

Contact allergy to cosmetics: testing with patients' own products

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In a 2-year period, 1527 patients with contact dermatitis were investigated in the patch-test clinic. In 531 patients, allergy to cosmetics was suspected from the history and they were tested with their own cosmetic products. 40 (7.5%) (of the 531 patients) had 1 or more positive reactions, 82 (15.4%) had doubtfully positive reaction(s) and 31 (5.8%) had irritant reaction(s). Skin-care products were tested most frequently and were also found to cause most positive, doubtfully positive and irritant reactions. 80% of the patients with positive reactions to their own products had no history of contact dermatitis prior to the presenting attack, and in 92.5% of the cases, the positive reaction was considered relevant or partly relevant. In patients with a positive reaction, ingredients that could be responsible were found in 60% of the cases by testing with the European standard series and a series of common cosmetic ingredients. Fragrance mix and formaldehyde were found to be the ingredients most often responsible and were significantly more frequent in patients with positive reactions to their own products, compared to a control group of eczema patients also seen in the patch-test clinic.

Key words: cosmetic allergy; own cosmetic products; patch testing technique; standard series; cosmetic ingredients; formaldehyde; fragrances. © Munksgaard, 1999.

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In a population-based study, approximately 95% of Danish women used cosmetic products daily and 43.9% claimed they had ever had side-effects from cosmetics. Patch testing with the European standard series revealed that 4.2% of all women had a positive reaction to 1 or more of the ingredients frequently used in cosmetics (1). Contact dermatitis caused by cosmetics may be a challenge to the dermatologist and testing with patients' own products often seems a necessary and relevant procedure. The aim of this retrospective study was to evaluate the prevalence of positive, doubtfully positive and irritant patch test reactions to cosmetics in consecutive eczema patients who visited our patch-test clinic in a 2-year period: a further aim was to relate this finding to the outcome of patch testing with the European standard series and selected cosmetic allergens.

Materials and Methods

Study population

The study included 1527 consecutively patch tested eczema patients in the Department of Derma-

tology, Gentofte Hospital, Denmark, in the period of October 1994 – October 1996. In 531 patients (35%, 404 female, 127 male), contact allergy to cosmetics was suspected from the clinical history, and patch testing with the patients' own cosmetic products was performed. In addition, the patients were tested with the standard series and a series of cosmetic ingredients.

Patch-test materials

Routine testing with The European standard series and a series of common cosmetic ingredients provided by Hermal, Germany, was performed.

Own products. Patients were told to bring all the cosmetic products that they had used for the last 2 months. These included moisturizing products, eye make-up, lip products, nail cosmetics, sunscreens, hair colouring products, deodorants, perfumes and shaving products. Soaps and shampoos were not included. Closed patch tests were performed using the undiluted cosmetic product. Solid products (powders, lipsticks) were suspended in 0.01 N HCl. Nail lacquers were air dried for

10–15 min. The test material was applied in Finn Chambers (8 mm) on Scanpor tape.

Patch testing procedure

The patches were applied on the upper back for 2 days. Readings were taken after 2, 3 and 7 days. Readings were taken according to ICDRG guidelines. In the case of several positive reactions, the maximum reaction was used in the analysis.

Relevance

A positive patch test to 1 or more of the patient's own products was considered relevant if there was a temporal relationship between the use of the product on a certain body area and the outbreak of eczema, and a complete or partial resolution of the eczema when the use of the product was discontinued.

Data handling and statistics

A comparison of certain characteristics was made between the group of patients with positive patch test reactions to their own cosmetic products (A) and the control eczema population (C), and between the group of patients with ?+ reactions to their own cosmetic products (B) and the control eczema population (C). The control eczema population ($n=1405$) was defined as eczema patients consecutively patch-tested with the standard series in the same period ($n=1527$), excluding patients with positive or ?+ reactions to their own products. Odds ratios (OR) and confidence intervals (estimating sample size errors) were calculated from log-likelihood estimation. OR expresses the relative risk of an event (e.g., fragrance sensitization) in a group with a certain characteristic (e.g., positive reaction to own cosmetic products) in comparison with a specified reference group, in this case a group of consecutively patch tested eczema patients negative on testing or not patch tested with their own cosmetic products. A confidence interval of 95% was chosen.

Results

Skin-care products were tested in 79% of the patients tested with their own cosmetic products, eye make-up products in 39%; deodorants were tested in 26% and perfumes in 20%. Most patients were tested with 1–5 products (61%). Less than 4% of the patients were tested with more than 30 different products.

