

Allergic contact dermatitis in Iran

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The frequency of sensitization to contact allergens varies in different countries because of both genetic and, more importantly, allergen exposure variations. The objective is to determine the frequency of sensitization to contact allergens in Iranian patients with dermatitis. 250 patients with a clinical diagnosis of contact dermatitis and/or atopic dermatitis were evaluated with a 28-allergen screening series recommended by the German Contact Dermatitis Research Group from September 2002 to April 2004 in Tehran, Iran. The patches were applied on the back of the patients, removed after 24 hr and the readings were taken on 24 hr, 48 hr and 72 hr after application. 126 patients (50.4%) showed at least 1 positive reaction, and 23 patients (9.2%) had more than 2 positive reactions. 189 (84.4%) of 224 positive reactions had past and/or present clinical relevance. The 5 most common allergens were nickel sulfate 70 (28.0%), cobalt chloride 32 (12.8%), paratertiarybutyl phenol formaldehyde resin 20 (8.0%), potassium dichromate 13 (5.2%) and colophony 13 (5.2%). Contact allergy to nickel sulfate was significantly more common in female patients and in patients under 40 years of age ($P < 0.05$). Nickel sulfate is the most common contact allergen in Iran, mostly affecting women and younger patients probably because of more exposure.

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Contact allergy develops in predisposed individuals as a consequence of environmental exposure to allergens. Exposure patterns change over time because of fashion trends, technological developments, official regulations (1), regional traditions or environmental specifications. It appears that some persons are more easily sensitized to common haptens than others because of their genetic background; however, environmental factors seem to be more important, because the total number of sensitized persons in the population depends on the degree of cutaneous exposure and environmental factors influence the degree of it (2).

It has been estimated that there are more than 6 million chemicals in the environment, and 2 800 of these have allergic properties (3, 4). Contact dermatitis from these allergens is common, representing approximately 9.7% of all dermatology visits (5). Patch testing is a vital component in making the diagnosis of allergic contact dermatitis (ACD). Also, it has been mentioned that 10–15% of healthy individuals have 1 or more positive reactions in patch tests (6, 7).

Patch test studies in different countries and groups can provide information for direct preven-

tive measures such as exposure reduction to prevent sensitization as well as elicitation of contact dermatitis (8). There are no published data of contact dermatitis from Iran. Hence, the purpose of this study was to examine some features of ACD in a referral dermatology clinic with the use of patch tests and to compare it with regional and major results published across the world.

Patients and Methods

Patients

250 consecutive patients with a clinical diagnosis of contact and/or atopic dermatitis (AD) primarily attending or referred from other dermatologists to a referral skin clinic in Tehran, Iran, from September 2002 to April 2004 were investigated. Each patient underwent a comprehensive history taking and physical exam, and necessary data (including demographics, location and duration of dermatitis, personal and family history of atopy including AD, asthma and hay fever) were filled in a questionnaire. The diagnosis of AD was based on the UK Working Party diagnostic

criteria (9). Patients who were taking more than 20 mg/day oral corticosteroids in the past 2 weeks were excluded.

Patch testing

The patients were tested with the 28-allergen screening series recommended by the German Contact Dermatitis Research Group (DKG) (10) provided from Hermal, Reinbek, Germany. Patch tests were performed and read in accordance with the guidelines of the International Contact Dermatitis Research Group (2) and DKG (10), Finn chamber on scanpor was used to apply allergens, and patches were attached for 24 hr. First readings were performed between 20 min and 40 min after removal of patches and then 24 hr and 48 hr later. 2 investigators (Alireza Firooz and Mansour Nassiri Kashani) performed all readings. The relevance of positive reactions was determined by asking patients whether they had any exposure to substances containing that allergen (the list of these substances was kindly provided by Hermal Company).

Data analysis

Data were stored and assessed using spss for windows released 10.1 standard version. Chi-square and Fisher's exact tests were used wherever needed and *P* values < 0.05 were considered as significant.

Results

The patients consisted of 60 (24%) men and 190 (76%) women with an age range between 9 and 79 years (mean $\pm$ SD = 32.7 ± 13.1 years). The duration of eczema was between 1 month and 30 years.

