Review paper

CONTACT ALLERGY AND "ATOPY PATCH TESTS" IN ATOPIC DERMATITIS

B. Wüthrich

ABSTRACT

The prevalence of contact sensitization in atopic dermatitis (AD) patients varies considerably, in dependence of sex, age, occupation, the population tested, i.e. patients with a long history of the disease, the allergens used and the country. Because of the highly irritable atopic skin unspecific irritant reactions were seen in 24 % to 40 % of the AD patients. The chemicals most frequently involved in contact sensitation are nickel sulfate, potassium dichromate, cobalt chloride, neomycine and benzoyl peroxide.

The prevalence of atopic patch tests with aeroallergens (housedust mites, pollens, animal danders and moulds) also vary from few to 70 % of the various tested allergens and the different authors. These findings support the hypothesis that direct epidermal contact with aeroallergens may play a pathogenetic role in some patients with AD.

Positive atopic patch tests to aeroallergens are not only present in patients with AD and positive specific prick tests or serum IgE (RAST) but they can also occur in presence of negative prick test reactions or negative specific IgE levels. International recommendations for standardization and evaluation of atopy patch tests are urgently needed.

KEY WORDS

atopic dermatitis, contact allergy, atopy patch tests, aeroallergens

PREVALENCE OF CONTACT ALLERGY

Reports on the prevalence rate of contact sensitization in atopic dermatitis (AD) patients are contradictory. The International Contact Dermatitis Research Group (ICDRG) demonstrated that the incidence of contact allergy is similar in atopic, seborrhoic and nummular eczema (2). However,

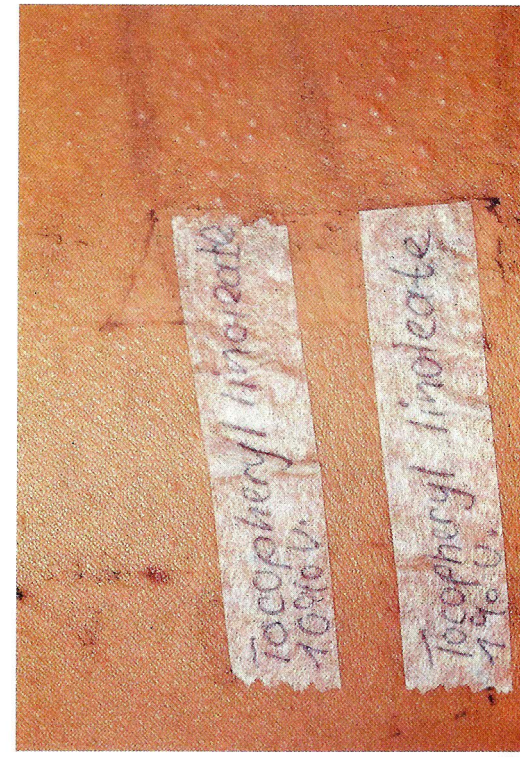

Fig. 1 An irritant, follicular reaction to tocopheryl linoleate (an ingredient in cosmetics) in atopic dermatitis.

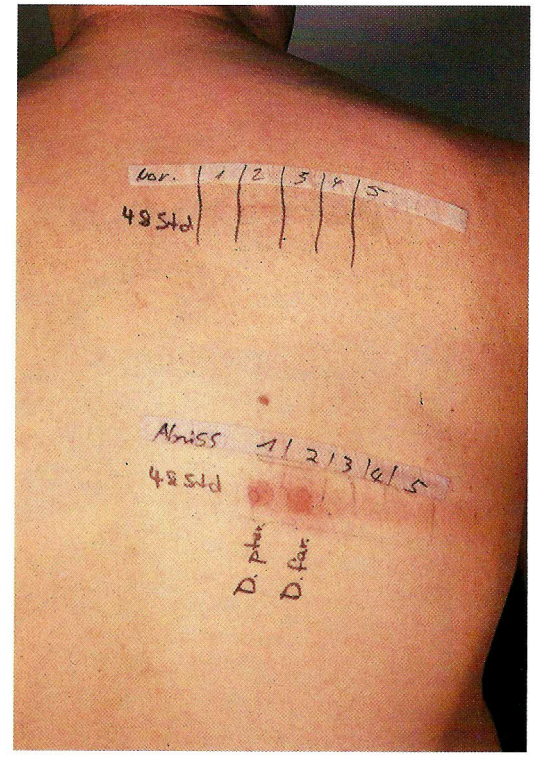

Fig. 2 Positive atopy patch test reactions to housedust mites Dermatophagoides pteronyssinus (1) and farinae (2) at the lecture on 48 hrs only on stripped (12x) skin, but not on intact skin. Negative reactions to birch (3), grass pollen (4) and saline control (5).

the rate of sensitization is much less pronounced than in the group of patients with stasis dermatitis. There are many articles which show that patients with severe AD and with high IgE values (>100 U/ml) display a decreased capacity to develop contact sensitivity as a consequence of an altered function of the cellular immunity (8, 11, 15). On the other hand, the irritant properties of the tested substances should not be understimated, especially when testing young children and patients with a widespread and long-lasting dermatitis with a high irritable skin. Irritant reactions were seen in 24 % to 40 % of the AD patients and the list of substances eliciting irritant or follicular reactions (Fig. 1) is very wide and contains pharmaceutical substances, vehicles and cosmetics, such as formaldehyde, fragrance-mix, carba-mix and propylenglycol, and environmental and professional haptens, such as rubber products and metals (5, 9, 10, 14).

