

Atopic Dermatitis in Adults

To the Editor:

In reference to atopic dermatitis (AD), the authors of “Atopic Dermatitis in Adults” (issue 1 of volume 22 of *Dermatitis*, 2011) clearly note, “the diagnosis of AD...is not always easy,” to which may I add, “not only in adults but also in younger patients.” When an entity can be diagnosed reliably through laboratory tests, an accurate definition becomes easier. However, when an ailment has no known cause and when its symptoms are subjective (by patient or health care provider) and its characteristics have been contested, competing case definitions are almost inevitable. Making a diagnosis becomes a “dilemma.” As the authors report, in 1983, Wüthrich proposed the 2 clinical subtypes (“intrinsic” and “extrinsic”) of what he labeled AD. I have, I believe, “debunked” the oxymoronic “nonatopic-atopic dermatitis” nomenclature with the same rationale presented in the next paragraphs.¹ Competing definitions lead only to an epidemiologic “Rashomon”—what you see depends on who is doing the looking, and this only stokes fierce debates among researchers and patient advocates on both sides of the Atlantic.

Europeans continue to proselytize intrinsic (or nonallergic) AD and extrinsic (or classic [allergic]) AD. The adjectives intrinsic and extrinsic were initially appended to “asthma,” but allergists and pulmonologists quickly appreciated that the separation was presumptive, and they no longer recognize asthma as is now insinuated for dermatitis. Interestingly, some Europeans considered AD as “asthma of the skin.” Like asthma, “eczema” is not a disease but a clinical symptom. Not all patients with asthma are “allergic/atopic”; similarly, not all patients with eczema are allergic/atopic.

The perplexity was prompted by the proselytizing of the concept of “atopy,” primarily by allergists. What does atopy mean? You infer that it is intimately associated with “allergy.” Therefore, I then ask, how do you define allergy? Is it possible to have a non-allergic allergic disease? I am essentially asking for a review of the vocabulary. (“A word is a symbol, and its meaning is constituted by the ideas, images, and emotion, which it raises in one’s mind”—Alfred North Whitehead).

Should we better appreciate AD not as a “disease” but as a “syndrome” (an aggregate of signs and symptoms associated with any morbid process and constituting together the picture of a dis-

ease)? Eczema, xerosis, keratosis pilaris, and so on are the signs, and pruritus and atopy are the major symptoms. You can then certainly appreciate the combination and permutations of more than 50 genes that have been identified in the atopic diathesis.² These polygenic factors are also significantly influenced by phenotypic (environmental) factors. The greater the gene dosage, the fewer environmental factors required, thus indicating the complexity of making a diagnosis of AD.³

Would it not be more prudent to define AD as a chronic, often relapsing, inflammatory dermatologic syndrome that often heralds the atopic diathesis (a hereditary, or acquired, susceptibility of the body to one or more diseases [ie, atopy])? Atopy is the expression of an array of polygenic (including *filaggrin* genetic mutations in AD) and phenotypic immunologic aberrations in which a spectrum of inflammatory reactions can occur in various organ systems (ie, the upper airway, lower airway, gastrointestinal tract, and skin), induced by the cytokine profile of a T helper 1–T helper 2 (Th2) reversal.⁴ These effector cells can be activated by both immunologic and nonimmunologic secretagogues, and the propensity of Th2 dominance with specific high-affinity immunoglobulin E (IgE) receptors differentiates atopic from nonatopic persons. (Elevated IgE and eosinophilia are merely epiphenomena of Th2-cell activation).

The authors’ medical file investigation of epidemiologic and clinical features can be criticized, as can all retrospective second-person (or third-person) reporting. This is especially pertinent to an entity that they recognize as being difficult to diagnose. The clinical and histologic differential diagnosis of spongiotic dermatitis (eczema) is lengthy and often challenging, especially in adults. The authors’ intrinsic AD criteria (“characterized by an absence of association with other atopic diseases, negative prick tests,... normal total serum IgE, level, and lack of allergen-specific serum IgE antibodies...and food allergens”) can be noted more often in adults with many dermatoses (ie, contact dermatitis, seborrheic dermatitis, LSC, and so on, as well as [without a biopsy CTCL] psoriasis). Conversely, Abramson and colleagues⁵ clearly noted that self-reported histories of seasonal allergic rhinitis or asthma are modest indicators of allergic sensitization (atopy). Only 68.3% of cases of physician-diagnosed seasonal allergic rhinitis or asthma were seropositive (specific IgE for aeroallergens).⁵ (Coincidentally, the concept of “immunosenescence,” in which the progressive age-dependent involution of the thymus plus the dramatic age-related shift in the proportion of naive and memory T cells contribute to the mosaic of responsive and hyporesponsive cells—the latter becoming more frequent with age⁶—accounts for the “growing out of” one’s allergies and the very rare patient’s developing AD after the age of 50 years). In their cornucopia of statistics (which is virtually minimally significant because the diagnostic dilemma is ignored), the authors identified AD (hopefully, spongiotic dermatitis) of the intrinsic type in 30.4%, without any other signs or symptoms of the atopic diathesis, of patients with nonatopic-atopic dermatitis. Could we then have nonmedical medical doctors?

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The author has no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0b013e31823e1f46

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A Response to Dr Beltrani's Letter

To the Editor:

"Consistency and accuracy of medical terminology" is important "for all health care providers and researchers,"¹ but nothing is absolute in medicine, and opinions can vary over time. Atopic dermatitis (AD) without atopy could seem to be an oxymoron, but it is undeniable that a more or less high percentage of AD patients do not show the biologic or clinical signs of atopy. Although elevated immunoglobulin E (IgE) and eosinophilia are epiphenomena of the transient T helper 1 (T_H1)–T helper 2 (T_H2) cell reversal, they are not exclusive for atopy. For example, almost half of patients with bullous pemphigoid have elevated total serum IgE (which is correlated with the presence of pruritus) and peripheral blood eosinophilia.²

For these reasons, the classification into extrinsic and intrinsic AD (or atopiform dermatitis, according to others) is still widely used, and the European Academy of Allergy and Clinical Immunology (EAACI) nomenclature task force suggested the term *atopic eczema/dermatitis syndrome* to cover the different subtypes of AD.³

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The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0b013e31823e1fa8

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The definition of AD proposed by Dr Beltrani is interesting, but the EAACI and the American Academy of Allergy, Asthma, and Immunology also believe AD to be a chronic inflammatory pruritic skin disease.⁴

Regarding the objection that our study is retrospective, our "Materials and Methods" section pointed out that AD in all enrolled subjects was diagnosed according to the criteria of Hanifin and Rajka (every patient had at least 3 major criteria and 3 minor criteria) and that all clinical data and the results of investigations (serum total IgE and results of skin prick and patch tests) were reported in the clinical record of patients. Moreover, our "intrinsic" AD criteria (normal IgE levels, no specific IgE, no association with respiratory diseases, and negative reactions to skin prick tests with common aeroallergens or food allergens) are those proposed by Wüthrich⁵ and the EAACI,³ and the clinical features and distribution of lesions (flexural folds, face) generally enable (at least for dermatologists!) the most important differential diagnosis with other forms of eczema also in young adult patients.

Finally, our "cornucopia of statistics" proves that extrinsic and intrinsic ADs are clinically identical and indistinguishable without skin and laboratory tests. Nevertheless, it is possible that some intrinsic AD patients could develop allergic conjunctivitis, rhinitis, and/or asthma with time, especially those with increased numbers of cutaneous T cells producing interleukins 4, 13, and 5⁶ and/or with high expression of FcεRI on epidermal dendritic cells.⁷

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