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Special Article

Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape

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ABSTRACT

The implementation of treatment guidelines for atopic dermatitis is challenging, in part because of different guidance documents being used by different groups of specialists and in part because the language of guidelines often reflects the evidence base rather than the practical "how to." The Atopic Dermatitis Yardstick is part of a series developed in response to the need to proactively address the loss of disease control for atopic illnesses at all levels of severity. It presents a comprehensive update on how to conduct a sustained step-up in therapy for the patient with inadequately controlled or poorly controlled atopic dermatitis. Patient profiles, based on current guidelines and the authors' combined clinical experience, provide a practical and clinically meaningful guide to aid physicians in helping their patients achieve the goal of clear to almost clear. The intent is not to replace guidelines but to complement their recommendations incorporating the latest research and therapies.

Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease—one of the most common inflammatory skin diseases worldwide, with an estimated prevalence of up to 25% of children and 7% of adults in the United States.[1–5] AD typically occurs in infancy and early childhood, with an onset in the first year of life reported for 60% to 85% of children and by 5 years of age for at least 85%.[2,6–8] However, AD can present at any age; and although most childhood-onset symptoms resolve before adulthood, persistence (albeit some in milder forms) is relatively common.[1,9–13] Up to 50% of adult patients are first diagnosed in adulthood, and 30% of childhood cases persist into the adult years.[1,14–16] Managing AD at any age can be challenging.

Atopic dermatitis is a diagnosis based on clinical presentation.[9–11,17] Current research detailing the underlying mechanisms of AD (Fig 1; eCommentary 1)[18] holds hope that biomarkers will be available to confirm the diagnosis and possibly differentiate various AD phenotypes (eg, intrinsic vs extrinsic AD, pediatric AD, Asian-origin AD),[19–31] but the current reality is that AD is diagnosed by symptoms and exclusion (Table 1).[5,9,11]

The clinical presentation of AD is characterized by (1) pruritus, (2) eczematous lesions (associated with T-helper cell type [T_H] 2 and T_H22 inflammation), and (3) dry skin (related to epidermal barrier

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Disclosures: Dr Boguniewicz is a member of the speakers' bureau and is a consultant for Regeneron and Sanofi-Genzyme and has done clinical research for Regeneron. Dr Farrar has no financial interests to disclose. Dr Fonacier serves on advisory boards for Regeneron and Genentech, is a member of the speakers' bureau for Regeneron, and has research receiving grant support from Baxter, Genentech, and Merck. Dr Guttman-Yassky serves on the boards of Sanofi-Aventis, Regeneron, Stiefel/GlaxoSmithKline, MedImmune, Celgene, Anacor, Leo Pharma, AnaptysBio, Celsus, Dermira, Galderma, Novartis, Pfizer, Vitae, Glenmark, AbbVie, and Asana Biosciences; serves as a consultant for Regeneron, Sanofi Aventis, MedImmue, Celgene, Stiefel/GlaxoSmithKline, Celsus, BMS, Amgen, Drais, AbbVie, Anacor, AnaptysBio, Dermira, Galderma, Leo Pharma, Novartis, Pfizer, Vitae Mitsubishi Tanabe, Eli Lilly, Glenmark, and Asana Biosciences; and receives grant support from Regeneron, Celgene, BMS, Janssen, Dermira, Leo Pharma, Merck, Novartis, and UCB. Dr Ong has no financial interests to disclose. Dr Silverberg serves on advisory boards and as a consultant for AbbVie, Eli Lilly, Galderma, GlaxoSmithKline, Kiniksa, Leo, Menlo, Pfizer, Realm, Roivant, and Regenron-Sanofi; and has research receiving grant support from GlaxoSmithKline.

