

Patch test results in 542 patients with suspected contact dermatitis in Turkey

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In this retrospective study, patch test results of 542 patients (303 female and 239 male), referred to our clinic between June 1996 and July 1999, were evaluated. All patients were patch tested with 32 allergens of an extended European standard series, 140 patients were tested with supplemental series, and 246 patients with their own substances. 280 (51.7%) patients had 1 or more positive results but allergic contact dermatitis, according to clinical relevance, was diagnosed in only 190 (67.9%) of these. Nickel sulfate was the most frequent sensitizer (19.1%), followed by potassium dichromate (11.8%), palladium chloride (9.4%), cobalt chloride (8.5%), and thiuram mix (7.7%). Frequencies of contact allergy to fragrance mix (5.5%), balsam of Peru (Myroxylon Pereirae resin) (2%), quaternium-15 (0.6%), and Kathon CG (methylchloroisothiazolinone+methylisothiazolinone) (0.2%) were relatively low, while no positive reactions were obtained to paraben mix in any case. Current clinical relevance to the present dermatitis was most frequently seen with carba mix (96.2%), thiuram mix (95.2%) and potassium dichromate (78.1%), whereas this rate was low for nickel (37.5%). In 85.8% of patients with allergic contact dermatitis, the responsible allergen was detected by testing with the extended standard series alone (18.4% identified by testing with the additional 10 allergens), in 11.6% by testing with the patients' own substances, and in 2.6% by testing with the supplemental series. Occupational contact dermatitis was diagnosed in 77 of the patients with positive reactions (27.5%), most of these being construction workers and house painters who showed relevant sensitizations to potassium dichromate, cobalt chloride, thiuram mix and carba mix. There was no statistically significant difference in the total contact sensitization rate between atopics and non-atopics, but contact sensitivity to nickel sulfate and palladium chloride was significantly higher among atopics. MOAHL index in % was: 44.1/14.2/24.9/ 54.4/2.4. In conclusion, we believe that similar large series of patients would be helpful to delineate the exact profile of contact dermatitis in Turkey.

Key words: patch testing; allergic contact dermatitis; atopy; occupational; nickel; chromate; construction industry; house painters; rubber chemicals; gloves. © Munksgaard, 2002.

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Patch testing is an important diagnostic tool to confirm allergic contact dermatitis. The positive reactions can be influenced by the variables such as age, sex or atopy (1). Our study aimed to find out the most common contact sensitizers in Turkey and to assess the results according to individual influencing factors such as age, sex, atopy and occupation, and to determine the necessity of testing with supplemental series and with patients' own substances to identify the responsible sensitizer.

Materials and Methods

542 patients suspected of having allergic contact dermatitis, who were referred to our clinic between June 1996 and July 1999 were patch tested with

a screening series of 32 allergens consisting of 22 allergens of the European standard series, excluding primin, and an additional 10 allergens (Table 1). 140 patients were additionally patch tested with supplemental series (Table 2) and 246 patients with their own substances (Table 3). Test allergens were supplied from Chemotechnique Diagnostics (Sweden) and Hal-Brial (Holland). Patients with either atopic dermatitis, mucosal atopy or atopic skin diathesis (2) were recorded as atopics. Atopic dermatitis was diagnosed according to the criteria of Hanifin & Rajka (3).

Patch testing was performed after written or oral consent of parents, or legal guardians in children. Patients were asked not to take any influencing drugs, antihistamines, or immunosup-

pressives, and not to use topical or systemic corticosteroids for at least 4 weeks before and during testing. Pregnant or lactating women were excluded. Patients were not patch tested if they had applied topical corticosteroids to the test site and if they had had sun exposure in the last month. Test allergens were applied in IQ® Chambers (Chemotechnique) to the upper back of the patients for 2 days (D). Test sites were evaluated at D2 and D3 and in some patients also at D4–D5, according to the criteria of the International Contact Dermatitis Research Group (ICDRG) (4). The degree of positivity of an allergic patch test reaction played no part in the final analyses. After patch testing, the current clinical relevance and occupational relevance of the positive patch test reactions were evaluated.

To avoid false-positive irritant reactions with patients' own substances, open patch testing (for shampoos, hair dyes, permanent-wave solutions

and antiseptics), occlusive patch testing in serial dilution (for mineral oils, cutting oils, and cooling fluids), and, in the case of a positive reaction, control testing in 15–20 unexposed individuals, were performed (4).

Data were stored and assessed using SPSS for Windows Release 6.1 standard version. The χ^2 was used for the comparisons. A 2-tailed p -value less than 0.05 was taken to indicate a statistically significant association.

