriented evidence.
- **B.** Recommendation based on inconsistent or limited-quality patient-oriented evidence.
- **C.** Recommendation based on consensus, opinion, case studies, or disease-orientedevidence.

In those situations where documented evidence-based data is not available, we have utilized expert opinion to generate our clinical recommendations.

This guideline has been developed in accordance with the American Academy of Dermatology (AAD)/AAD Association *Administrative Regulations for Evidence-based Clinical Practice Guidelines* (version approved May 2010), which includes the opportunity for review and comment by the entire AAD membership and final review and approval by the AAD Board of Directors.[7] This guideline will be considered current for a period of five years from the date of publication, unless reaffirmed, updated, or retired at or before that time.

## DEFINITION

Atopic dermatitis is a chronic, pruritic inflammatory skin disease that occurs most frequently in children, but can also affect adults. It follows a relapsing course. AD is often associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and asthma. Atopic eczema is synonymous with AD.

## INTRODUCTION

AD onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by 5 years of age.[8, 9] While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults.[10] AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Notable clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification, but these vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by patients and their families.

## DIAGNOSIS

The diagnosis of atopic dermatitis is made clinically and is based on historical features, morphology and distribution of skin lesions, and associated clinical signs. Formal sets of criteria have been developed by various groups to aid classification.

One of the earliest and most recognized sets of diagnostic criteria is the 1980 Hanifin and Rajka criteria, which requires that three of four major criteria and three of twenty-three minor criteria be met.[11] While comprehensive and often utilized in clinical trials, such a large number of criteria are unwieldy for use in clinical practice. Some of the minor criteria have been noted to be poorly defined or non-specific (such as pityriasis alba), while others, such as upper lip cheilitis and nipple eczema, are quite specific for AD but uncommon.[11, 12] Several international groups proposed modifications to address these limitations (e.g. Kang and Tian criteria, International Study of Asthma and Allergies in Childhood (ISAAC) criteria).[13–16] The United Kingdom (UK) Working Party, in particular, systematically distilled the Hanifin and Rajka criteria down to a core set that is suitable for epidemiologic/population-based studies and that can be used by non-dermatologists. These consist of one mandatory and five major criteria and do not require any laboratory testing. Both the Hanifin

and Rajka and UK Working Party diagnostic schemes have been validated in studies and tested in several different populations.[12, 13, 15, 17–23]

A 2003 consensus conference spearheaded by the American Academy of Dermatology suggested revised Hanifin and Rajka criteria that are more streamlined and additionally applicable to the full range of ages affected.[24] While this set has not been assessed in validation studies, it is felt by the current workgroup that an adaptation of this pragmatic approach for diagnosing AD in infants, children, and adults is well-suited for use in the clinical setting (Box 1). The original UK criteria cannot be applied to very young children, although revisions to include infants have since been proposed.[25–27]

The recommended criteria for the diagnosis of atopic dermatitis are shown in Table II, and the strength of the recommendation is displayed in Table VI. Atopic dermatitis should be differentiated from other red, scaly skin conditions. It is often difficult to separate AD from seborrheic dermatitis in infancy, and the two conditions may overlap in this age group. AD usually spares the groin and axillary regions, while seborrheic dermatitis affects these areas and tends not to be pruritic. Particularly if not responding to therapy, the diagnosis of AD should be re-reviewed and other disorders considered, including more serious nutritional, metabolic, and immunologic conditions in children and cutaneous T-cell lymphoma in adults. Allergic contact dermatitis may be both an alternative diagnosis to AD and/or an exacerbator of AD in some individuals (further discussed in Part 4 of the guideline series).

## BIOMARKERS

The diagnosis of AD remains clinical, as there is currently no reliable biomarker that can distinguish the disease from other entities. The most commonly associated laboratory feature, an elevated total and/or allergen-specific serum IgE level, is not present in about 20% of affected individuals.[28] Some denote “extrinsic” and “intrinsic” groups of disease based on the presence or absence of IgE elevation, but whether these are true variants remains controversial. Some individuals will later develop elevated IgE levels and recent knowledge of skin barrier defects and studies on epicutaneous sensitization suggest that elevated IgE may be a secondary phenomenon.[28] Elevated allergen-specific IgE levels are also non-specific, as they are found in 55% of the United States general population.[29] Although the total IgE level does tend to vary with disease severity, it is not a reliable indicator because some individuals with severe disease have normal values, and IgE may also be elevated in multiple non-atopic conditions (e.g. parasitic infection, certain cancers and autoimmune diseases).[28, 30, 31] Increases in tissue mast cells and peripheral eosinophil counts have also been evaluated, but with similar inconsistent association.[30, 32–34]

