SkinTopics™

Highlights of emerging topics in dermatology

Number 2 in a series–Provided as a professional service by Primus Pharmaceuticals®

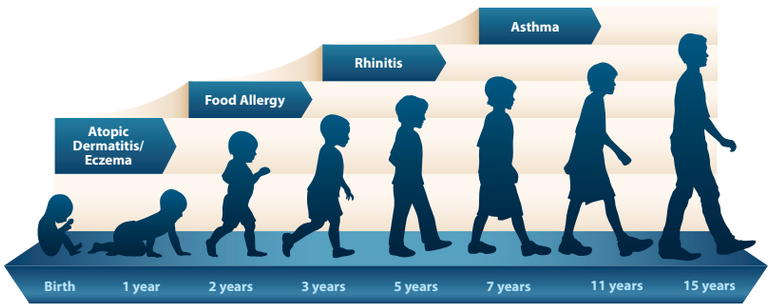
This issue reviews the impact of skin barrier dysfunction on atopic march

Welcome to SkinTopics™—an ongoing review of selected articles of importance to you

This issue of SkinTopics™ features relevant and important information from multiple clinical articles that discuss atopic march and the influence of the skin barrier. The following is presented to better understand skin barrier repair during the earliest years of life to potentially prevent atopic march.

Defining the atopic march

Atopic march describes the progression of atopic disorders from atopic dermatitis (AD) in infants to allergic rhinitis and asthma in children.[1] Typically, patients develop a sequence of atopy, beginning with AD, followed by allergic rhinitis and asthma. Atopic diseases have different peaks of incidence at different ages.[1] AD and food allergies have the highest incidence in the first 2 years of life. In later childhood, the prevalence of AD, food allergies, and food allergen sensitization decreases and the prevalence of asthma, allergic rhinitis, and sensitization to inhalant allergens rises.[2] For some children, atopy may persist for several years and, for others, it may resolve with increasing age.[1]



While food allergen sensitization decreases with age, the incidence of food allergy-related anaphylaxis has increased significantly, which indicates a rise in food allergy.[1] It is common for AD and food allergy to co-exist, and food allergy is known to provoke AD, with IgE-mediated food allergy prevalent in about 35% of children with AD.[1] It is unclear whether children with IgE-mediated food allergy are at increased risk of developing other allergic manifestations (asthma and allergic rhinitis).[1] Studies have shown that underlying atopy is considered to be critical in linking AD, allergic rhinitis, and asthma.[1] Many cross sectional and longitudinal studies highlight AD as a possible first step in the atopic march. Studies show that 30% to 50% of children who develop AD progress to develop asthma and two-thirds go on to have allergic rhinitis.[3] In a study of 2,270 children with physician-confirmed AD, the prevalence of allergic rhinitis and asthma was examined and results showed that by 3 years of age, nearly 66% of the subjects reported having allergic rhinitis, asthma, or both.[1] The data further demonstrated that the presence of the diseases correlated with poor AD control.

Dysfunctional skin barrier: where atopic march begins

Correlation between the atopic march and the strateum corneum has raised scientific attention in the study of the allergic diathesis.[3] This focus on epidermal barrier function provides a more extensive and meaningful understanding of AD and the initiation of the atopic march.[3]

Barrier permeability is bi-directional. With increase in water loss comes easier allergen incursion. Recent studies have shown that epicutaneous application of a protein allergen (ovalbumin OVA) on barrier-disrupted skin elicits both a local and systemic Th2 predominant response in the mouse model.[4] When protein antigens enter the skin, it causes a primarily T2 immune response. When later challenged, an asthmatic response is produced. The role of allergen sensitization through the barrier defective skin has been recognized as the onset of atopic march. However, the underlying mechanism has been poorly understood.
In a recent article, the impact of skin barrier dysfunction on thymic stromal lymphopoietin (TSLP) was shown (in the mouse model) to be the missing link.[4]

"The most modern theories seem to show that the most important factor which starts the atopic march is represented by an impaired epidermal barrier.[2]"

–Annalisa Patrizi, Division of Dermatology, Department of Internal Medicine, Geriatrics and Nephrology, University of Bologna, Italy

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Making strides toward barrier repair

Studies examining skin barrier dysfunction demonstrate that a deficiency of ceramides is a major contributing factor in damaging the permeability barrier of the skin.[3] A murine model of AD illustrates the importance of ceramide in preventing allergen-induced atopic dermatitis.[3] Research also suggests that an intact lipid matrix in the stratum corneum may actually prevent epidermal penetration of allergens and allergic AD.[3]

The identification of ceramide as a critical element in barrier function has led to the development of ceramide-based emollients.[3] In a study of patients with mild-to-moderate AD, application of ceramide emollient resulted in 69% of patients having no symptoms of eczema and skin hydrations scores improving significantly.[3] In another study, a ceramide-dominant lipid-based emollient was used in 24 children with stubborn AD, resulting in improvements in skin cohesion, transepidermal water loss levels, and AD scores as a result of the reestablishment of extracellular lamellar membranes in the stratum corneum.[3]

Are there ways of stopping atopic march?

Multiple lines of evidence (clinical, genetic, and experimental studies) suggest that previous expression of AD is a prerequisite for the development of allergic rhinitis and asthma and specific sensitization highlighting the importance of the epidermal barrier in the pathogenesis of these disorders.[1] Still under study, therapy that targets the maintenance and repair of the stratum corneum barrier in infants with AD may prevent the subsequent development of asthma and allergic rhinitis.[1]

Many clinicians also believe that early identification of at risk individuals, coupled with ongoing research and evolving skin barrier treatment strategies, may make it so the atopic march is not an inevitability for certain predisposed individuals.[3]

What was the clinical relevance of this review article?

The findings in this review suggest that maintenance of an intact skin barrier or repair of a dysfunctional skin barrier that is a result of AD may prevent the onset of atopic march, which can begin in infancy with AD and may progress to allergic rhinitis and asthma as a child ages.

Review at a glance

- "Atopic march" is the progression of atopic disorders from (AD) in infants to allergic rhinitis and asthma in children.
- Evidence suggests that previous expression of AD is a prerequisite for the development of allergic rhinitis and asthma.
- Studies show that 30% to 50% of children who develop AD progress to develop asthma and two-thirds progress to allergic rhinitis.
- A key component in AD is dysfunction of the strateum corneum skin barrier.
- Studies show that a deficiency of ceramides is a major contributing factor in damaging the barrier of the skin and in the development of allergen-induced AD.
- Clinicians state that improving barrier function might be an important way to control the onset of the atopic march.

Access the full articles referenced below

Zheng: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3062798/
Patrizi: http://www.hindawi.com/journals/ja/2011/279425/
Hogan: http://www.hindawi.com/journals/ja/2012/901940/
Leyva: http://www.nature.com/jid/journal/v133/n1/full/jid2012239a.html

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