Positive reaction(s) to own cosmetic products

A total of 40 of the 1527 patients (2.6%) tested had 1 or more positive patch test reactions to their own cosmetic products (Table 1) and 16 of these did not have reactions in the standard series. 5 (12.5%) had current or previous atopic eczema and 32 (80%) had no contact dermatitis prior to the present attack. Among the 40 patients, face (57.5%), axillae (22.5%) or hands (17.5%) were most commonly affected sites. 30 were female and 10 male. This sex distribution was not significantly different from the control group of consecutive eczema patients tested with the standard series in the same time period (Table 2). In 37 cases (92.5%), the positive patch test reactions to the cosmetic product(s) were considered fully or partly relevant to the patients, presenting dermatitis (Table 1). Most patients reacted only to 1 type of cosmetic product, either moisturizers (14), nail polish (6), deodorants (5), perfumes (5), sunscreens (3), make-up (5) or shaving preparations (3). 3 patients reacted to several product categories (Table 1).

In 24 of the cases (60%), a positive patch test reaction was found to 1 or more of the allergens from the standard series or cosmetic ingredient series that might be present in cosmetics. A positive reaction to the fragrance mix was found in 27.5% of the cases, to formaldehyde in 12.5%, to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) in 7.5% and to methyldibromomethylglutaronitrile and phenoxyethanol (Euxyl K400) in 7.5% of the cosmetic-positive patients, which is statistically significantly more often than in the control eczema population (Table 2). The frequency of positive reactions to nickel did not differ significantly from the control group.

Doubtful reaction(s) to own cosmetic products

A maximum reaction of ?+ to own cosmetic products was found in 82 of consecutively tested eczema patients (5.4%) and 86% of these were female. In 24 of the cases (29%), the reaction to the cosmetic product was considered relevant or partly relevant to the patients presenting eczema. In 9 cases, the information was missing. Most reactions were due to skin-care products/lotions (54), followed by perfumes (6), deodorants (6) and nail polish (4). 27 of the 82 patients (33%) had 1 or more positive patch tests to cosmetic allergens from the standard or cosmetic series. No significant difference in the frequency of positive patch test reactions to fragrance mix ($n=7$), MCI/MI ($n=3$) or nickel ($n=10$) was found in comparison to the control eczema population, while formaldehyde contact allergy was found significantly more

Table 1. Types of reactions, causative products, eczema location and relevance are given for each of the 40 patients having positive reaction(s) to their own products

Case No.	Product type	No. positive products/patient	Reactions to allergens from standard and cosmetic series	Eczema location	Relevance ^{a)}
nail polish					
1		9+	tosylamide/formaldehyde resin	face, neck	yes
2		4+	tosylamide/formaldehyde resin, ++ nickel	face	yes
3		1+	no	face, neck	yes
4		3++	++ formaldehyde ^{b)} , + nickel	hands	partly
5		1++	++ formaldehyde ^{b)}	face, hands	partly
6		3+	tosylamide/formaldehyde resin	face	partly
deodorants					
7		2 ++, + ^{c)}	no	axillae	yes
8		1+	fragrance mix	axillae	yes
9		2+	fragrance mix, Euxyl K 400, nickel NT	axillae, hands, face	partly
10		1+	no	axillae	yes
11		1++	Euxyl K 400	axillae	yes
perfumes					
8		1+	fragrance mix	axilla	yes
12		1+	no	axilla, neck	partly
13		1+	no	legs ^{d)}	yes
14		1+	fragrance mix	axilla	yes
15		1+	no	neck, face	yes
16	aftershave	1+	fragrance mix	face	yes
moisturizers					
3		1++	no	face, arms, legs	yes
18		1+	no	face	no
18		2+	no	face	no
19		1+	no	hands	partly
20		1+	Euxyl K 400	face	yes
21		1+	fragrance mix, span 80	face	yes
22		1+	formaldehyde, imidiazolidinyl urea, diazolidinyl urea, nickel, NT	hands	partly
23		1+	Amerchol L-101	scalp	yes
24		1+	Amerchol L-101	perianal	yes
25		1+	fragrance mix	face	partly
26		1+	nickel	hands	yes
27		1+	MCI/MI, balsam of Peru, formaldehyde ^{b)}	face, axillae, leg	yes
			oleamidopropylamine		
28		1+	no	face	yes
29		1+	no	legs	yes
30		1+	MCI/MI, balsam of Peru, fragrance mix	neck	yes
sun protection lotion					
31		1++(+light)	4-aminobenzoic acid, formaldehyde ^{b)}	face	yes
32		1+	no	arms, legs	yes
33		1+	fragrance mix, nickel, MCI/MI, oleamidopropylamine	face	yes
make-up					
34	mascara	1+	no	face, neck	yes
35		1+	fragrance mix	face	yes
36	make-up creme	1+	no	face	yes
37		1+	fragrance mix, nickel	face	yes
27	rouge	1+	MCI/MI, balsam of Peru, formaldehyde ^{b)}	face, axilla	yes
27	make-up remover	1++	oleamidopropylamine		yes
shaving products					
38		1+	no	face	no
39		1+	fragrance mix	hands/body	no
40		1+	diazolidinyl urea	face	yes