Discovery of new T-lymphocyte subsets, as well as novel cytokines and chemokines, have generated a myriad of additional potential biomarkers. These include serum levels of CD30, Macrophage-Derived Chemoattractant (MDC), interleukins (IL)-12, -16,-18,-31, and Thymus and Activation-Regulated Chemokine (TARC). Some have demonstrated correlation with AD disease severity using the SCORing Atopic Dermatitis (SCORAD) index and other severity scales.[35–40] But to date, none have shown reliable sensitivity or specificity for AD to support general clinical use for diagnosis or monitoring. Most studies

suffer from small cohort size and involve selection from tertiary care centers with more severe disease, rather than from general populations. Few have compared levels in AD with that in other eczematous conditions or other atopic conditions to assess whether the biomarker is a specific indicator for AD.

Markers for prognosis are also inconsistent, although high total serum IgE levels and *filaggrin* gene null mutations do tend to predict a more severe and protracted course of disease (discussed further in RISK FACTORS).[9, 28, 41, 42] Recommendations for the use of biomarkers in the assessment of atopic dermatitis are shown in Table III, and the strength of the recommendation is summarized in Table VI.

## DISEASE SEVERITY AND CLINICAL OUTCOMES ASSESSMENT

### Disease severity scales

For measurement of disease severity, twenty-eight different scales were identified, without a single gold-standard emerging.[43–56] They employ various methods that include grid patterns, objective disease features and extent, and some scales incorporate subjective disease features. The most commonly used disease severity scales are the SCORAD index, the Eczema Area and Severity Index (EASI), Investigator's Global Assessment (IGA), and Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score.[43] These scales are primarily used in clinical trials and rarely in clinical practice, as they were generally not designed for this purpose.

Scale development in many cases included rigorous testing and evaluation of the following statistical properties: inter-and intra-rater reliability, validity (construct, content and concurrent), internal consistency reliability, responsiveness to change, and minimal clinically important difference.[44, 45] The available literature suggests that the SCORAD index, the EASI score, and the Patient-Oriented Eczema Measure (POEM) severity scale have been adequately tested and validated and therefore, their use can be considered when practical.[44] Of note, EASI utilizes objective physician estimates of disease extent and severity, while SCORAD incorporates both objective physician estimates of extent and severity and subjective patient assessment of itch and sleep loss.[50] POEM was specifically designed to measure severity from the patient perspective and utilizes seven questions regarding symptoms and their frequency. [43] The Three Item Severity Scale (TISS) is another simplified scale that shows promise for future use in clinical practice, but needs further testing.[44, 54]

Recognizing the lack of uniformity in disease-severity scale use, international efforts are underway to standardize measured outcomes. [57] This includes development of a core set of valid measures of signs and symptoms that can be feasibly recorded in controlled trials, which is directed toward improving comparisons across trials and facilitating meta-analyses.

### Quality of life scales and disease impact measurements

Twenty-two different AD-specific, dermatology-specific, and generic scales were identified that measure quality of life and other psychological outcomes in patients with atopic dermatitis.[43, 58–66] These scales have been used to assess the impact of the disease and the

effects of interventions, as well as to make comparisons with the impact of other disorders. Careful consideration of the scale properties should occur prior to use, including validity (content, construct, concurrent, discriminative), reliability (test-retest and internal consistency), responsiveness to change, and minimal clinically important difference.[58, 60, 67, 68] In clinical trials, the most commonly used scale is the Children's Dermatology Life Quality Index (CDLQI), followed by the Dermatitis Family Impact (DFI), the Dermatology Life Quality Index (DLQI), and the Infant's Dermatology Life Quality Index.[43] But these scales were not generally designed for use in routine clinical practice.[69]

