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Allergic hyperreactivity to microbial components: A trigger factor of "intrinsic" atopic dermatitis?

To the Editor:

Atopic dermatitis (AD) is a common, chronic, relapsing inflammatory skin disease characterized by typically distributed eczematous skin lesions and intense pruritus. A majority of patients with AD have high concentrations of total and allergen-specific IgE in the blood and skin. This form has been individualized as the IgE-mediated/allergic or *extrinsic* form of AD. In the so-called non-IgE-mediated/nonallergic or *intrinsic* form, which has been reported to represent 10% to 30% of all patients with AD, patients have normal total serum IgE levels and no allergen-specific IgE against aeroallergens or food allergens, although they exhibit the same clinical phenotype.² However, factors contributing to the development of this subtype of AD are completely obscure.

The skin of patients with AD exhibits a striking susceptibility to colonization and infection with microbial components, such as *Staphylococcus aureus*, *Pityrosporum ovale*, or *Candida albicans*. Recently, it has been

shown that *S aureus* strains isolated from AD skin produce enterotoxins, such as staphylococcal enterotoxins A (SEA), B (SEB), C (SEC), D (SED), and toxic shock syndrome toxin 1 (TSST-1), which display superantigenic activities. As a hallmark, superantigens facilitate the binding of MHC class II to the T-cell receptor independent of the peptide groove and stimulate T cells expressing a particular T-cell receptor β -chain. After superantigenic stimulation, skin-homing cutaneous lymphocyte antigen-positive T cells from patients with AD undergo a T-cell receptor V β expansion and perpetuate the inflammatory immune response in this way.³ Additionally, these exotoxins can act as classical allergens and induce the production of functional relevant specific IgE antibodies, which trigger mediator release from sensitized basophils after IgE antibodies have been cross-linked with the appropriate antigen.⁴

It is assumed that IgE antibodies directed against the commonly found skin yeasts *P ovale* and *C albicans* might potentially play analogous roles in triggering humoral immune responses.

Because skin colonization with microbial components is a common feature of both patients with high (ie, >150 kU/L IgE) and low serum IgE levels (ie, <150 kU/L IgE), it was the aim of our study to determine the prevalence of circulating IgE antibodies with specificity to microbial products in the intrinsic subgroup of patients with AD. For this purpose, a total of 114 patients with AD and 30 nonatopic healthy volunteers were recruited. Total serum IgE and specific IgE levels to SEA, SEB, SEC, SED, TSST-1, *P ovale*, *C albicans*, and various aeroallergens and food allergens, such as *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, *Alternaria tenuis*, timothy grass and birch pollen, wall pellitory, mugwort, cat dander, peanut, hazelnut, egg white, cow milk, fish, wheat, green apple, kiwi, and tomato, were assessed with the help of a CAP RAST system (Pharmacia, Germany).

As a result, 23 (20%) of 114 patients with AD had IgE serum levels of less than 150 kU/L and no allergen-specific IgE against aeroallergens or food allergens. In 53% of these patients with AD, specific IgE toward microbial components could be found (Table I). In 47% of patients displaying classical features of intrinsic AD, neither specific IgE antibodies to aeroallergens and food allergens nor to microbial components were detectable (Table I). In the extrinsic form of AD, in 85% of the patients, allergen-specific IgE against aeroallergens or food allergens in combination with allergen-specific IgE against microbial components was detectable, whereas no allergen-specific IgE against microbial components was detectable in the control group, in which the serum IgE level was 11.4 ± 5.4 kU/L. Statistical analyses with the χ^2 test demonstrated a significant difference ($P < .001$) in IgE reactivity versus no reactivity against microbial components for patients with intrinsic AD in comparison with healthy control subjects. Together, these findings underline the hypothesis that in a subgroup of patients with AD with low serum IgE levels, an allergic reactivi-

TABLE I. Prevalence of allergen-specific IgE against microbial components in patients with intrinsic atopic dermatitis

	IgE (kU/L)	SEA	SEB	SEC	SED	TSST-1	<i>C albicans</i>	<i>P ovale</i>
1	5	++						
2	137							+
3	25						+	+
4	39	++						
5	123							++
6	38							+
7	35							+
8	148					++		
9	137	++				++	+	
10	24		+					++
11	22						++	
12	26			+	+			

$P < .001$, χ^2 test. No allergen-specific IgE against microbial components was detectable in the sera of the 30 healthy individuals tested.

ty exclusively to microbial components, such as SEA, SEB, SEC, SED, *P ovale*, and *C albicans* (analogous to the allergic hyperreactivity to aeroallergens or food allergens in patients with extrinsic AD), might be an important trigger factor of the immune response. As an assumption, the allergic hyperreactivity to microbial components, together with the direct hyperstimulatory effect of the superantigens themselves and in combination with the lower level of antimicrobial defensins in the skin of patients with AD,⁵ might be potent enough to contribute to the typical pathognomic features of AD, even in the absence of other environmental allergens. Nevertheless, at present, the presence and relevance of these allergen-specific antibodies in the skin of patients with AD has not been proved sufficiently. If this were the case, the clinical effect of IgE antibodies to microbial antigens might derive from their capability to promote the itch-scratch cycle in these patients, which later contributes the release of mast cell-derived mediator, leading to intense pruritus and the typical skin lesions of AD.

Taken together, we conclude that the determination of allergen-specific IgE levels against microbial components in the peripheral blood is important to classify a subgroup of patients with AD in which the immune response might be predominated by a solely allergic hyperreactivity to microbial components. In this subgroup of patients with AD, the benefit of antimicrobial therapies seems to be the major strategy for effective allergen avoidance.

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Anaphylaxis to ingestion of hempseed (*Cannabis sativa*)

To the Editor:

Hemp (*Cannabis sativa*) is a tall annual herb of the family Cannabinaceae.¹ Marijuana is one variant that has a relatively high concentration of the psychoactive cannabinoid tetrahydrocannabinol (THC), whereas other variants contain little THC. Industrial hemp, low in THC, is used for manufacture of cloth, cosmetics, and other materials. Hempseed is the fruit of the plant, and a THC-free hulled form and its oil are being popularized as a food product with potential health benefits. We describe a case of anaphylaxis to this food.

A 44-year-old man with a history of seasonal allergic rhinitis, mild asthma, and occasional use of marijuana but no food allergies or prior anaphylaxis entered a restaurant that specializes in hempseed ingredients. He was, at one time, a fairly heavy marijuana pipe smoker and had inhaled the smoke of "many hundreds" of marijuana seeds. There was an exhaust fan blowing cooking fumes into the dining area, and shortly after entering the establishment, the subject noted ocular pruritus. He then ingested a meal of hempseed-crusted catfish, calamari, and other foods he routinely ingests. During the meal, urticaria developed on the scalp, axillae, and groin, and the patient went immediately to an emergency department where generalized urticaria, facial angioedema, dyspnea, and dysphonia were observed. Symptoms resolved with epinephrine and antihistamines. No other diners were ill.

Skin prick testing was performed with fresh extracts of the raw ingredients of the meal obtained from the restaurant. Results for the potentially causal foods revealed the