3 patients had more than 1 reaction. All reactions to the standard and cosmetic series were ++, +++ or ++++ reactions. Follicular and ?+ reactions were not included.

^{a)} Relevance of patch test reaction to product for current eczema.

^{b)} Formaldehyde analysis of products positive.

^{c)} Usage test positive.

^{d)} Perfume oil had been used on the legs. NT: not tested.

Table 2. A comparison of certain characteristics was made between the group of patients with positive reactions (A) and the control eczema population (C) and between the group of patients with ?+ reactions (B) and the control eczema population (C)

	Positive reactions to own cosmetic products (n=40) group A	?+ reactions to own cosmetics products (n=82) group B	Control eczema population (n=1405) group C	Comparison (odds ratio and 95% confidence interval) group A versus C	Comparison (odds ratio and 95% confidence interval) group B versus C
female	30 (75%)	70 (85.4%)	892 (63.5%)	1.68 (0.81–3.46)	3.25 (1.74–6.05)
age, median and percentiles	50 yrs (42–61)	46 yrs (37–55)			
atopic dermatitis	5 (12.5%)	12 (14.6%)	169 (12%)	1.17 (0.45–3.03)	1.4 (0.74–2.65)
fragrance mix positive	11 (27.5%)	7 (8.5%)	94 (6.7%)	5.29 (2.56–10.92)	1.3 (0.66–2.59)
formaldehyde positive	5 (12.5%)	6 (7.3%)	27 (1.9%)	7.29 (2.65–20.05)	4.03 (1.6–10.05)
MCI/MI positive	3 (7.5%)	3 (3.7%)	22 (1.6%)	5.10 (1.46–17.70)	2.39 (0.70–8.15)
nickel positive	6 (15%)	10 (12.2%)	130 (9.2%)	1.73 (0.71–4.2)	1.31 (0.66–2.59)
balsam of Peru positive	2 (5%)	0	25 (1.8%)	2.91 (0.66–12.77)	
Euxyl K400 positive	3 (7.5%)	0	11 (0.87%), (n=1257)	9.2 (2.46–34.36)	
diazolidinyl urea positive	2 (5%)	3 (3.7%)	12 (0.95%), (n=1257)	5.47 (1.11–25.29)	3.98 (1.1–4.41)

Odds ratio and 95% confidence intervals are given for each comparison. The control eczema populations (n=1,405) are defined as eczema patients consecutively patch-tested with the standard series in the same period (n=1,527) excluded patients with positive or ?+ reactions to their own products (n=40+82=122).

often in patients with a ?+ reaction to their own cosmetic products (Table 2). 14.6% had current or previous atopic dermatitis and 58% had no contact dermatitis prior to the presenting attack. Because of the difference in the sex distribution in the 2 groups, a similar analysis was performed in females only with the same result.

Irritant reaction(s) to own cosmetic products

A maximum reaction of IR was seen in only 31 out of the total 531 patients. Moisturizers 8 (26%) most often caused irritant reactions, followed by perfumes 6 (18%), deodorants 4 (13%) and skin tonics 4 (13%).