Further development and evaluation of practical clinical quality of life scales are needed. This could be done by modifying existing scales into short clinical versions or by testing existing scales in a clinic population. Of note, inclusion of patient assessment of pruritus is critical given its central contribution to the morbidity of AD.[70, 71] Ratings of itch intensity, whether made by parents for young children or by older individuals for themselves, significantly and inversely correlate with quality of life.[72, 73] The difficulties due to itching and the resultant scratching are typically the first to be mentioned by parents when asked about the effects of their child's disease.[74] The mechanisms underlying AD-associated itch remain unclear, and are an area of much active research. Sleep disturbance, impedance of daily activities (including effects on work or school performance), and persistence of disease are other key measures of disease impact, and represent a patient's status and overall well-being. [69, 75, 76] Recommendations on assessment are summarized in Table IV and the strength of recommendation in Table VI.

## CLINICAL ASSOCIATIONS

Common associations/comorbidities of AD that have been supported by studies include other atopic conditions: namely, food allergies, asthma, and allergic rhinitis/rhinoconjunctivitis.[77–84] Some consider AD to be the start of the "atopic march," given the frequent subsequent development of one or more of the other atopic conditions. However, the association of other atopic conditions with AD is complex and multifactorial, as this progression does not happen in all individuals. Patients living in humid climates or developing countries may manifest AD only after changing their locale and/or following onset of respiratory allergies.[85–88]

Sleep disturbance is also common and stems in large part from the significant itch associated with AD.[69, 70, 89, 90] Sleep is disrupted in up to 60% of children with eczema, increasing to 83% during exacerbation.[91] Along with the affected individual, other family members may also suffer as a result of being awakened.[68] Even when in clinical remission, individuals with eczema demonstrate more sleep disturbance than do healthy individuals.[91] Greater skin disease severity appears to have an effect on mood as well. Depression has been noted in both teens and adults affected with AD.[92, 93] More recently, there has been a suggested association of AD with behavior disorders, e.g. attention deficit hyperactivity disorder (ADHD), especially in children.[94, 95] However, association does not establish causality and the precise nature of the relationship requires further study, including the role of sleep disturbance and ADHD-like behaviors, as well as the possibility of non-specific linkage to any chronic disease of childhood.[94]

Cancer and obesity have been inconsistently associated with AD. There does not appear to be an increased risk of skin cancer or of internal malignancies, although some data is suggestive of higher rates of lymphoma and lower rates of glioma.[96–100] At present, there is insufficient data to warrant special screening or caution. AD has been linked to obesity in a few epidemiologic studies.[101, 102] However, short stature and poor growth have also been documented, particularly in children who suffer from severe skin disease.[103–106]

The recommendations regarding the assessment for clinical associations of atopic dermatitis (Table V) are based on group consensus, as there is no high-quality, conclusive evidence to show that screening for them leads to improved patient outcomes. The benefits of taking an integrated, multidisciplinary clinical approach to the care of AD patients with common associations are mainly limited to a few case reports.[107, 108] Eczema schools and other educational programs will be discussed in Part 4 of the guidelines.

## RISK FACTORS FOR DISEASE DEVELOPMENT

Two risk factors appear to be consistently and strongly associated with the development of atopic dermatitis: 1) a family history of atopy and 2) loss of function mutations in the *filaggrin* (*FLG*) gene.

Approximately 70% of AD patients have a positive family history of atopic diseases.[109] The odds of developing AD are 2- to 3-fold higher in children with one atopic parent, and this increases to 3- to 5-fold if both parents are atopic.[110, 111] A maternal history of AD is possibly more predictive.[112] The FLG gene encodes profilaggrin, which is degraded to filaggrin monomers, and these proteins play key roles in the terminal differentiation of the epidermis and formation of the skin barrier including the stratum corneum. Filaggrin breakdown products are part of natural moisturizing factor, which contributes to epidermal hydration and barrier function. FLG null mutations confer a risk for earlier-onset AD, and for more severe, persistent disease.[113, 114112] They also lead to an increased tendency for eczema herpeticum. Different defects in *FLG* have been noted in different ethnic populations with AD, demonstrating its importance to pathogenesis. However, a significant number of patients with AD have no known *FLG* mutations, and conversely, approximately 40% of individuals with *FLG* null alleles do not develop AD.[113]

The type of delivery during childbirth (caesarean or vaginal) does not appear to alter AD risk.[115] Elevated birth weights may be a risk factor for disease development, but the effect size is likely small as studies have been conflicting, with some showing a negative association.[116–118]

