

LETTER TO THE EDITOR

A defective inflammatory response may underlie cases of atopic dermatitis

Editor

An investigation of atopic dermatitis (AD) proposes an association between susceptibility to developing allergic contact sensitization (ACS) and a possible defect in the delayed

hypersensitivity inflammatory response.¹ Current research supports the predominant pathogenesis of AD to be T-helper cell 2 (Th2)-mediated type I hypersensitivity response and allergic contact dermatitis (ACD) to be a T-helper cell 1 (Th1)-mediated type IV hypersensitivity response.²

However, several studies introduce a diminished proclivity to develop ACD in AD (Table 1). Of note, Jones *et al.*'s³ use of the common antigen *Rhus oleoresin*, which is highly sensitizing, find that their atopic subjects are less responsive compared to healthy

Table 1 Epidemiological and experimental studies of AD and ACS

Researchers	Objectives	Methods	Results	Conclusions
Epidemiological studies				
Ref. [5]	Prospective study of the frequency of ACS in atopic patients with dermatitis compared to non-atopics with dermatitis	Dermatitis patients >15 years old investigated from 1987 to 1988 Patch test: European standard series, methyl(chloro)isothiazolinone Prick test: 24 inhalant and 11 food allergens Atopics ($n = 214$): selected via clinical dermatitis and two positive prick tests or one positive prick test, family hx. atopic diseases Controls ($n = 285$): dermatitis with negative prick tests	79 (37%) atopic patch test reactions compared to 149 (52%) controls Statistically significant difference ($P < 0.05$)	Adults presenting with dermatitis and atopy are less frequently sensitized than those presenting with dermatitis alone High percentage of positive patch tests in the atopic does not rule out routine patch testing
Ref. [6]	Study the potential for sensitization to topical antibiotics and antiseptics in patients with atopic eczema	Patch test results from 1995 to 1999 collected from Departments of Dermatology in the Information Network of Departments of Dermatology German database Exclusion criteria: current leg ulcers or stasis dermatitis	No additional risk of ACS in atopic patients when controlling for confounding variables (age, sex)	Considering the methodological limitations of this study, the data do not show an increased risk of sensitization to topical medications
Ref. [7]	Study of clinical databases for association between contact sensitization and atopic disease (AD and asthma)	Linkage of records from two databases: 1 Tertiary hospital records of AD patients patch-tested for ACS 2 Danish National Patient Registry of national hospital discharge diagnoses and outpatient contacts	Inverse association between ACS and assumed severe AD (OR, 0.70; 95% CI, 0.61–0.81) when linkage performed Positive relationship seen with fragrance sensitization assumed mild–moderate AD	Severe AD and mild–moderate AD have different ACS prevalence Severe AD suppresses ACS, while mild–moderate does not All AD patients have higher prevalence of fragrance ACS; scented therapeutics should be avoided

Table 1 Continued

Researchers	Objectives	Methods	Results	Conclusions
Experimental studies				
Ref. [3]	Comparison of frequency of <i>Rhus oleoresin</i> sensitization in AD patients and age-matched non-atopics	Three comparison groups: 1 AD participants ($n = 40$) not receiving systemic or topical meds near the patch test sites 2 1st test controls ($n = 44$) with no hx. of skin or respiratory atopy 3 2nd test controls ($n = 67$) Two <i>Rhus</i> patch test: applied to upper back for 48 h Irritant reactions: erythema at 30 min; faded by 24 h, not graded Allergic reactions: erythema after 24 h – graded 1+ (erythema only) 2+ (erythema, oedema) 3+ (erythema, oedema, papules) 4+ (erythema, confluent oedematous vesicular dermatitis)	First test: 15% (6 of 40) AD and 61% (27 of 44) controls, positive ACS, significant P-value (0.01) Second test: 6% (1 of 16) AD and 31% (8 of 24) controls positive ACS 1+ to 4+ scoring system not able to determine intensity of atopic vs. non-atopic response	Infrequent ACS to <i>Rhus</i> family of antigens in AD patients may be due to a cellular immunity defect Clinical hx. of <i>Rhus</i> exposure and subclinical sensitization cannot be ruled out
Ref. [8]	Determine whether diminished contact sensitivity in AD patients is primary or secondary to AD	Longitudinal observation study of experimental contact sensitivity to DNCB in AD patients AD ($n = 150$; 24 severe, 86 moderate, 40 mild) Controls ($n = 70$) DNCB patch test: induction on the left arm (24 h) Challenge 2 weeks later on the right arm; read in 2–3 days Allergic reaction: red, palpable induration and/or vesiculation	Challenge results: AD (87%) and controls (100%), ($P < 0.01$) Challenge among the three severities of AD: severe (33%), moderate (95%), mild (100%) 18/20 AD patients, non-responsive to 1st challenge responded to 2nd challenge during disease remission No difference between the moderate AD and control subjects regarding frequency of positive reactions ($P > 0.5$)	Patients with severe AD are less easily sensitized to DNCB than moderate to mild AD when compared to controls Suppression of sensitization occurs with widespread, severe dermatitis but upon remission, sensitization is possible
Ref. [9]	Study contact sensitization response in mild atopic eczema patients with DNCB	Mild AD patients ($n = 22$) without active disease or on systemic corticosteroids Controls ($n = 27$) Induction: DNCB patch to medial thigh or 48 h Challenge: 1 month later, three challenge doses placed on upper arm for 6 h and skinfold thickness measured before and 48 h after challenge	Although the difference was not statistically different, 78% ($n = 17$) of atopics and 85% ($n = 23$) of controls showed clinical sensitization Significant difference in the dose responses between atopics and controls ($F_{1,90} = 7.5$, $P = 0.008$)	Response to new antigens in atopics is reduced; the use of quantifiable measures to evaluate clinical responses helps determine variability in responses rather than binary ($\pm$) responses Not able to determine whether the differences observed are from the atopic state per se or result from minimal skin disease present during testing

Table 1 Continued

Researchers	Objectives	Methods	Results	Conclusions
Ref. [10]	Evaluate frequency between atopy and ACS in a general population using objective measures	Prospective study of $n = 135$ randomly selected students Atopic markers were tested: skin prick test; Phadiatop test, total IgE > 120 kU/L Sensitization tests: patch test Analysis included: Fisher exact test; Mann–Whitney U -test; odds ratio	For atopic patients, odds ratio for contact hypersensitivity (1.0–3.2) No statistical significance reached ($P > 0.05$) between atopy markers and ACS	Atopy and ACS are independent of each other

ACS, allergic contact sensitization; AD, atopic dermatitis; DNCB, dinitrochlorobenzene; hx., history.

controls. They conclude that a defective cell-mediated immune response in AD may explain the decreased frequency of ACS, but noted that prior subclinical sensitization cannot be ruled out.

Additionally, a few studies raise the hypothesis of a possible defective inflammatory response per se in AD patients that can lead to a decreased propensity for developing ACD. Johnson *et al.*⁴ in their examination of the response of cancer patients to the development of a response when challenged with 2,4-dinitrochlorobenzene (DNCB), an uncommon antigen, assert that an intact inflammatory response must be present to establish whether there is a delay in its reactivity. Without the presence of an intact inflammatory response, the ability to mount a delayed hypersensitivity reaction is impaired.

While the previous work of hypersensitivity response reactions in non-atopics compared to atopics is mainly binary comparisons, future research may include a third comparison group of patients with defective inflammatory reactions (i.e. immunosuppressed patients) which may dramatically improve our understanding of the pathogenesis of ACS in AD patients.

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