Discussion

40 patients (2.6%) seen in the patch test clinic had 1 or more positive reactions to their own cosmetic products and 82 (5.4%) a doubtful one. A Spanish survey reported that 182 out of 5539 patch tested patients (3.2%) had a positive reactions to their own cosmetics (2), and De Groot (3) found 61 of 1781 patients with contact dermatitis (3.4%) to have positive patch test(s) with own cosmetics. A frequency of 2.6% patients with a positive reaction to their own cosmetic may seem a modest result, but almost all these reactions were found to be partly or fully clinical relevant. Cosmetic products

often produce rather weak allergic reactions because of a low concentration of the eliciting allergen; thus, in the present study, no +++ reactions were found. This means that the patients with a positive reaction to a cosmetic product probably constitute only the most sensitive portion of patients with allergy to cosmetic ingredients, and that patients with a relevant contact allergy may also be found in the group with a doubtful patch test reaction to their own products. In the present study, 1/3 of the doubtful reactions to patients' own products were judged to be relevant to their present eczema. Furthermore, patients with a false-negative reactions to their own cosmetic products may be expected. In a European multi-centre study, 141 out of 4713 patients (3.0%) had a positive patch test to 100 ppm MCI/MI, and when 117/141 of the patients were re-patch tested with 100, 50 and 25 ppm MCI/MI, only 20% had a positive reaction to 25 ppm, which exceeds the maximum allowed concentration of 7.5 ppm recommended for leave-on products in the EU (4).

Product testing may be a valuable supplement to the standard series as it is relevant to patients actual exposure. Furthermore, it makes it possible to detect sensitivity to rare allergens in the products or effects produced because of additive or synergistic actions of several ingredients in combination (5). First and foremost it should be recommended to perform such testing when the

Table 3. Arguments pro and contra testing with patients, own cosmetic products

Pro	Contra
relevant to patient's exposure	false-negative reactions, as the concentration of the offending allergen is low
unknown or rare allergens (e.g., vehicles)	false-positive reactions, as it is not standard materials that are tested
additive or synergistic effects	many doubtful reactions, which make the reactions difficult to judge
in cases of no reactions in the standard series	expense
labelling may be incorrect or missing	time-consuming
for detecting fragrance allergy (labelling in the EU does not include individual fragrance substances)	

patient has had facial dermatitis/rash (in the present study, 57.5% of the patients with positive reactions to their own products had had face involvement), and in cases with no reaction to the standard series. Since 1997, ingredient labelling of cosmetics products has been compulsory in the EU. However, a Swedish study showed that the declaration of cosmetic products was incorrect in 17% of 100 moisturizers tested for the presence of 9 preservatives (6). This provides a yet further argument for not only testing with cosmetic ingredients but also with the product itself (Table 3).

Most patients (80%) in the present study had no contact dermatitis prior to the present attack; thus, contact allergy to cosmetic ingredients is a significant primary cause of contact eczema. A similar result was reported from the North American Contact Dermatitis Group, who, in a 5-year survey, found the majority of patients with cosmetic-related reactions (501/713, 70%) to have no prior history of contact dermatitis (7).

Moisturizers were most frequently suspected of eliciting the dermatitis and accounted for most cases of both positive reactions and ?+ reactions. This is in agreement with other studies also reporting skin care products as producing the most frequent positive reactions (7, 8), and is not surprising, since skin care products are one of the most sold cosmetic product categories (9). A Swedish study of a young population revealed that as many as 75% used moisturizers daily (10). Next after moisturizers, deodorants, perfumes and nail polish were the products causing most positive reactions, which is in general agreement with other studies (7, 8), while in Spain, nail polish was the product causing most allergic reactions (2).

Patients with positive reactions to their own products had a significantly higher number of positive reactions to cosmetic ingredients (fragrance mix and preservatives), as compared to the control eczema population. The ingredient found most frequently responsible was fragrance mix, which was positive in 27.5% of the patients with

positive reactions, thus supporting what has been found by others, namely fragrance mix being the most common causative agent, accounting for 30–45% of allergic reactions to cosmetics (3, 7). Positive reactions to balsam of Peru were no more frequent in patients with positive or ?+ reactions to their own cosmetics than in the background population of eczema patients. This may corroborate what has recently been reported, that balsam of Peru is not necessarily a relevant marker for fragrance allergy (11). The preservative formaldehyde was found to be a causative ingredient in significantly more of the cosmetic-allergic patients (patients with both positive and ?+ reactions to own products) compared to the control eczema population. It is known from other studies that formaldehyde patch testing has a relatively low degree of reproducibility (12, 13). The reason may be that formaldehyde is of a volatile nature and easily evaporates. This may also complicate testing with cosmetic products containing formaldehyde, and doubtful reactions may occur in some of the patients that are actually sensitized. One study by Flyvholm et al. (14) showed that, when re-testing 20 formaldehyde-sensitive patients, only 1/2 of them reacted to a diagnostic patch test concentration of 10,000 ppm and none had positive reactions to either non-occluded patch tests or repeated open application tests (ROAT) with cosmetic products containing 300 ppm free formaldehyde. However, Marzulli et al. (15) found that 2–5/10 formaldehyde-sensitized persons developed a positive use-test to a product containing 4000 ppm formaldehyde used 2× daily for 21 days (15).

