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CONTACT DERMATITIS IN THE ATOPIC

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Abstract. In five European contact dermatitis clinics 4,000 patients were patch tested to an identical series of 20 standard allergens. Of this group 233 had atopic eczema. It was found that atopics are no more likely to develop an allergic contact dermatitis than patients with other types of endogenous eczema such as seborrhoeic or nummular eczema. The absolute and relatively commonest allergens in atopics were balsams and topical medicaments. The incidence of occupational dermatitis was almost similar in patients with atopic and nummular eczema. Of the patients with atopic, contact and nummular eczema an equally high incidence of 68% had their hands affected.

Reports in the literature differ as to whether there is an increased incidence of contact dermatitis in patients with atopic dermatitis.

Wilson (18) contrasted the patch test results, to a standard series of allergens, in 50 patients with atopic, discoid and contact eczema and normal controls. He concluded that atopic patients are not more likely to develop contact dermatitis than normal persons. Caron (3) found no evidence of an atopic background in 37 patients sensitive to nickel and in Calnan's (2) study of contact dermatitis to nickel, only 1% of 400 nickel-sensitive patients had had atopic eczema. Similarly Rostenberg & Sulzberger (15), Skog & Thyresson (17) and Skog (16) found no evidence that atopic patients are particularly prone to develop contact dermatitis. In 1963 Fregert & Möller (8) patch tested 101 children with eczema and found no significant difference in the incidence of positive reactions between the 37 atopic children and the rest of the group. In a detailed investigation of hand eczema, Agrup (1) observed that the atopic is prone to develop an irritant dermatitis but observed no significant difference in the frequency of positive tests between atopic, irritant, nummular and unclassifiable hand eczema. Forsbeck et al. (7) patch tested 101 pairs of twins and found no correlation between atopy and positive patch test reactions. A Scandinavian Committee tested a group of 1,027 patients to a routine test series and found that 13% of the atopics and 31% of the non-atopics had positive patch test reactions (11).

In contrast Malten (12) patch tested 80 atopic patients to a series of 43 substances and reported that 34% gave positive reactions. Meneghini (13, 14) found that of 75 atopic children 6 gave positive test reactions to a routine test series. Epstein & Mohajerin (5) reported that 28 of 100 atopics gave positive patch tests compared with 9 of 100 psoriatics and 0 of 20 patients with acne. The reactions in the atopic patients were principally to medicaments. In a further study of 120 patients sensitive to neomycin, Epstein (4) classified 55–75% of this group as atopics. The Scandinavian Committee could not confirm this predominance of neomycin sensitivity in atopic patients (11). Fifty patients with hand eczema were studied by Glickman & Silvers (10). Of these 82% had a personal or family history of atopy compared with only 28% among 50 normal controls. A relationship between contact allergy and atopic dermatitis was also suggested in the investigation of Forsbeck et al. (6), who found a high frequency of atopy among the children of patients with allergic contact dermatitis.

No definite conclusions can be drawn from these conflicting findings, which may partly be due to differences in the selection of patients for patch testing and the composition of the patch test series.

MATERIAL AND METHODS

In eight European contact dermatitis clinics we decided to investigate patients with eczema by patch testing to a

Table I. *Numbers of male and female patients tested at each of five clinics*

Clinic	♂	♀	Total
1. Copenhagen	300	500	800
2. Gothenburg	262	538	800
3. London	358	442	800
4. Lund	320	480	800
5. Munich	377	423	800
Total 1–5	1,617	2,383	4,000

standard battery of allergens (9). In 12 months, 800 patients were tested in each of the following clinics, Copenhagen (Denmark), Gothenburg and Lund (Sweden), London (England), and Munich (Germany), Table I. The data from these 4,000 patients was analysed with a computer (Data Center, University of Lund, Sweden. Project No. 205238) and forms the basis for this study. As the numbers tested in Bari, Nijmegen and Wycombe were smaller, being a total of 825, their results were not included in the computer analysis.

The twenty chemicals and their concentrations are listed in Table II, each chemical was diluted in petrolatum except for oil of turpentine and formaldehyde. The test substances for each clinic were obtained from one source (K. Trolle-Lassen, Høyrups Alle 1, Hellerup, Denmark).