Results

542 patients (303 female (55.9%) and 239 male (44.1%)) were patch tested with the 32 allergens. The average age of the patients was 33.5 years (range 3 to 82 years). The duration of their disease ranged from 1 week to 30 years (mean 38.8 months).

Table 1. Patch test results of the extended standard series

No	Allergen ^{a)}	% Vehicle	No. patients with positive reactions (n=542)	Females (n=303)	Males (n=239)	p-value ^{b)} (NS: not significant)
1	nickel sulfate	5.0 pet.	104 (19.1)	91 (30)	13 (5.4)	<0.001
2	potassium dichromate	0.5 pet.	64 (11.8)	12 (3.9)	52 (21.7)	<0.001
3	<i>palladium chloride</i>	1.0 pet.	51 (9.4)	45 (14.8)	6 (2.5)	<0.001
4	cobalt chloride	1.0 pet.	46 (8.5)	18 (5.9)	28 (11.7)	0.04
5	thiuram mix	1.0 pet.	42 (7.7)	8 (2.6)	34 (14.2)	<0.001
6	fragrance mix	8.0 pet.	30 (5.5)	13 (4.2)	17 (7.1)	NS
7	<i>carbamix</i>	1.0 pet.	26 (4.8)	4 (1.3)	22 (9.2)	<0.001
8	p-phenylenediamine (PPD)	1.0 pet.	20 (3.7)	13 (4.2)	7 (2.9)	NS
9	<i>mercury ammonium chloride</i>	1.0 pet.	15 (2.8)	5 (1.6)	10 (4.1)	NS
10	neomycin sulfate	20.0 pet.	14 (2.6)	7 (2.3)	7 (2.9)	NS
11	<i>thimerosal</i>	0.1 pet.	12 (2.2)	5 (1.6)	7 (2.9)	NS
12	balsam of Peru (Myroxylon Pereirae resin)	25.0 pet.	11 (2)	5 (1.6)	6 (2.5)	NS
13	mercaptobenzothiazole	2.0 pet.	9 (1.7)	3 (0.9)	6 (2.5)	
14	mercapto mix	2.0 pet.	9 (1.7)	2 (0.6)	7 (2.9)	
15	colophonium	20.0 pet.	7 (1.3)	3 (0.9)	4 (1.6)	
16	N-isopropyl-N-phenyl-p-PPD	0.1 pet.	7 (1.3)	1 (0.3)	6 (2.5)	
17	<i>diaminodiphenylmethane</i>	0.5 pet.	6 (1.1)	4 (1.3)	2 (0.8)	
18	<i>Euxyl K 400</i> (methylidibromo glutaronitrile)	0.5 pet.	6 (1.1)	3 (0.9)	3 (1.2)	
19	quinoline mix	6.0 pet.	5 (0.9)	2 (0.6)	3 (1.2)	
20	epoxy resin	1.0 pet.	5 (0.9)	2 (0.6)	3 (1.2)	
21	lanolin alcohol	30.0 pet.	4 (0.7)	1 (0.3)	3 (1.2)	
22	sesquiterpene lactone mix	0.1 pet.	3 (0.6)	1 (0.3)	2 (0.8)	
23	quaternium-15	1.0 pet.	3 (0.6)	1 (0.3)	2 (0.8)	
24	<i>turpentine</i>	10.0 pet.	3 (0.6)	1 (0.3)	2 (0.8)	
25	formaldehyde	1.0 aq.	3 (0.6)	3 (0.9)	0	
26	benzocaine	5.0 pet.	1 (0.2)	1 (0.3)	0	
27	p-tert-butylphenol-formaldehyde resin	1.0 pet.	1 (0.2)	1 (0.3)	0	
28	<i>toluenesulfonamidelformaldehyde resin</i>	10.0 pet.	1 (0.2)	1 (0.3)	0	
29	<i>ethylenediamine dihydrochloride</i>	1.0 pet.	1 (0.2)	0	1 (0.4)	
30	Kathon CG (methylchloroisothiazolinone+ methylisothiazolinone)	0.01 aq.	1 (0.2)	0	1 (0.4)	
31	paraben mix	12.0 pet.	0	0	0	
32	<i>white petrolatum</i>	100.0	0	0	0	
	total no. of patients		510	256	254	

^{a)}Additionally tested allergens (nos. 3, 7, 9, 11, 17, 18, 24, 28, 29 and 32) are marked in italics.

^{b)}Statistical analysis was carried out for those allergens that were positive in >10 patients.

