

Short Communications

Contact and bacterial allergy in children with atopic dermatitis*

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Cell-mediated immunity to bacterial antigens was studied by intradermal testing, and to contact antigens (cosmetics, environmental chemicals and topical medicaments) by patch testing in 270 children with atopic dermatitis. The incidence of delayed-type immune cutaneous reactions in these patients was lower than in the controls. Contact allergy is a rare finding in the first 4 years of life but its incidence increases subsequently. In subjects with atopic dermatitis the incidence of sensitization by contact with allergens contained in topical medicaments proved to be lower than in subjects with eczema of other types.

The data collected points to a reduced cell-mediated immune reactivity in a proportion of subjects with atopic dermatitis.

Recent publications support the hypothesis (Parish & Champion 1973) that in atopic dermatitis (AD) there is a fundamental defect in T-lymphocytes with corresponding excessive production of reagins. Reduced response to phytohaemagglutinin by lymphocytes of two patients with AD has been demonstrated *in vitro* by Lobitz et al. (1972). Schöpf (1974) and Gottlieb & Hanifin (1974) observed disturbance of cell-mediated immune reactions in AD with reduction in the number of T-lymphocytes forming rosettes and a corresponding increase in the IgE. Luckasen et al. (1974), McGeady & Buckley (1974) and Blaylock (1976) obtained results also pointing to a moderate reduction in T-lymphocytes in patients with AD.

Similarly, and still in patients with AD, Andersen & Hjorth (1975) demonstrated a moderate but significant reduction in the number of T-lymphocytes forming rosettes, and a depressed response to phytohaemagglutinin of lymphocytes placed in culture with the addition of autologous serum; this phenomenon thus takes place only in the presence of a serum factor, presumably IgE.

In vivo studies produced satisfactorily concordant results indicative of poor cutaneous

reactivity in atopic subjects to tuberculin and bacterial antigens (Gudjonsson et al. 1966, Palacios et al. 1966, tuberculin, bacterial and viral antigens (Rajka 1967, Rajka 1968, Grove et al. 1975), with negative responses to tuberculin especially in patients with severe eczema (Hovmark 1975).

Data on the incidence of contact hypersensitivity of the delayed type, i.e. of allergic contact dermatitis (ACD) in AD showed some discrepancies. According to some (Fregert & Möller 1963, Epstein & Mohajerin 1964) it is increased; to others (Gudjonsson et al. 1966, Jones et al. 1973) it is diminished. Palacios et al. (1966) have demonstrated experimentally that the capacity for sensitization to dinitrochlorobenzene in patients with AD is reduced compared to controls. In the ICDRG series (Cronin et al. 1970) the incidence of ACD in atopic dermatitis does not differ from the statistical means for normal subjects. According to Rudzki & Grzywa (1975) the incidence of positive patch tests to various chemicals, excluding certain drugs, is less in subjects with AD than in all subjects with ACD. It must be pointed out also that data on contact allergy to chemical agents in AD have been collected

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in most cases without reference to the age of the subjects. Binazzi et al. (1974) in their study of the incidence and variations of delayed hypersensitivity reactions in AD, reported 10 % of positive patch tests in children aged 6 months to 6 years, as against 36% in subjects aged 7 to 15 years, and 41.5% in those aged 15 to 42 years.

The aim of our study was to collect further data on the behaviour of cell-mediated immunity in children with special reference to

1. delayed cutaneous reactions to bacterial antigens administered by intradermal injection
2. the incidence of ACD to various chemical agents including drugs.

Material and Methods

Skin responses to bacterial antigens were studied in a series of 100 children under the age of 12 years with atopic dermatitis with exudative lesions or with active Besnier's prurigo. The following antigens in doses of 0.1 ml were injected intradermally into the flexor surface of the forearm by means of a 1-ml insulin syringe

1. Candidicin (Institut Pasteur, Paris) diluted 1:10,000 in saline
2. PPD (Statens Seruminstitut, Copenhagen) 0.1-ml dose containing 1 unit of purified tuberculin
3. Streptokinase-streptodornase (Varidase, American Cyanamid Company, Wayne, N. J.) 0.1-ml dose containing 40 units of streptokinase.

