

Atopic Dermatitis: Looking Beyond the Skin

Atopic dermatitis (AD) is a chronic disease affecting 10%-20% of children.¹ It commands the attention of pediatricians and various subspecialists alike because of its chronic nature and daily impact on the patient's and family's quality of life. For affected children, multiple factors, including frequent pruritus, superficial skin infections, and impaired sleep, lead to significant stress. In older children, AD can contribute to attention and behavior problems that affect academic performance as well as social and family interactions. All of these factors lead to additional anxiety, which further provokes the itch-scratch cycle of AD. For caregivers, the depth of commitment required cannot be underestimated.

In this issue of *The Journal*, Saavedra et al² report the results of a survey of patterns of clinical management of AD by 3 physician specialties in the US. This survey reveals significant differences in the management of this disease by different specialists, and highlights the need for a more unified approach to the diagnosis and treatment of AD.

In their study, Saavedra et al issued a survey to pediatricians, dermatologists, and allergists regarding their approach to managing AD in patients aged <37 months, including referrals, laboratory tests, and management. They concluded that pediatricians and allergists were more likely to use formula change as a management strategy, with allergists specifically more likely to use laboratory tests (eg, immunoglobulin E, skin prick) or an elimination diet with a food challenge test, and that dermatologists favor a pharmacologic approach to treatment and are less likely to consider food allergy as a cause of AD.²

A unified approach should be based on the possible etiology of AD in affected children. This requires an understanding of the mechanisms of hypersensitivity to food and some environmental allergens that are frequent causes of the most severe forms of AD in infants and small children. It also requires knowledge of the benefits and pitfalls of testing for allergies, because not all patients who test positive for a food protein actually have an allergic reaction to that food. Erroneous interpretation of allergy tests can lead to extensive elimination diets that can further complicate the patient's life and may lead to nutritional problems.³ Because AD is often the first step in the "allergic march" toward rhinitis and persistent asthma, the clinician must treat the patient's current problems effectively while monitoring for the development of related problems.

Comprehensive management of AD requires a multifaceted approach including avoidance of allergens and irritants, skin moisturization, topical anti-inflammatory agents, and

anti-itch and anti-infection measures. For many patients, all of these interventions are necessary to some degree. The first-line basic therapeutic measures are often the most important, especially aggressive moisturization with fragrance-free, nonirritating creams or ointments. Adherence

to daily treatment is essential to maintain good control of this condition. For this purpose,

it helps caretakers to understand that reestablishing the normal skin barriers helps prevent further allergic sensitization through the skin and also helps prevent secondary infections. Caretakers also need to understand that AD is a systemic condition that causes visible lesions in injured skin areas. Areas that appear healthy require frequent moisturization to prevent breakdown. The fear of steroid use can be significantly reduced by selecting a topical steroid with low systemic bioavailability, which is especially important for patients requiring frequent and extensive topical steroid applications. Bacterial, viral, and fungal infections may play a prominent role in acute AD flares, and may explain why many severe cases are refractory to standard topical management. The valuable input from allergists and dermatologists in developing a comprehensive plan for diagnosing and managing AD will certainly help pediatricians become more comfortable with a standard initial approach and understand when to consult with an AD specialist.

Understanding the genetic contributors to AD is becoming increasingly important. A skin barrier defect that may be partly genetic and partly acquired plays a significant role in the development of AD. Although many specific epidermal barrier defects have been identified, mutations in the gene for filaggrin, a stratum corneum structural protein (*FLG*), may confer the greatest genetic predisposition for AD.⁴ More than 80 different candidate genes have been implicated in this disease process, each suspected of playing a role in the impaired epidermal barrier, defective innate immune response of the skin, or development of an amplified response by type 2 helper T cells (helper T cells that produce "allergic" cytokines) response.^{4,5} Type 2 helper T cell cytokines may further down-regulate several components of the innate and adaptive immune system, contributing to impaired barrier defense.⁵ Even though testing for *FLG* mutations and other specific defects is not yet of clinical relevance, it will be important to include advice on how and when to use genetic testing in future recommendations for the management of AD.

If an eczematous rash does not respond to first-line therapy, the diagnosis of AD should be called into question. A

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AD	Atopic dermatitis
PIDD	Primary immunodeficiency disease

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thorough review of systems, past medical history, and family history should be performed. Early-onset eczematous skin lesions may be involved in multiple forms of primary immunodeficiency disease (PIDD), including Wiskott-Aldrich syndrome and hyperimmunoglobulin E syndromes. Onset of a persistent rash during the first weeks of life should always raise suspicion for severe combined immune deficiency. Although infections eventually are present in all of the aforementioned PIDDs, eczematous skin lesions may be the presenting sign. The pediatrician should always have a high index of suspicion for these disorders, because a delayed diagnosis of PIDD will result in significant morbidity and possibly even mortality. Any child with AD associated with pathology of other organ systems or with a history of recurrent, unusual, or invasive infections (including recurrent or persistent infections of the skin) should be referred to a pediatric immunologist experienced with the diagnosis and management of PIDD.

For severe, refractory cases of AD, additional measures, such as UV light therapy, may be offered by dermatologists. Allergy immunotherapy has been shown to offer significant improvement in selected patients with aeroallergen sensitization. For these interventions, patients must be carefully selected and the risks and benefits considered. Systemic corticosteroids, which mask the skin symptoms only temporarily, are not recommended.

Management of AD with conventional measures should be possible for the vast majority of patients. Recommendations for a common approach to management have been published. The Joint Task Force on Practice Parameters has issued a 2012 update to its parameter on AD (available at

jcaai.org).¹ This comprehensive recommendation, prepared by subspecialists in allergy and immunology as well as dermatology, specifies a consensus approach based on the available literature and expert opinion. ■

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