Table 2. Patch test results of supplemental series

Supplemental series	No. (%) of tested series ^{a)}	No. (%) of series with a positive result ^{b)}
cosmetics series	134 (41.8)	10 (21.7)
fragrance series	27 (8.4)	3 (6.5)
bakery series	15 (4.7)	4 (8.7)
topical medicaments series	16 (5)	11 (23.9)
corticosteroid series	20 (6.3)	0
eye medicaments	7 (2.2)	3 (6.5)
dental series	26 (8.2)	2 (4.4)
textile series	10 (3.1)	0
leather series	3 (0.9)	0
plastics and glues series	9 (2.8)	0
metals series	19 (5.9)	3 (6.5)
oil and cooling fluid series	13 (4.1)	2 (4.4)
rubber series	10 (3.1)	4 (8.7)
hairdressing series	9 (2.8)	4 (8.7)
printing series	2 (0.7)	0
total	320	46

^{a)} Total no. of patients tested with supplemental series=140.

^{b)} Total no. of patients with a positive result=40; reactions were evaluated as clinically relevant in 32 of these (80%).

Patch test results

280 patients (51.6%) had 1 or more positive patch test reactions (Tables 1–3). In 67.9% of these, allergic contact dermatitis was diagnosed according to current relevance of the allergens. Table 4 shows the distribution of the responsible allergens according to the tested series. The dermatitis was judged to have an occupational cause in 40.5% of patients with allergic contact dermatitis.

Regarding the extended standard series, patch test reactions showed an almost equal distribution among male and female patients (Table 1). Positive

reactions were most frequently caused by nickel sulfate (19.1%) (Table 1). Frequencies of contact allergy to fragrance mix (5.5%), balsam of Peru (Myroxylon Pereirae resin) (2%), quaternium-15 (0.6%), and Kathon CG (methylchloroisothiazolinone+methylisothiazolinone) (0.2%) were relatively low, while no positive reactions were obtained to paraben mix in any case. Current clinical relevance to the present dermatitis was most frequently seen with carba mix (96.2%), thiuram mix (95.2%) and potassium dichromate (78.1%), whereas this rate was low for nickel (37.5%).

Regarding supplemental series (Table 2), most positive reactions were obtained with a topical medicaments series (11 patients), followed by a cosmetics series, the latter being the most frequently applied.

Among patients' own substances (Table 3), topically applied medicaments (35.2%) (nitrofurazone and neomycin the leading agents) and cosmetics (16.9%) were the most frequent sensitizers. Rubber chemicals (gloves) were found to be the most frequent occupationally relevant sensitizers, in both construction workers and hospital workers.

Age and sex

Positive reactions to nickel sulfate and palladium chloride were more frequently observed among young women. The difference in nickel and palladium sensitization rates between women and men under 40 years was statistically significant ($p<0.001$). Men had a higher frequency of positive reactions to potassium dichromate, thiuram mix and carba mix, especially in the 20–59 year age

Table 3. Patch test^{a)} results of the patients' own substances

Substances with clinical relevance	No. patients	Substances with occupational relevance	No. patients
cosmetic creams	12	rubber gloves	8
neomycin + bacitracin cream	8	permanent wave solution	2
nitrofurazone cream	7	steering wheel material	1
other topical medicaments	10	mineral oil	1
mascara	4	cooling fluid	1
hair dye	3	shoe polish	1
makeup	2	cutting oil	1
lipstick	1		
nail polish	1		
shampoo	1		
Mersol® (tincture containing mercury ammonium chloride)	1		
dental metal	1		
wig adhesive	1		
rose oil	2		
pine resin + beeswax	1		
eau de Cologne	1		
total (n=71)	56		15

^{a)} Total no. of patients tested with their own substances=246; total no. of patients with a positive result=71 (28.9%); all reactions evaluated as clinically relevant.

Table 4. Distribution of patients with allergic contact dermatitis and occupational contact dermatitis according to the source of the relevant allergens

	No. (%) of patients with a positive reaction	No. (%) of patients with allergic contact dermatitis	No. (%) of patients with occupational contact dermatitis
extended standard series	253 (90.3)	163 (85.8)	75 (97.4)
supplemental series	5 (1.8)	5 (2.6)	0
patients' own substances	22 (7.9)	22 (11.6)	2 (2.6)
total ($n=542$)	280 (51.7)	190 (35.1)	77 (14.2)

group. Compared with female patients in the same age group, the difference was statistically significant ($p<0.001$). Significantly more frequent positive reactions were seen with balsam of Peru and fragrance mix among patients above 40 years ($p<0.001$), independent of sex. Fragrance mix showed more positive reactions among young women and older men.