The clinical diagnoses of patients before patch test were ACD 54%, irritant contact dermatitis (ICD) 9.6%, AD 27.6%, ACD and AD 7.6%, ACD and ICD, ICD and AD each 0.4%.

Positive personal history of atopy existed in 40% of patients and 53.6% of them had positive familial history of atopy.

Important demographic characteristics of the patients according to the MOAHLFA index (10) are summarized in Table 1. Table 2 summarizes the results of patch test in different sex, age groups and their relevance. 126 patients (50.4%) had at least 1 positive reaction, and there were a total of 224 positive reactions in these patients, 84.4% of these reactions had past or present clinical relevance.

Of these patients, 60 were positive to 1 substance, 43 to 2 substances, 17 to 3 substances, 4

Table 1. Demographic characteristics of 250 Iranian patients according to MOAHLFA index

M (Male)	60 (24%)
O (Occupation)	29 (11.6%)
A (Atopic dermatitis)	89 (35.6%)
H (Hand involvement)	171 (68.4%)
L (Leg involvement)	79 (31.6%)
F (Face involvement)	117 (46.8%)
A (Age > 40)	65 (26%)

to 4 substances, 1 to 5 and 1 to 7 substances. Patients with more than 2 positive reactions were significantly more likely to have acute vesiculobullous dermatitis at the time of test ($P < 0.05$). In addition, none of the patients were sensitive to 5 of 28 tested allergens including benzocaine, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine, cetyl stearyl alcohol, Bufexamac and mercapto mix.

Females and patients younger than 40 years had more nickel sensitivity than males and older patients ($P < 0.05$). Besides, positive reactions to fragrance mix and composite mix were more prevalent in patients older than 40 years and allergy to paratertiarybutyl phenol formaldehyde resin (PTBP) was more common in patients who had eczema on their feet and legs ($P < 0.05$). There was a significant association between positive reactions to cobalt and positive reactions to nickel and potassium dichromate ($P < 0.00001$).

Discussion

The purpose of this study was to obtain information about the responsible allergens for ACD in Iran and to compare it with previous results from this region (Middle East) and worldwide. In this study, 126 of 250 patients (50.4%) showed at least 1 positive reaction, and the 5 most common allergens were nickel sulfate (28.0%), cobalt chloride (12.8%), PTBP (8.0%), potassium dichromate (5.2%) and colophony (5.2%). This positivity rate may indicate that patch testing is underused in Iran (11).

Hand was the most frequent site of involvement in this study (68.4%), which was similar to previous reports (12, 13). Although hand involvement is more often associated with occupational dermatitis (14), we could not find such relationship in this study.

In this study, 50.4% of all patients showed positive reactions to at least 1 substance; this figure is lower than most of other reports from Middle East (15, 16). This may be explained by a selection bias, because we offered patch testing to all patients with a suspected diagnosis of contact dermatitis and/or atopic dermatitis. We applied

Table 2. Patch test results in 250 Iranian patients in different sex, age groups and their clinical relevance