While patients with atopic dermatitis are often sensitized to certain foods, the timing of solid food introduction or withholding of allergenic foods does not appear to alter the risk for AD.[119] Most studies of dietary modification of the maternal or infant diet do not show a protective effect, although recently published studies of hydrolyzed formula and probiotic supplementation suggest that these approaches could have a beneficial effect in preventing disease development in some high-risk infants who are not exclusively breast fed.[120–125] But at present, there is insufficient evidence to recommend any specific dietary or other measures as being effective for the primary prevention of AD. Breastfeeding for the first 6

months of life is encouraged for its other benefits for the infant and mother (e.g. bonding, passive immunity).

There are no consistent findings to suggest that gender affects AD risk, but being of black race does appear to increase risk.[126] A higher level of parental education is a risk factor for disease, but the effect of socioeconomic status is unclear.[126, 127] Previous studies found a higher risk of AD in higher socioeconomic groups, but more recent studies failed to confirm these findings.[128, 129] Living in urban areas appears likely to increase the risk of atopic dermatitis, but studies attempting to identify causative environmental agents have not been conclusive.[130] Day care may influence the risk of AD development, but studies that offer better control for confounders are needed before further conclusions can be made.[126, 131]

The effect of exposure to pets is unclear, with conflicting data.[132–134] Two recent studies have shown that cat, but not dog, ownership enhanced the effect of filaggrin mutations in promoting the development of AD.[135, 136] While patients with atopic dermatitis are often sensitized to house dust mites, there is no strong evidence to show that dust mite avoidance strategies prevent atopic dermatitis.[137, 138] The most recent systematic review regarding early life microbial exposures found evidence that exposures to endotoxin, farm animals, and dogs may protect against AD.[139] The consumption of unpasteurized milk, as well as acquired helminth infections may also be protective, but are not recommended measures due to their potential associated health risks.

No definitive conclusions can be drawn regarding early antibiotic exposure and the risk of AD.[85, 140, 141] Although studies are inconsistent, personal and secondhand/household smoking status do not appear to significantly affect AD development; [142–145] however, smoking is detrimental to those with asthma and has many other negative health risks.

## GAPS IN RESEARCH

In review of the currently available highest level of evidence, the expert work group acknowledges that while much is known about the diagnosis and evaluation of AD, much has yet to be learned. Significant gaps in research were identified, including but not limited to: validation studies of the AAD workgroup diagnostic criteria, development, validation, and uniformity in use of disease severity and quality of life measurements applicable to a busy clinical practice environment, interventional studies testing impact of multidisciplinary management on AD outcomes, and additional quality, controlled studies on epidemiologic risk factors for disease. It is hoped that additional knowledge of AD pathogenesis will soon lead to a proven biomarker for diagnosis and/or monitoring, and that AD-associated pruritus is better understood to generate improved therapeutic options.

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## Publishable Conflict of Interest Statement

The American Academy of Dermatology (AAD) strives to produce clinical guidelines that reflect the best available evidence supplemented with the judgment of expert clinicians. Significant efforts are taken to minimize the potential for conflicts of interest to influence guideline content. Funding of guideline production by medical or pharmaceutical entities is prohibited, full disclosure is obtained and evaluated for all guideline contributors, and recusal is used to manage identified relationships. The AAD conflict of interest policy summary may be viewed at www.aad.org.

The below information represents the authors' identified relationships with industry that are relevant to the guideline. Relevant relationships requiring recusal for drafting of guideline recommendations and content were not noted for this section.

Lawrence F. Eichenfield, MD, served as a consultant for Anacor, Bayer, Leo Pharma receiving honoraria , and TopMD receiving stock options; was a consultant and speaker for Galderma receiving honoraria; served as a consultant, speaker and member of the advisory board for Medicis/Valeant receiving honoraria; and was an investigator for Anacor, Astellas, Galderma, and LeoPharma receiving no compensation.

Sarah L. Chamlin, MD, served on the advisory boards for Galderma and Valeant receiving honoraria.