Localization

The dermatitis was mainly localized on the hands (54.4%) followed by the face and neck (13.1%). The most frequent clinically and occupationally relevant allergen on the hands was potassium dichromate, whereas on the face, the most frequent clinically relevant allergen was fragrance mix. 48.1% of the patients with nickel sensitization had hand eczema, but current clinical relevance could be found in only 26% of them.

Nummular eczema and nickel sensitivity

Nummular (discoïd) eczema was seen in 4.2% of the patients. No significant association was found between nummular eczema and nickel sensitivity ($p=0.83$).

Occupational contact dermatitis

Occupational contact dermatitis was diagnosed in 77 patients, most of these being construction workers and house painters (61%) who showed relevant sensitizations to potassium dichromate, cobalt chloride, thiuram mix and carba mix (Table 5). Hospital workers, hairdressers and metalworkers followed behind. Hospital workers were most frequently sensitized to thiuram mix and carba mix from rubber gloves, whereas para-phenylenediamine was the most frequent occupational allergen for hairdressers.

Atopy

135 patients (24.9%) were assessed as atopic, comprising 111 patients with mucosal atopy, 21 pa-

tients with atopic skin diathesis and 15 patients with atopic dermatitis. There was no statistically significant difference in the total contact sensitization rate between atopics and non-atopics ($p=0.14$), but contact sensitivity to nickel sulfate and palladium chloride was significantly higher among atopics ($p<0.001$). On the other hand, thiuram mix and carba mix sensitization rates were significantly higher among non-atopic patients ($p<0.05$).

Metal sensitivity

94.6% of the patients with a positive patch test reaction had positive reactions to metal allergens, comprising nickel sulfate, palladium chloride, potassium dichromate and cobalt chloride. A history of metal sensitivity was present in 58.5% of these. The compatibility rates between a positive history of metal sensitivity and a positive patch test reaction to metal allergens were significantly higher in atopic patients than in non-atopics ($p<0.001$ for nickel and palladium and $p<0.05$ for chromate and cobalt).

The *MOAHL index* (men-occupational-atopy-hand eczema-leg ulcer) in % was: 44.1–14.2–24.9–54.4–2.4.

The *angry back* was diagnosed in 3 patients (1.3%).

Discussion

Nickel sulfate was the most common allergen in our study (19.1%), reflecting the worldwide incidence (1, 5–8). Nickel allergy was observed significantly more frequently among young women, as reported previously (1, 5, 7). The high nickel sensitivity rate among young women is explained by early ear piercing (9, 10). It is generally accepted that the hand eczema of a nickel-sensitive housewife is not due to nickel-containing detergents because of the insufficiently high level of nickel in detergents (11). In our study, if there was no clear history of contact with metals, housewives' hand eczema was evaluated as irritant contact dermatitis due to wet working conditions and alkaline detergents. On the other hand, nickel sensitizations were

Table 5. Characteristics of patients with occupational dermatitis

Occupation (no. patients) (%)	Localization of eczema (no. patients)	Relevant allergen (no. patients)	Onset of eczema
Construction workers and house painters (47) (61%)	hand eczema with or without foot eczema (44) generalized eczema (3)	potassium dichromate (41) thiuram mix (27) cobalt chloride (22) carba mix (17) mercapto mix (4) mercaptobenzothiazole (4) nickel sulfate (4) rubber gloves (4)	9th year
hospital workers (7) (9.1%)	hand eczema (6) generalized eczema (1)	thiuram mix (7); carba mix (4) mercaptobenzothiazole (1) mercury ammonium chloride (1) formaldehyde (1) rubber gloves (3) iodine (1)	4th year
hairdressers (7) (9.1%)	hand eczema (7)	p-phenylenediamine (6) permanent wave solution (2)	1st year
metalworkers (5) (6.5%)	hand eczema (3) generalized eczema (1) baboon syndrome (1)	nickel sulfate (3) potassium dichromate (1) mercaptobenzothiazole (1) mercapto mix (1) diaminodiphenylmethane (1) chromium sulfate (1) mercury (1)	4th year
shipwright (2) (2.6%)	airborne eczema (2)	epoxy resin (2); pine tar (1) N-isopropyl-N-phenyl-p-PPD (1)	1st year
shoemakers (2) (2.6%)	hand eczema (2)	thiuram mix (1); carba mix (1) shoe polish (1)	8th year
electrician (1) (1.3%) lathe operator (1) (1.3%)	hand eczema (1) generalized eczema (1)	N-isopropyl-N-phenyl-p-PPD (1) cobalt chloride (1); copper sulfate (1) 4-tert-butylcatechol (1) cooling fluid (1); mineral oil (1)	10th year 20th year
miner (1) (1.3%) architect (1) (1.3%)	hand eczema (1) hand eczema (1)	potassium dichromate (1) diaminodiphenylmethane (1)	4th year 1st year
house cleaner (1) (1.3%) jeweler (1) (1.3%)	hand eczema (1) hand eczema (1)	carba mix (1) ; rubber glove (1) cutting oil (1)	23rd year 3rd year
driver (1) (1.3%)	hand eczema (1)	steering wheel material (1)	8th year