The results were read 2-3 days later using the following criteria:

- a. negative reaction (-): no evidence of inflammation
- b. weak positive reaction (+): presence of erythema (this type of reaction was ignored)
- c. positive reaction (++;+++): presence of an erythematous infiltrative lesion 8-10 mm or more in diameter (this type of reaction was the only one taken into consideration).

The results were compared with those obtained in 100 children under 12 years of age with moderately severe dermatitis of noneczematous type and not caused by microbial agents.

Allergological investigation was carried out in a total of 270 patients, 154 boys and 116 girls under the age of 12 years, all with active

Table 1. Test substances used in the standard series (TL = Trolle Lassen)

Substance*	Concentration %
Balsam of Peru (TL)	25
Benzocaine (TL)	5
Chloramphenicol (TL)	5
Cobalt chloride (TL)	1
Colophony (TL)	20
Ethylenediamine (TL)	1
Formaldehyde (Merck), aqueous	2
Mercaptobenzothiazole (TL)	2
Mercapto-mix (TL)	2
Mercury (TL)	0.5
Neomycin sulfate (TL)	20
Nickel sulfate (TL)	5
Paraphenylenediamine (TL)	1
Parabens (TL)	15
Penicillin (Squibb)	5
Potassium dichromate (TL)	0.5
Promethazine (Farmitalia)	2
Sulfonamide (De Angeli)	5
Tetramethylthiuramdisulphide (TL)	1
Trichlorocarbaniide (Bouty)	5
Triethanolamine (Merck)	5
Turpentine (Carmagnani)	10
Vioform (Ciba)	3
Wool alcohols (TL)	30

*All prepared in petrolatum except formaldehyde.

lesions of AD, observed during the period 1970-1975. Two thirds of the patients were hospitalized. A standard series of 24 allergens was employed (Table 1), chosen from those commonly responsible for contact sensitization of the delayed type. While most of the test substances were supplied by Trolab of Copen-

Table 2. Positive intradermal reactions to bacterial antigens in 100 children with atopic dermatitis and in 100 controls

Bacterial antigens	Atopic dermatitis	Controls
<i>Candida albicans</i>	0	7 (7.0 %)
PPD - tuberculin	3 (3.0 %)	17 (17.0 %)
Streptokinase-streptodornase	14 (14.0 %)	21 (21.0 %)

Table 3. Contact allergy in atopic dermatitis; 270 patients tested; 25 patients with positive reactions, according to age and sex

Age (years)	Patients tested	Positive reactions	Sex	Substance
0-1	13	0		
1-2	54	2	M	paraphenylenediamine
			M	turpentine
2-3	37	4	F	cobalt chloride
			F	potassium dichromate
			M	nickel sulfate
			M	balsam of Peru, potassium dichromate
3-4	18	0		
4-5	28	3	M	neomycin sulfate
			M	potassium dichromate
			M	promethazine
5-6	17	4	F	neomycin sulfate
			F	potassium dichromate
			M	potassium dichromate
			M	potassium dichromate
6-7	18	1	F	cobalt chloride
7-8	16	1	F	promethazine
8-9	17	2	M	neomycin sulfate
			M	turpentine
9-10	20	3	F	benzocaine
			F	colophony
			F	potassium dichromate
10-11	15	2	F	parabens, potassium dichromate
			M	benzocaine, nickel sulfate
11-12	17	3	F	cobalt chloride
			F	formaldehyde
			M	neomycin sulfate, potassium dichromate

hagen, some were prepared by ourselves by dissolving the substances in standard petroleum (Carlo Erba, Milan). The technique for applying and reading the patch tests was that described by Fregert et al. (1969).

Results

The variations in delayed-type reactivity to intradermally introduced microbial antigens were as follows (Table 2). Of 100 subjects with AD only three became sensitized to tuberculin as against 17 of 100 controls (same age group and free from tuberculosis). The response to streptococcal antigens was positive in 14 % of subjects with AD as against 21 % of controls. The corresponding figures for *Candida albicans* positivity were nil for the AD group as against 7 % for the controls.