The distribution of the haptens that are most frequently involved in eliciting true positive patch test (PT) reactions in AD can also vary considerably, in dependence of sex, age, occupation, the population tested (i.e. patients with a long history of the disease), the allergens used, and the country. Nevertheless, the chemicals most frequently involved are nickel sulfate, especially among women and younger atopics, potassium dichromate, cobalt chloride, neomycine and benzoyl peroxide (2, 3, 6, 9, 10, 12).

On the other hand, the clinical relevance of such positive PT is often hard to verify. In a recent study it was shown that no differences concerning the occurence of positive responses existed in atopics with and without hand manifestation and that in only 3/136 patients the result of PTs did explain the occurrence of hand eczema (4).

In conclusion, despite standardization of PT methods and development of test materials and devices, i.e. with the TRUE test system, it remains difficult to distinguish between true allergic and irritant reactions in patients with irritable skin and to judge about the clinical relevance of such positive PTs. Therefore, epicutaneous patch testing in atopic dermatitis should only be performed by well trained and experienced physicians.

"ATOPY PATCH TEST" WITH AEROALLERGENS

Patients with AD, also without concomitant respiratory allergies, frequently show sensitization to aeroallergens of the immediate type in skin tests and/or in RAST (27, 28). The skin lesions, however, are clinically and histologically those of a subacute or chronic eczema with the features of a delayed type hypersensitivity reaction (1). Therefore, the immediate type reactions to inhalant were often regarded as an epiphenomenon without clinical significance for the atopic skin manifestation or as an indicator for a respiratory allergy of the airways. Nevertheless, some clinical observations of flares of AD in springtime by pollen exposures (AD as hay fever equivalent) or of improvements after allergen avoidance, such as house dust mites or chironomides in fishfood, and IgE sensitization to the relevant allergens, stressed the pathogenetic significance of aeroallergens at least in a subgroup of AD patients (28). In these cases it was assumed that haematogenous skin contact after inhalation of inhalant allergens can elicit a flare-up of AD.

Already 1945 it was shown that patch tests to human dander from the scalp of normal adults produced positive eczematous reactions in a high percent of patients with AD. Subsequently, several authors have reported positive PT reactions of the delayed type to house dust mites, pollens, animal epithelia and mould extracts (1, 5, 7, 9, 10, 13, 14, 16, 17, 19, 20, 21, 22, 24, 26) (Fig. 2). The frequency of these positive PT differs from few to 70 % percent for the various tested allergens and the different authors, supporting the hypothesis that direct epidermal contact with such aeroallergens may play a pathogenetic role in some patients with AD. It was subsequently shown that positive patch tests to aeroallergens are a specific feature of AD as they were not observed in atopic patients with rhinitis or asthma without eczema, also in the presence of a strong IgE sensitization to the tested allergens. Viceversa, there were no difference between patients with "pure" AD and those with associated respiratory allergies (5, 18).

Originally, it was thought that "atopy patch tests" (APT) were present only in patients with AD and positive specific prick tests or serum IgE. Recent works show that positive APT also occur in presence of negative prick tests reactions or negative specific IgE levels (25). So far, there was no correlation between dust mite-specific IgE and PT reaction for dust mite antigens. Recently, it has been suggested that the results of APT and specific serum IgE could be used to divide AD patients into four distinct groups, each with its own particular clinical morphology, suggesting the heterogeneity of this disease (7). However, the existence of these four different subtypes must await further investigations.

Parallel to these clinical findings, the mechanisms underlying positive APT in patients with AD were investigated by several groups. The presence of IgE on epidermal Langerhans cells and the isolation of antigen-specific T cell clones from the test sites - as a link between specific IgE and cell-mediated immune response - is now seen as a possible pathogenetic mechanism in AD or at least acting in positive APT reactions (1, 20).

Unfortunately, in contrast to classical PT for contact dermatitis, there have been until now no international

recommendations for standardization and evaluation of APT (18). In fact, there exist important differences between the different authors concerning the carrying-out of these APT:

- conditions of application on the skin (intact, slightly abraded, stripped or scratched skin (Fig. 2),
- site and size of the test area,
- application period (24 or 48 hrs),
- nature, origin and concentration of allergen extracts

(Der pI/fI, Der pII/fII, body antigens, fecales, whole mite cultures a.o.; same or stronger concentration than prick test solutions etc),

- nature of vehicles used (glycerol, saline, vaseline),
- patient selection,
- classification of test reactions (grading, allergic or irritative reaction?).

The editing of such recommendations could be the task of the European Society of Dermatology.