assessed as clinically relevant in patients who had current dermatitis on the ears, neck, abdomen or wrists, reflecting the localizations of contact with metal jewelry such as ear piercing, necklaces, belts or watches, respectively. Therefore, the current clinical relevance of nickel sensitization was relatively low in our series (37.5%). The relationship between nickel allergy and nummular eczema is another debatable issue (12, 13). In our study, no statistically significant association could be found between these 2 conditions.

Multiple positive patch test reactions to metals like nickel sulfate, palladium chloride, cobalt chloride and potassium dichromate is a well-known finding (14–16). Metal instruments are usually made of various combinations of these metals, so that considerable contact with nickel,

for example, implies correspondingly heavy contact with other metals (17). In our study, the most frequent associated metal allergy was found between nickel sulfate and palladium chloride, in 48 patients, followed by potassium dichromate and cobalt chloride in 29 patients.

In this study, the relatively low frequencies of contact allergy to fragrance mix, balsam of Peru, and to some of the cosmetic preservatives, in particular quaternium-15, Kathon CG and parabens (no case) is a striking finding when compared to other studies (1, 6, 7, 17). Allergens from the supplemental cosmetic series also had a lower positivity rate when compared to previous American and European studies. Though this is speculative, this could be due to less cosmetic product use in Turkey.

Most patients with occupational contact dermatitis were construction workers and house painters. The high rate of potassium dichromate and cobalt chloride sensitivity, when compared to other European countries, was attributed to sensitization to cement in the construction industry. Asian countries like India and Saudi Arabia have also reported similarly high sensitization rates to chromate due to the cement used in developing construction industries (14). High potassium dichromate sensitization was explained by the expansion in the construction industry in parallel with the increasing population and the inadequacy of protective methods among workers. On the other hand, the decline in chromate sensitivity in certain other European countries is explained by the addition of ferrous sulfate to cement, thus transforming water-soluble hexavalent chromium into non-water-soluble trivalent chromium (5, 18).

Rubber chemical allergens like thiuram mix and carba mix were the other common occupational sensitizers. A history of wearing rubber gloves only during work, worsening of eczema during work times and improvement during holidays directed us to evaluate these rubber sensitivities as occupational. Sensitization to rubber chemical allergens was more frequent among construction workers and hospital workers. Mercapto mix and mercaptobenzothiazole were less important rubber allergens in our study.

A contact sensitization rate in atopics has been reported up to 57% in various studies (19, 20). It is only temporarily diminished in patients with atopic dermatitis who have extensive skin lesions (21). In our study, no statistically significant difference could be found in the total contact sensitization rate between atopics and non-atopics, but sensitization to nickel sulfate and palladium chloride was significantly more frequent among atopics. The relationship between atopy and nickel allergy is well known; it has even been postulated that nickel allergy should be regarded as a further diagnostic criterion for atopic dermatitis (3, 19). On the other hand, one should be careful to evaluate the patch test results of nickel, chromium or cobalt salts, as false-positive irritant reactions are common with such metal salts, especially in atopic patients (22).

In 85.8% of patients with allergic contact dermatitis, the responsible allergen could be detected by testing with the extended standard series alone; 67.4% of these were identified by testing with the 22 allergens of the European standard series and 18.4% by testing with the additional allergens. In other words, testing with the standard series is sufficient for detection of the majority of clinically relevant allergens, though testing with extended

standard series might eventually become more important. Palladium chloride, carba mix, mercury ammonium chloride and Euxyl K 400 (methyl-di-bromo glutaronitrile) were the most frequently detected additional allergens in our study. Moreover, testing with patients' own substances is an easy and cost-effective way to find out the responsible allergen, as long as false-positive irritant reactions are excluded. Interestingly, testing with supplemental series, a cosmetics series and a fragrance series being the most commonly tested series, enabled us to detect only a small minority of relevant allergens (2.6%).

In conclusion, this study provides a comprehensive profile of allergic contact dermatitis in Turkey. Routine patch testing with a standard series and patients' own substances is essential, whereas it is more advisable to test supplemental series in selected cases. The contact sensitization rate of some allergens with a relatively low frequency of positive patch test reactions, like parabens and other preservatives as well as fragrance mix and balsam of Peru, should be further investigated.

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