Table II. *The twenty allergens used as a routine test series*

Test substance	Conc. (%)	Vehicle
Metals		
Potassium dichromate	0.5	Petrolatum
Nickel sulphate	5	Petrolatum
Cobalt chloride	2	Petrolatum
Rubber chemicals		
Tetramethylthiuramdisulphide	2	Petrolatum
Mercaptobenzthiazole	2	Petrolatum
Phenyl-cyclohexyl-PPD	2	Petrolatum
Diphenyl-PPD	2	Petrolatum
Medicaments		
Neomycin sulphate	20	Petrolatum
Benzocaine	5	Petrolatum
Vioform	5	Petrolatum
Parabens (methyl-, ethyl-, propyl-, butyl-, benzyl-) 3% each	15	Petrolatum
Wool alcohols	30	Petrolatum
Sterosan	5	Petrolatum
Balsams		
Colophony	20	Petrolatum
Wood tars	25	Petrolatum
Balsam of Peru	25	Petrolatum
Oil of turpentine	5	Olive oil
Others		
p-Phenylenediamine	1	Petrolatum
Coal tar	5	Petrolatum
Formaldehyde	2	Water

The A1-test (IMECO, Astra Agency Co., Stockholm, Sweden) was used as the patch test unit and the allergens were applied to the upper back in strips of five. The adhesive plaster was Leukoplast (Beiersdorf & Co., Hamburg, West Germany), except in those who gave a history of irritation from plaster, when Dermicel (Johnson and Johnson, New Brunswick, N.J., USA) was substituted. The patches remained on for 24 hours in the first half of the study and for 48 hours in the second half. Two readings were done whenever possible, the first at 24–28 hours after application and the second at 72, 96 or 120 hours after application. More precise details are given by Fregert et al. (9). Although we endeavoured to make the selection of patients the same in each clinic, this was not achieved owing to local differences in the way each department is run. For instance, in Copenhagen every patient with eczema is patch tested, whereas in the other centres as in London, it is mainly patients suspected of having contact dermatitis who are so referred. Before patch testing each patient was assessed clinically and a "primary diagnosis" made, in this way the patients were clinically grouped into six following types of eczema, contact (allergic or irritant), seborrhoeic, atopic, nummular, stasis, and unclassifiable (unable to be put into any of the other five categories) eczema.

In each of the five clinics, the diagnosis of atopic dermatitis was based on the history, morphology and clinical appearance of the patient. The definition conformed with that given by Agrup (1).

RESULTS

In the series 233 patients (6%) had atopic eczema, of these 80 were men and 153 women. The num-

Table III. *Number of patients in each of the six classifications of eczema (primary diagnosis)*

	Atopic	Contact	Seborrhoeic	Nummular	Stasis	Unclassified
Number	233	2,266	143	85	302	971
%	6	57	4	2	8	23
Males (%)	5	57	4	3	5	26
Females (%)	6	56	4	2	9	23

Table IV. *Duration of eczema before patch testing in the atopic patient compared with the rest of the series*

	>5 y.	<5 y.	<1 y.	<1 mo.
Atopic (%)	53	26	16	5
Non-atopics (%)	22	22	43	13

Table V. *Incidence of positive reactions* (%) *to 20 allergens in the six categories of eczema* (*primary diagnosis*)

Atopic	Contact	Seborrhoeic	Nummular	Stasis	Unclassified
26	43	22	19	60	34

Table VII. *Contact dermatitis* (*definite diagnosis*) *in per cent of 233 patients with atopic dermatitis* (*primary diagnosis*)

Allergic	Irritant	Allergic and irritant	Not a contact dermatitis
16	10	2	72

bers and six incidence in the other primary diagnoses are also given in Table III.

Duration of eczema prior to patch testing

At the time of patch testing half of the atopics (53%) had had their eczema for longer than 5 years compared with a fifth with this length of history among the other patients. Only 5% of the atopics had a history shorter than a month compared with 13% among those with other types of eczema (Table IV).

Incidence of reactions to the allergens tested

Of the 4,000 patients a total of 1,600 (40%) had positive reactions to one or more of the 20 allergens. Of these positive reactors 4% were atopics; the proportion with positive tests was the same in males and females. The incidence of positive reactions was similar for atopic, seborrhoeic and nummular eczema, varying from 26% to 19%; it was higher in the group initially diagnosed as having contact dermatitis (43%), and for those with stasis eczema (60%) (Table V).