Testing with patients' own cosmetic products provides the possibility of detecting cases of contact allergy that would otherwise not be found, and judging from the present investigation, will be relevant in a large number of the cases (40% of the cases in this study). The problem is to identify the offending allergens in the products. The present study shows a relatively high concordance rate be-

tween positive reactions to cosmetic products and allergens known to be used in cosmetic products. The problem is still the cases where no such reaction is found. The present study is based on data from before 1997, when ingredient labelling of cosmetic products became compulsory in the EU. Identification of the causative ingredient(s) may be less complicated in the future, when full labelling of the products is or should be available, which is of great advantage for both the allergic patient and the dermatologist. Since rules about cosmetics are made according to cosmetic regulations rather than drug regulations, governmental control is still very limited, and more public-administered research in the field of adverse reactions to cosmetics is desirable.

References

1. Nielsen N H, Menné T. Sensibilisation de contact aux constituants des cosmétiques dans une population danoise non sélectionnée. La Glostrup allergy study, Danemark. *Ann Dermatol Venereol* 1993; 120: 33–36.
2. Romaguera C, Gamarasa J M G, Alomar A, Grimalt F. Patch test with allergens related to cosmetics. *Contact Dermatitis* 1983; 9: 167–168.
3. De Groot A. Contact allergy to cosmetics: Causative ingredients. *Contact Dermatitis* 1987; 17: 26–34.
4. Menné T et al. Contact sensitization to 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (MCI/MI). A European multicentre study. *Contact Dermatitis* 1991; 24: 334–341.
5. Johansen J D, Skov L, Vølund A, Andersen K, Menné T. Allergens in combination have a synergistic effect on the elicitation response: a study of fragrance-sensitized individuals. *Br J Dermatol* 1998; 139: 264–270.
6. Gruvberger B, Bruze M, Tammela M. Preservatives in moisturizers on the Swedish market. *Acta Dermato-venereologica* 1998; 78: 52–56.
7. Adams R M, Maibach H I. A 5-year study of cosmetic reactions. *J Am Acad Dermatol* 1985; 13: 1062–1069.
8. Dooms-Goossens A, Kerre S, Drieghe J, Bossuyt L, Degreef H. Cosmetic products and their allergens. *Eur J Dermatol* 1992; 2: 465–8.
9. The European Cosmetic Toiletry and Perfumery Association 1995 (COLIPA). *The European cosmetic, toiletry and perfumery market* 1994.
10. Berne B, Lundin Å, Malmros P E. Side-effects of cosmetics and toiletries in relation to use. A retrospective study in a Swedish population. *Eur J Dermatol* 1994; 4: 189–193.
11. Johansen J D, Andersen T F, Veien N, Avnstorp C, Andersen K E, Menné T. Patch testing with markers of fragrance contact allergy. Do clinical tests correspond to patients self-reported problems. *Acta Dermato-venereologica* 1997; 77: 149–153.
12. Trattner A, Johansen J D, Menné T. Formaldehyde concentration in diagnostic patch testing: comparison of 1% with 2%. *Contact Dermatitis* 1998; 38: 9–13.
13. Bratsch J, Henseler T, Aberer W, Bäuerle G, Frosch P J, Fuchs T. Reproducibility of patch tests. A multicenter study of synchronous left-versus right-sided patch tests by the German Contact Dermatitis Research Group. *J Am Acad Dermatol* 1994; 31: 584–591.
14. Flyvholm M-A et al. Threshold for occluded formaldehyde patch test in formaldehyde-sensitive patients. Relationship to repeated open application test with a product containing formaldehyde releaser. *Contact Dermatitis* 1997; 36: 26–33.
15. Marzulli F N, Maibach H I. The use of graded concentrations in studying skin sensitizers: experimental contact sensitization in man. *Cosmet Toxicol* 1974; 12: 219–227.

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