Steven R. Feldman, MD, PhD, served on the advisory boards for Amgen, Doak, Galderma, Pfizer, Pharmaderm, Skin Medica, and Stiefel receiving honoraria; was a consultant for Abbott, Astellas, Caremark, Coria, Gerson Lehrman, Kikaku, Leo Pharma, Medicis, Merck, Merz, Novan, Peplin, and Pfizer receiving honoraria, and Celgene, HanAll, and Novartis receiving other financial benefits; was a speaker for Abbott, Amgen, Astellas, Centocor, Dermatology Foundation, Galderma, Leo Pharma, Novartis, Pharmaderm, Sanofi-Aventis, Stiefel, and Taro receiving honoraria; served as a stockholder and founder for Causa Technologies and Medical Quality Enhancement Corporation receiving stock; served as an investigator for Abbott, Amgen, Anacor, Astellas, Basilea, Celgene, Centocor, Galderma, Medicis, Skin Medica, and Steifel receiving grants, and Suncare Research receiving honoraria; and had other relationships with Informa, UptoDate, and Xlibris receiving royalty, and Medscape receiving honoraria.

Jon M. Hanifin, MD, served on the advisory board for Chugai Pharma USA receiving honoraria; was a consultant for GlaxoSmithKline, Merck Elocon Advisory Board, Pfizer, and Valeant Elidel Advisory Board receiving honoraria; and served as an investigator for Asubio and Merck Sharp & Dohme receiving grants.

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## ABBREVIATIONS

| | |
|---|---|
| **AAD** | American Academy of Dermatology |
| **AD** | atopic dermatitis |
| **ADHD** | attention deficit hyperactivity disorder |
| **CLDQI** | Children’s Dermatology Life Quality Index |
| **DFI** | Dermatitis Family Impact |
| **DLQI** | Dermatology Life Quality Index |
| **EASI** | Eczema Area and Severity Index |
| **FLG** | filaggrin |
| **GREAT** | Global Resources for Eczema Trials |
| **IGA** | Investigator’s Global Assessment |
| **IgE** | immunoglobulin E |
| **IL** | interleukin |
| **ISAAC** | International Study of Asthma and Allergies in Childhood |
| **MDC** | macrophage-derived chemoattractant |

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|---|---|
| **POEM** | Patient-Oriented Eczema Measure |
| **SASSAD** | Six Area, Six Sign Atopic Dermatitis |
| **SCORAD** | SCORing atopic dermatitis |
| **SORT** | strength of recommendation taxonomy |
| **TARC** | thymus and activation-regulated chemokine |
| **TISS** | Three-Item Severity Scale |
| **UK** | United Kingdom |

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**BOX 1**

Adapted from Journal of the American Academy of Dermatology, Volume 49, Eichenfield, LF, Hanifin JM, Luger TA, Stevens SR, Pride HB. Consensus conference on pediatric atopic dermatitis, pages 1088–1095, Copyright 2003, with permission from the American Academy of Dermatology.

Features to be considered in diagnosis of patients with atopic dermatitis

- **ESSENTIAL FEATURES**; must be present:
  - Pruritus
  - Eczema (acute, subacute, chronic):
    - Typical morphology and age-specific patterns*
    - Chronic or relapsing history

  *Patterns include:*
  *1) facial, neck, and extensor involvement in infants and children;*
  *2) current or prior flexural lesions in any age group;*
  *3) sparing of groin and axillary regions.*

- **IMPORTANT FEATURES**; seen in most cases, adding support to the diagnosis:
  - Early age of onset
  - Atopy
    - Personal and/or family history
    - IgE reactivity
  - Xerosis

- **ASSOCIATED FEATURES** ; these clinical associations help to suggest the diagnosis of AD but are too non-specific to be used for defining or detecting AD for research and epidemiologic studies:
  - Atypical vascular responses (e.g., facial pallor, white dermographism, delayed blanch response)
  - Keratosis pilaris / pityriasis alba / hyperlinear palms / ichthyosis
  - Ocular / periorbital changes
  - Other regional findings (e.g., perioral changes / periauricular lesions)
  - Perifollicular accentuation / lichenification / prurigo lesions

- **EXCLUSIONARY CONDITIONS;** it should be noted that a diagnosis of AD depends on excluding conditions such as:
    - scabies
    - seborrheic dermatitis
    - contact dermatitis (irritant or allergic)
    - ichthyoses
    - cutaneous T-cell lymphoma
    - psoriasis
    - photosensitivity dermatoses
    - immune deficiency diseases
    - erythroderma of other causes