The allergens to which the atopic patients reacted most frequently have been listed in Table VI and their incidence compared with those in the other patients. Among the atopics the highest incidence of reactions was to the balsams. None of the atopic men but 4.6% of the atopic women reacted to nickel and 7.5% of the male atopics compared with 1.3% of the female atopics reacted to potassium dichromate. The analysis also showed an unexplained difference in the number of reactions to medicaments in male atopics, which was 7.5% compared with an incidence of 2.6% in females.

One per cent of both male and female atopic patients reacted to wool alcohols, this was comparable to all the rest of the patients, except those with stasis eczema where the incidence of sensitivity was 11% for men and 20% for women.

The final assessment of the importance of contact factors

When the results of the patch tests were completed a final assessment was made as to whether contact factors, either allergic or irritant, played any part in the patient's eczema or if it was concluded that the eczema was "not a contact dermatitis". Of the 233 patients with atopic eczema 16% were considered to have an allergic contact dermatitis, 10% an irritant dermatitis, 2% an allergic combined with an irritant dermatitis, the rest (72%) were considered to be uninfluenced by contact factors (Table VII).

Occupational dermatitis

After patch testing the results were reviewed in each case to decide whether the patient had an occupational contact dermatitis. A total of 769 patients

Table VI. *Positive reactions* (%) *in atopics and other patients tested with 20 allergens*

The allergen groups according to Table II

	Neomycin	Cr	Ni	Co	Rubber	Medicaments	Balsams	Benzocaine	PPD
Atopics, males	1.2	7.5	0.0	2.5	1.2	7.5	13.8	0.0	1.2
Non-atopics, males	3.6	10.1	1.8	7.3	4.7	7.2	17.2	3.1	5.3
Atopics, females	0.0	1.3	4.6	3.9	0.7	2.6	15.7	1.3	1.3
Non-atopics, females	4.4	2.8	10.5	6.7	5.2	9.7	19.7	4.8	4.8

Table VIII. *Primary diagnoses of the 769 patients with occupational dermatitis among 4,000 tested*

	Atopic	Contact	Seborrhoeic	Nummular	Stasis	Unclassified
Number of cases tested	233	2,266	143	85	302	971
Occupational dermatitis (%)	10	29	3	9	1	8

Table IX. *Primary diagnosis of 427 patients with involvement of their hands and feet among 4,000 tested*

	Atopic	Contact	Seborrhoeic	Nummular	Stasis	Unclassified
Number of cases tested	233	2,266	143	85	302	971
Hands and feet (%)	16	8	3	21	3	17

Table X. *Patients with hand dermatitis (%) in the various groups of eczema (primary diagnosis)*

Atopic	Contact	Seborrhoeic	Nummular	Stasis	Unclassified
68	67	20	68	11	54

among the 4,000 were finally diagnosed as being occupational. The distribution of these cases among the six eczema categories (primary diagnosis) is given in Table VIII. The incidence of occupational dermatitis was about equal (from 10% to 8%) in the atopic, nummular and unclassified eczema patients.

Eczema of the hands and feet

There were 427 patients with both hands and feet involved. Their distribution among the six eczema categories is given in Table IX. In only 3 atopic patients was the eczema confined to their feet.

The incidence of hand eczema with or without involvement of the feet in the atopic patients varied in the different clinics and ranged from 49% to 80% of the atopics tested.

In the series of 4,000 patients hand eczema was commonest in the following types of eczema: atopic 68%, nummular 68%, contact 67% (Table X).

DISCUSSION

In this series of 4,000 patients with eczema, there was a definite bias towards patch testing those in whom a contact dermatitis was suspected. This applied to all the clinics except Copenhagen where all patients with eczema are patch tested. Therefore the 233 atopic patients in this study are a selected group in that most of them have probably been included as it was thought that they might have a contact dermatitis. This bias towards the presence of a contact sensitivity applied equally to the other five categories of eczema into which the patients were divided, Table III, so that a comparison between each of the six eczema groups is valid.

When patch tested, the atopic patients had a considerably longer history of eczema than the rest of the series, thus having had more opportunity to become sensitized, TableIV. Despite this their incidence of positive reactions of 26%, Table V, was similar to the incidence in the seborrhoeic and nummular eczema patients which is in accordance with the findings of Agrup (1). This data strongly suggests that the atopic patient is no more likely to develop a contact sensitivity than patients with other types of endogenous eczema such as discoid or seborrhoeic.

When sub-dividing the patients with occupational dermatitis into their categories of primary diagnoses the findings were similar. The incidence of occupational dermatitis was about equal in atopic nummular and unclassified eczema patients (Table VIII). It is noteworthy that a relatively low incidence of contact dermatitis occurred in the indogenous eczema groups despite the preselection of patients on the possibility of their having a contact dermatitis.