Patch test designed to demonstrate sensitivity

to contact allergens in 270 children under 12 with AD produced positive results in 25 cases (93 %), including four positive responses to two allergens. More specifically, positive results were recorded in 6 of 122 children under 4; in 9 of 79 children aged 5 to 8 years, and in 10 of 69 children aged 9 to 12 years. The sex distribution of positive results was 13 of 154 males (8.4 %) and 12 of 116 females (10.3).

The distribution of results according to the type of allergen is shown in Table 3. As four patients showed two positive responses each, the total number of positive results was 29. The double positive responses were obtained with

1. Balsam of Peru and potassium dichromate
2. Nickel sulfate and benzocaine
3. Potassium dichromate and parabens
4. Cobalt sulfate and neomycin sulfate.

Table 4. Sensitivities to medicaments in eczematous patients of different types

15%	in post-traumatic ecz. (168 cases)
39%	in leg ulcers (259 cases)
26%	from clothing accessories (145 cases)
26%	of the face (104 cases)
20%	in anoperineal ecz. (152 cases)
20%	in occupational d. (770 cases)
10%	in dyshidrotic ecz. (186 cases)
9%	in atopic d. (176 cases)

Discussion

The incidence of positive delayed-type skin immune reactions to tuberculin, streptococcal and *Candida albicans* antigens in subjects with atopic dermatitis was lower than in the controls. This indicates a reduced cell-mediated immune response in a group of atopic children. An interesting finding was the low incidence of positive reactions to streptococcal antigens, inasmuch that in the course of the disease subjects with atopic eczema show spontaneous or scratch lesions which in nonatopic subjects usually favour pyogenic infections with the corresponding immune responses.

Contact allergy has been demonstrated in children with AD after the second year; its incidence increased with age.

The relatively low incidence of sensitivity in the first years of life may be attributable to:

- small number of contacts with potential allergens
- a defect of cell-mediated immunity in atopic subjects.

As regards the changes of contact with potential allergens it is obvious that young children are less at risk of environmental exposure to metals, garments, textile dyes and finishes, etc., but may be subject to the sensitizing effects of soaps, lotions, creams, substances in the linen, and topical applications, often used over prolonged periods.

The patterns of sensitivity demonstrated by patch testing in atopic children under the age of 12 years point to the major aetiopathogenic importance of contact with environmental factors in the second six compared with the first six years of life.

The sensitivity to chromate may be attributed to some aspects of the way of life currently prevalent in Italy, especially in the villages of the southern part of the country. In their play younger children often imitate their mothers'

domestic chores, including handwashing of garments with soaps, detergents and bleaches; poor families cannot afford washing machines. Older children are more likely to come into contact with various substances when they are called upon to help adults in various types of work including building; in fact, an Italian farmer or peasant still depends on his own and his family's labour for minor building and artisan jobs.

The defect of cell-mediated immunity in the atopic subject, as raised by Parish & Champion (1973), might explain the relatively low incidence of sensitization in the first four years of life. The data reviewed in our introduction and indicative of a fundamental defect in T-lymphocytes as demonstrated *in vitro* and the poor reactivity to microbial antigens observed in subjects with AD are in favour of this interpretation.

It is likely that contact allergy also develops with greater difficulty in subjects with AD, especially in the first few years of life, compared with those suffering with other forms of dermatitis. To explore this possibility we compared the results of patch testing with a series of drugs listed in Table 1, in groups of subjects with eczematous dermatitis of various types (post-traumatic, leg ulcers, pompholyx, etc.) and in subjects with AD, mainly children; the incidence of positive reactions was lower (9%) in the latter (Table 4).

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Contact allergy to onion

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A 24-year-old housewife began helping in a restaurant more than 1 year ago. She makes what is called in this country "brochette". Her work consists of putting slices of meat and onion on metal pins. Since then she developed eczema of the hands. She denied ever having touched garlic. Patch tests with a standard tray

of contact allergens were all negative. A test with pieces of onion however showed erythema, edema and vesicles.

Subsequently we prepared water, ethanol and acetone extracts of onion and garlic, according to Bleumink et al. (1972). Results are shown in Table 1. They resemble the test results in the