## SCOPE

This guideline addresses the diagnosis and assessment of pediatric and adult atopic dermatitis (AD, atopic eczema) of all severities. Other forms of dermatitis, such as irritant dermatitis and allergic contact dermatitis in those without atopic dermatitis, are outside the scope of this document. Recommendations on AD treatment and management are subdivided into four sections given the significant breadth of the topic, and to update as well as expand on the clinical information and recommendations previously published in 2004. This document is the first part of the series and covers methods for diagnosis and monitoring of AD, disease severity and quality-of-life scales for outcomes measurement, and common clinical associations that affect patients. A discussion on known risk factors for the development of AD is also presented. The second guideline in the series will address the management and treatment of AD with pharmacological and non-pharmacological topical modalities; the third section will cover phototherapy and systemic treatment options; and the fourth section will address the minimization of disease flares, educational interventions, and use of adjunctive approaches.

**Table I**

Clinical questions used to structure the evidence review for the diagnosis and assessment of atopic dermatitis

| |
|---|
| • What are the most valid and reliable methods for diagnosing atopic dermatitis?* |
| • What are the most useful tools to assess the severity and course of atopic dermatitis?* |
| • What are the patient-specific and disease-specific outcome measures used to determine the relative effectiveness of a given treatment for atopic dermatitis? |
| • What common clinical associations may affect patients with atopic dermatitis?* |
| • What are the epidemiological risk factors associated with atopic dermatitis?* |

* Indicates new clinical questions

**Table II**

Recommendation for the diagnosis of atopic dermatitis

| |
|---|
| Patients with presumed atopic dermatitis should have their diagnosis based on the criteria summarized in Box 1. On occasion, skin biopsy or other tests (such as serum IgE, potassium hydroxide (KOH) preparation, patch testing, and/or genetic testing) may be helpful to rule out other or associated skin conditions. |

**Table III**

Recommendations for the use of biomarkers in the assessment of atopic dermatitis

| |
|---|
| For patients with presumed atopic dermatitis, there are no specific biomarkers that can be recommended for diagnosis and/or assessment of disease severity. |
| Monitoring of IgE levels is not recommended for the routine assessment of disease severity. |

**Table IV**

Recommendations for disease severity and clinical outcomes assessment

| |
|---|
| For the general management of patients with atopic dermatitis, available disease severity measurement scales are not recommended for routine clinical practice, as they were not usually designed for this purpose. |
| For the general management of patients with atopic dermatitis, available patient quality-of-life measurement scales are not recommended for routine clinical practice. |
| It is recommended that clinicians ask general questions about itch, sleep, impact on daily activity, and persistence of disease, and currently available scales be used mainly when practical. |

**Table V**

Recommendations for the assessment of clinical associations of atopic dermatitis

| |
|---|
| Physicians should be aware of and assess for conditions associated with AD – such as rhinitis/rhinoconjunctivitis, asthma, food allergy, sleep disturbance, depression, and other neuropsychiatric conditions—and it is recommended that physicians discuss them with the patient as part of the treatment/management plan, when appropriate. |
| An integrated, multidisciplinary approach to care may be valuable and is suggested for atopic dermatitis patients who present with common associations. |

**Table VI**

Strength of recommendations for the diagnosis and assessment of atopic dermatitis

| Recommendation | Strength of Recommendation | Level of Evidence | References |
|---|---|---|---|
| Diagnosis made using criteria in Box 1 | *C* | III | [12], [13], [15–23], [146–149] |
| No specific biomarkers for diagnosis or severity assessment | *B* | II | [30–40], [150–164] |
| IgE levels not routinely Recommended | A | I | [5], [30], [31], [34], [35], [165], [166] |
| Available disease severity scales not for routine clinical use | *C* | II | [44], [45], [48], [49], [54], [66], [67], [167–176] |
| Available quality of life severity scales not for routine clinical use | C | II | [58], [60], [67], [6837] |
| Should query itch, sleep, impact on daily activity, and disease persistence | C | III | [69–76] |
| Awareness and discussion of common associations | *C* | I,II | [69], [70], [77–84], [92–98], [103], [104] |
| Integrated, multidisciplinary approach to care | C | III | [107], [108] |