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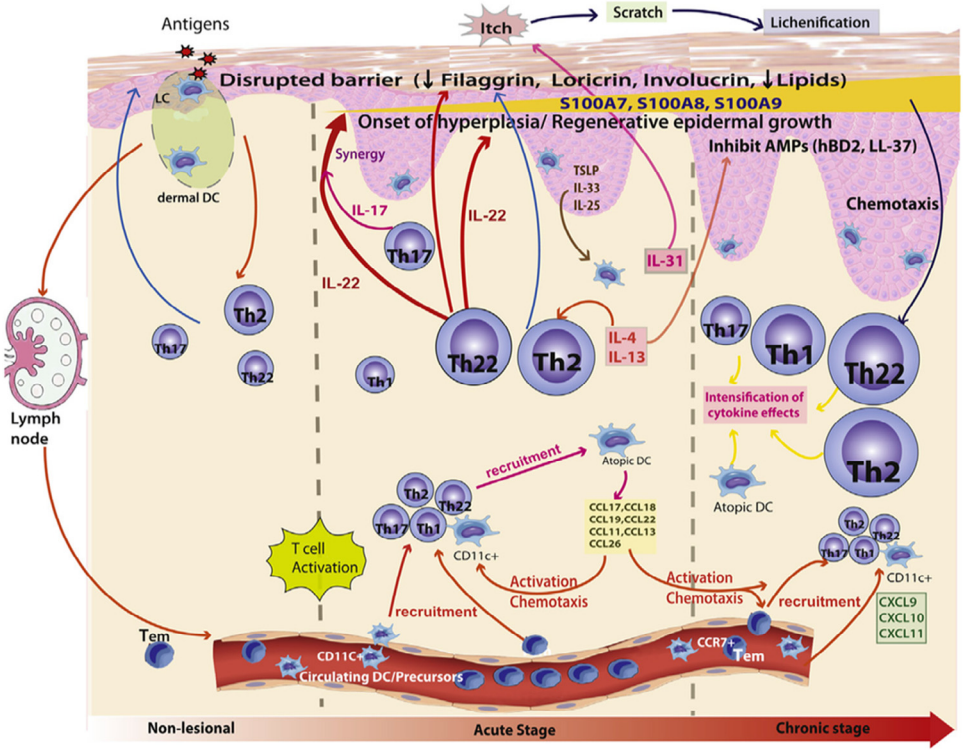

Figure 1. Immunopathologic mechanisms underlying atopic dermatitis. Reprinted with permission from Leung D, Guttman-Yassky E. Deciphering the complexities of atopic dermatitis: shifting paradigms in treatment approaches. *J Allergy Clin Immunol.* 2014;134:769–779,[18] with permission from Elsevier. AMP, adenosine monophosphate; CCR7, C-C chemokine receptor type 7; CXCL, chemokine ligand; DC, dendritic cell; hBD2, human β-defensin 2; IL, interleukin; Tem, effector memory T-cell; Th, T-helper cell type; TSLP, thymic stromal lymphopoietin.

dysfunction; Fig 1; eCommentary 1).[7,9–11,17,32] Pruritus is the hallmark of AD; and the cycle of itching and scratching exacerbates the cellular damage in skin lesions and facilitates secondary infections, which can be serious.[29,33–36] These patients are at increased risk for cutaneous infections, and in a recent study, also at risk for multiorgan and systemic infections.[37] Symptoms usually wax and wane, and patients with AD can present with a range of disease severity, from mild intermittent disease to severe difficult-to-control disease (Fig 2). For greater depth, the reader is directed to current guidelines and review publications.[7,9–11,17,32]

Current guidance documents recommend a "control-based" and "risk-based" model of disease management in which an initial diagnosis is followed by treatment according to categorization of severity[9–11] (Fig 2). However, for AD, validated measures to assess severity are not commonly used in the clinic, making it difficult to assess the impact of treatment and monitor disease progression. Although several validated clinical scoring systems are available, they are used mostly as tools for clinical research. Others await validation.[38–52] These are presented in Table 2. The Food and Drug Administration's (FDA) preferred primary efficacy end point categorizes AD severity according to a subjective, static Investigator's Global Assessment (IGA) or Investigator's Static Global Assessment (ISGA) score. The IGA has not been validated for AD in any setting.[1,48] The lack of validated clinical measures with standardized

Table 1
Diagnostic Criteria for Atopic Dermatitis[17]

Essential (must be present)	Important (supports diagnosis)	Associated (nonspecific but supports diagnosis)	Exclusionary (excludes diagnosis)
Pruritus	early age of onset	atypical vascular responses (eg, facial pallor, white dermographism, delayed blanch response)	scabies
Eczema (acute, subacute, chronic)	atopy	keratosis pilaris, pityriasis alba, hyperlinear palms, ichthyosis	seborrheic dermatitis
Morphology—typical or atypical? Age-specific patterns:	personal and/or family history	ocular, periorbital changes	contact dermatitis (irritant or allergic)
Infants and children: facial, neck, extensor involvement	immunoglobulin E reactivity	other regional findings (eg, perioral changes, periauricular lesions)	ichthyoses
Any age group: current or previous flexural lesions; sparing of groin and axillary regions	xerosis	perifollicular accentuation, lichenification, prurigo lesions	cutaneous T-cell lymphoma
History—chronic or relapsing?			psoriasis photosensitivity dermatoses immune deficiency diseases erythroderma of other causes