ORIGINAL ARTICLE

Inflamed skin predisposes to sensitization to less potent allergens

Nita Kohli, MD, MPH, and Susan Nedorost, MD
Cleveland, Ohio

Background: Irritant dermatitis, caused by genetic barrier dysfunction in atopic dermatitis or wet work in hand dermatitis, induces innate immune response that might predispose to allergic contact sensitization to less potent sensitizers.

Objectives: We sought to determine if positive patch test results to less potent allergens are more prevalent in patients with a history of childhood flexural dermatitis or current wet work.

Methods: We examined our database of patients presenting to a contact dermatitis clinic tested to potential contact allergens as indicated by their history. Allergens from our most recent standard were studied if they could be classified as weak, moderate, or strong sensitizers based on published data from the local lymph node assay. Patients were stratified by a history of childhood-onset flexural dermatitis as a proxy for atopic dermatitis and by occupation.

Results: History of childhood-onset dermatitis predisposed to contact allergy to weak sensitizers and wet work to medium-potency sensitizers. Neither predisposed to contact allergy from strong sensitizers.

Limitations: Association cannot prove causation.

Conclusions: We conclude that strong sensitizers do not require wet work or atopy to cause sensitization. Barrier defects associated with childhood eczema and wet work may promote sensitization to weak antigens. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.03.010.)

Key words: atopic dermatitis; contact sensitization; irritant dermatitis; occupational hand dermatitis; potency of contact allergens; systemic contact dermatitis; wet work.

Irritant dermatitis may increase the risk of allergic sensitization through danger signals such as danger-associated molecular patterns[1] or alarmins released by damaged epithelium that result in inflammatory cytokines and chemokines modulating Th2 adaptive immune response.[2] Genetic mutations that render the epidermis more susceptible to barrier disruption predispose to irritant contact dermatitis.

Innate immune signals from barrier disruption might enhance sensitization to very-low-potency allergens. An example of a low-potency allergen is propylene glycol, which is not considered a sensitizer in the local lymph node assay (LLNA), has minimal dermal irritancy even when applied at 100% concentration to mice,[3] and is allowed in many products designed to treat dermatitis including emollients and topical corticosteroids.

In contrast, the contact allergens most often used for patch testing are potent allergens that induce their own irritant/innate immune response and cause contact allergy in a substantial proportion of the general population. Methylchloroisothiazolinone, a potent sensitizer, is a strong irritant at a

From the Department of Dermatology, University Hospital Case Medical Center, Case Western Reserve University.
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Correspondence to: Susan Nedorost, MD, Department of Dermatology, University Hospital Case Medical Center, Case Western Reserve University, 11100 Euclid Ave, Cleveland, OH 44106. E-mail: stn@case.edu.
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concentration of 1.5%[4] and is restricted in products designed to stay on the skin. Neomycin, another strong sensitizer, is a component of triple-antibiotic ointment that has been demonstrated to cause cutaneous irritation.[5]

Atopic dermatitis patients seem to be less susceptible to strong sensitizers such as poison ivy and are harder to sensitize to the potent allergen dinitrochlorobenzene.[6] There may be a tipping point at which damage to the epidermis no longer enhances cutaneous sensitization via danger-associated molecular patterns but rather is of sufficient severity that cutaneous sensitization does not occur. This may explain the decreased prevalence of positive patch test findings in patients with severe atopic dermatitis that is not seen in patients with moderate or mild disease.[7]

CAPSULE SUMMARY

- Inflamed skin is a risk factor for development of allergic sensitization.
- Inflamed skin is associated with increased incidence of sensitization to antigens of weaker potency.
- Patch test series designed for the general population include mostly potent sensitizers and miss less potent antigens that cause dermatitis in specific cohorts.

Knowledge of decreased sensitization to potent allergens in patients with atopic dermatitis was extrapolated years ago to conclude that patch testing would not benefit patients with atopic dermatitis. However, there are now many reports of atopic dermatitis patients with relevant allergic contact dermatitis to less potent allergens, including fragrances[7] that include both weak and moderate sensitizers. The weak sensitizer propylene glycol was found by the North American Contact Dermatitis Group to be currently relevant in over 88% of patients with a positive patch test result, with over 20% of these patients classified as having atopic dermatitis.[8]

Recent studies have shown that in skin from patients with atopic dermatitis, the potent allergen dinitrochlorobenzene can induce both T helper (Th) 1 and Th2 responses. The Th2 responses likely contribute to the atopic march. The Th1 response to this allergen is of shorter duration in patients with atopic dermatitis compared with healthy control subjects, and in fact disappears within a few months of sensitization in the majority, but it does persist for months in a substantial minority of patients with atopic dermatitis.[9] This confirms that patients with atopic dermatitis can be sensitized and a substantial minority of patients retains delayed-type hypersensitivity even to a potent allergen.

Allergenicity of chemicals is commonly measured by the LLNA that classifies allergens by potency.[10-12]

We examined our database of patients presenting for evaluation of allergic contact dermatitis to determine if patients with a history of childhood flexural dermatitis or current wet work (both known to be associated with irritant dermatitis) had a higher incidence of sensitization to less potent allergens. A priori we selected only allergens from our 2013 standard series (Appendix A; available at http://www.jaad.org), representing the most frequently tested allergens, which could be classified by the LLNA as strong, medium, or weak sensitizers. These allergens are shown in Table I.

METHODS

This was a retrospective study using a database of all 1828 patients patch tested for suspicion of allergic contact dermatitis in the University Hospital Case Medical Center Dermatology Clinic, 2003 through 2013. The statistics reported here were for the 1650 subjects evaluable for occupational classification of wet or dry work. The study was granted approval from the university institutional review board. All patents underwent patch testing with the university's standard series and specialty series as indicated for suspicion of allergic contact dermatitis.

Atopic dermatitis was defined as history of childhood flexural dermatitis for purposes of this study where irritant dermatitis is the focus of our hypothesis. Although we recognize that atopic dermatitis is characterized both by barrier deficit and by generation of antigen-specific IgE manifesting as respiratory atopy and often by abnormal immune responses to commensal micro-organisms, we defined childhood flexural dermatitis with or without any combination of seasonal rhinitis and asthma as a proxy for atopic dermatitis. Of the 291 patients with a history of childhood flexural dermatitis, 94 reported a history of only dermatitis, and 197 reported a history of flexural dermatitis with seasonal rhinitis, asthma, or both.

The wet versus dry work classifications were determined by the principal investigator at the time the patient was seen in clinic, taking into account the individual's job duties. The job tasks represent the exposures and were fit to the group that represents the exposures as shown in Table II. For example, a nursing supervisor was classified as "office worker" rather than "health care worker" and would be grouped under dry worker. Retirees who functioned as caregivers were classified as homemakers. Using the database, 1650 patients were classifiable as wet or dry workers. There were 178 patients who were