In the group of 233 atopic patients 68% had hand eczema, which is as high an incidence as that which occurred in the patients with contact dermatitis and nummular eczema (Table X).

There was a rather wide variation in the frequency of hand eczema in the atopic patients tested in the various clinics ranging from 49% in Gothenburg to 80% in Lund. This is likely to have been due to the differences in the selection of patients rather than a true difference in the topographical distribution of eczema in the atopics of different countries.

When considering the positive reactions to individual allergens, the numbers calculated for

this series are not applicable to all atopic patients. Thus an incidence of 4.6% female atopics being sensitive to nickel is likely to be due to their having given positive histories of nickel sensitivity, which was the reason why they were patch tested. This assumption applies equally to the 7.5% of male atopics who reacted to potassium dichromate (Table VI). The selection of patients must also be remembered in the comparison of the incidence of positive reactions to the individual allergens in the atopics compared with the rest of the series. The high incidence of sensitivities in "the rest of series" is due to the heavy weighting of the group in favour of positive reactions, as patients suspected of having contact dermatitis are included in this group.

Although the atopic patients tended to be selected on the possibility of their having a contact sensitivity only 16% had clinically relevant allergic reactions, 10% were judged to have an irritant dermatitis and 2% had a combined allergic and irritant dermatitis (Table VII).

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REFERENCES

1. Agrup, G.: Hand eczema. Acta Dermatovener (Stockholm) *49:* Suppl. *61.* Lund, 1969.
2. Calnan, C. D.: Nickel dermatitis. Brit J Derm *68:* 229, 1956.
3. Caron, G. A.: Nickel sensitivity and atopy. Brit J Derm *76:* 384, 1964.
4. Epstein, S.: Neomycin sensitivity and atopy. Dermatologica *130:* 280, 1965.
5. Epstein, S. & Mohajerin, A. H.: Incidence of contact sensitivity in atopic dermatitis. Arch Derm (Chicago) *90:* 284, 1964.
6. Forsbeck, M., Skog, E. & Ytterborn, K. H.: The frequency of allergic disease among relatives of patients with allergic eczematous contact dermatitis. XIII Congressus, Intern Dermat München: 268, 1967.
7. — Delayed type of allergy and atopic disease among twins. Acta Dermatovener (Stockholm) *48:* 192, 1968.
8. Fregert, S. & Möller, H.: Contact allergy to balsam of Peru in children. Brit J Derm *75:* 218, 1963.
9. Fregert, S., Hjorth, N., Magnusson, B., Bandmann, H. J., Calnan, C. D., Cronin, E., Malten, K., Meneghini, C. L., Pirilä, V. & Wilkinson, D. S.: Epidemiology of contact dermatitis. Trans St John's Hosp Derm Soc *55:* 17, 1969.
10. Glickman, F. S. & Silvers, J. H.: Hand eczema and atopy in housewives. Arch Derm (Chicago) *95:* 487, 1967.
11. Magnusson, B., Fregert, S., Hjorth, N., Høvding, G., Pirilä, V. & Skog, E.: Routine Patch Testing V. Fifth report by the Scandinavian Committee for Standardisation of Routine Patch Testing. Acta Dermatovener (Stockholm) *49:* 556, 1969.
12. Malten, K. E.: The occurrence of hybrids between contact allergic eczema and atopic dermatitis (and vice versa) and their significance. Dermatologica *136:* 404, 1968.
13. Meneghini, C. L. & Rantuccio, F.: Eczematous contact hypersensitivity in children. Contact Dermatitis Newsletter *2:* July 1967.
14. Meneghini, C. L.: Patch test in atopic dermatitis children. Contact Dermatitis Newsletter *6:* 132, 1969.
15. Rostenberg, A. & Sulzberger, M. B.: Some results of patch tests. Arch Derm (Chicago) *35:* 433, 1937.
16. Skog, E.: Sensitisation to *p*-Phenylenediamine. Arch Derm (Chicago) *92:* 276, 1965.
17. Skog, E. & Thyresson, N.: The occupational significance of some common contact allergens. Acta Dermatovener (Stockholm) *33:* 65, 1953.
18. Wilson, H. T. H.: Standard patch tests in eczema and dermatitis. Brit J Derm *67:* 291, 1955.

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