REFERENCES

1. Bruynzeel-Koomen CAFM, Wichen van DF, Spry CJF: Active participation of eosinophils in patch test reactions to inhalant allergens in patients with atopic dermatitis. Br. J. Dermatol. 1988; 118:229-238

2. Cronin E, Bandman HJ, Calnan CD et al: Contact dermatitis in the atopic. Acta Derm Venereol (Stockh) 1970; 50:183

3. Epstein S: Neomycin sensitivity and atopy. Dermatologica (Basel) 1965; 130:280

4. Forsbeck M, Skog E, Aesbrink E: Atopic hand dermatitis. A comparison with atopic dermatitis without hand involvement, especially with respect to influence of work and development of contact sensitization. Acta Derm Venereol (Stockh) 1983; 63:9-13

5. Gebhardt M: Aeroallergens and atopic dermatitis. Contact sensitivity in children and adults with atopic dermatitis. Z. Hautkr. 1992; 67:682-685

6. von Huber A, Fartasch M, Diepgen TL: Auftreten von Kontaktallergien beim atopischen Ekzem. Dermatosen 1987; 35:119-123

7. Imayama S, Hashizume T, Miyahara H et al: Combination of patch test and IgE for dust mite antigens differentiates 130 patients with atopic dermatitis into four groups. J. Am. Acad. Dermatol. 1992; 37:531-538

8. Jones HE, Lewis CHW, Stacey MAJ: Allergic contact sensitivity in atopic dermatitis. Arch. Dermatol. 1973; 107:217-222

9. Lammintausta K, Kalimo K, Fagerlung VL: Patch test reactions in atopic patients. Contact Dermatitis 1992; 26:234-240

10. Lisi P, Simonetti S: Contact sensitivity in children and adults with atopic dermatitis - A chronological study. Dermatologica 1985:171:1-7

11. Lobitz WC jr, Honeymean JF, Winkler NW: Suppressed cell-mediated immunity in two adults with atopic dermatitis. Brit Derm 1972;86:317

12. Malten KE: Nickel-allergic contact dermatitis and atopy. Dermatologica 1971;142:113

13. Mitchell EB, Chapman MD, Pope FM et al: Basophils in allergen-induced patch test sites in atopic dermatitis. Lancet 1982/1;127-130

14. Nexmand PH: Clinical studies of Besniers Prurigo. Rosenkilde and Bagger, Kopenhagen, 1948

15. Palacios J, Fuller EW, Blaylock WK: Immunological capabilities of patient with atopic dermatitis. J invest Derm 1967;47:484

16. Reitamo S, Visa K, Kähönen K et al: Eczematous reactions in atopic patients caused by epicutaneous testing with inhalant allergens. Br J Derm 1986;114:303-306

17. Räsänene L, Reunala T, Lehto M et al: Immediate and delayed hypersensitivity reactions to birch pollen in patients with atopic dermatitis. Acta Derm Venereol (Stockh) 1992;72:193-196

18. Ring J: "Atopie-Patch-Test": Chancen und Probleme, ALLERGO J. 1993;2:8

19. Rudzki E, Grzywa Z: Contact sensitivity in atopic dermatitis. Contact Dermatitis 1975;1:285-287

20. Sager N, Feldmann A, Schilling G et al: House dust mite-specific T cells in the skin of subjects with atopic dermatitis: Frequency and lymphokine profile in the allergen patch test. J. Allergy Clin. Immunol. 1992;89:801-810

21. Seidenari S, Manzini BM, Danese P et al: Patch test modificati con colture intere di dermatophagoides. Esperienza su 31 soggetti affetti da dermatite atopica. G. Ital. Dermatol. Venerol. 1991;126:5-10

22. Seidenari S, Manzini BM, Danese P: Patch testing with pollens of gramineae in patients with atopic dermatitis and mucosal atopy. Contact Dermatitis 1992;27:125-126

23. Simon FA: Cutaneous reactions of persons with atopic eczema to human dander. Arch Derm 1945;51:402-404

24. Uehara M, Ofuji S: Patch test reactions to human dander in atopic dermatitis. Arch. Dermatol. 1976;112:951-954

25. Vieluf B, Kunz B, Bieber T et al: "Atopy patch test" with aeroallergens in patients with atopic eczema. ALLERGO J. 1993; 2:9-12

26. Vocks E, Drosner M, Szliska CHR et al: Epikutantestungen mit Schimmelpilzen, Grundnahrungsmitteln und Mikro-organismen bei Patienten mit Neurodermitis constitutionalis atopica. Allergologie 1990;13:415-419

27. Wüthrich B: Zur Immunpathologie der Neurodermitis constitutionalis. Eine klinisch-immunologische Studie mit besonderer Berücksichtigung der immunglobuline E und der spezifischen Reagine im zeitlichen Verlauf. Huber, Bern, Stuttgart, Wien, 1975

28. Wüthrich B: Atopic dermatitis flares provoked by inhalant allergens. Dermatologica 1989;178:51-53

AUTHOR'S ADDRESS
Brunello Wüthrich M.D., Professor of Dermatology and Allergology, Head Allergy Unit, Department of Dermatology, University Hospital, Gloriastrasse 31
CH-8091 Zurich, Switzerland