Allergens*	Total 250 (%)	Male 60 (%)	Female 190 (%)	Age < 40 184 (%)	Age > 40 65 (%)	Relevance 189/224 (%)
Nickel sulfate	70 (28.0)	7 (11.7)	63 (33.2)	61 (33.2)	9 (13.8)	64/70 (91.4)
Cobalt chloride	32 (12.8)	8 (13.3)	24 (12.6)	29 (15.8)	3 (4.6)	23/32 (71.9)
PTBP	20 (8.0)	3 (5.0)	17 (8.9)	14 (7.6)	6 (9.2)	16/20 (80)
Potassium dichromate	13 (5.2)	5 (8.3)	8 (4.2)	10 (5.4)	3 (4.6)	11/13 (84.6)
Colophony	13 (5.2)	4 (6.7)	9 (4.7)	9 (4.9)	4 (6.2)	13/13 (100)
Paraben mix	11 (4.4)	5 (8.3)	6 (3.2)	7 (3.8)	4 (6.2)	9/11 (81.8)
Fragrance mix	10 (4.0)	2 (3.3)	8 (4.2)	1 (0.5)	9 (13.8)	7/10 (70)
Formaldehyde	7 (2.8)	1 (1.7)	6 (3.2)	2 (1.1)	5 (7.7)	7/7 (100)
Balsam of Peru	6 (2.4)	2 (3.3)	4 (2.1)	3 (1.6)	3 (4.6)	3/6 (50)
Paraphenylenediamine	5 (2.0)	2 (3.3)	3 (1.6)	3 (1.6)	2 (3.1)	4/5 (80)
Mercury ammonium chloride	5 (2.0)	0 (0.0)	5 (2.6)	5 (2.7)	0 (0.0)	4/5 (80)
Thiuram mix	4 (1.6)	1 (1.7)	3 (1.6)	3 (1.6)	1 (1.5)	4/4 (100)
Wool wax alcohols	4 (1.6)	0 (0.0)	4 (2.1)	4 (2.2)	0 (0.0)	4/4 (100)
MCI/MI	4 (1.6)	2 (3.3)	2 (1.1)	3 (1.6)	1 (1.5)	3/4 (75)
Propolis	4 (1.6)	0 (0.0)	4 (2.1)	2 (1.1)	2 (3.1)	4/4 (100)
Composite mix	3 (1.2)	1 (1.7)	2 (1.1)	0 (0.0)	3 (4.6)	2/3 (66.7)
Neomycin sulfate	2 (0.8)	1 (1.7)	1 (0.5)	2 (1.1)	0 (0.0)	1/2 (50)
Epoxy resin	2 (0.8)	1 (1.7)	1 (0.5)	2 (1.1)	0 (0.0)	2/2 (100)
Turpentin	2 (0.8)	1 (1.7)	1 (0.5)	1 (0.5)	1 (1.5)	1/2 (50)
Dibromodicyanobutane	2 (0.8)	0 (0.0)	2 (1.1)	2 (1.1)	0 (0.0)	2/2 (100)
Mercaptobenzothiazole	2 (0.8)	1 (1.7)	1 (0.5)	1 (0.5)	1 (1.5)	2/2 (100)
Lyril	2 (0.8)	0 (0.0)	2 (1.1)	2 (1.1)	0 (0.0)	2/2 (100)
Zinc diethyl dithiocarbamate	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	1/1 (100)

*No positive reactions were observed to benzocaine, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine, cetyl stearyl alcohol, Buxefamox and mercapto mix.

MCI/MI = methylchloroisothiazolinone and methylisothiazolinone; PTBP = parateritarybutyl phenol formaldehyde resin.

patch tests for 24 hr, although most centres have an application time of 48 hr. Also, the readings were done after 24 hr, 48 hr and 72 hr after application. Late readings after 96 hr and 120 hr have also been recommended to detect some delayed responses, and such reactions may be missed in our study (17). The results of clinical patch testing should be interpreted cautiously because of limitations of defining allergic and irritant reactions, determining the relevance of reactions to the patient's dermatitis and trends in which screening allergens are patch tested. Past or current clinical relevance of positive patch test reactions in this study was 84.4%, which was comparable to the report from Turkey (18) and more than Pakistan (16).

Nickel was the most common allergen in this study. Nickel is the leading allergen in the Middle East, and its sensitivity rates vary from 15% to 39.5% in this region; these rates are much higher than those in large studies done in the other parts of the world (19).

There is no doubt that nickel is the most frequent allergen in majority of countries (20, 21), but there are reports of some declination in frequency of nickel sensitivity in young German (22) and Danish (23) females that may be because of EU regulations that limited the nickel-release threshold at 0.5 µg/cm² per week from nickel-

containing alloy and coatings that are in prolonged contact with skin (24). Although a German multicentre study showed a stable prevalence of nickel allergy from 16.7% in 1992 to 16.3% in 1996 (21). Nickel sensitivity was significantly more common in females in this study, which is in accordance with most previous studies (10, 12). The fact that ear piercing is a very common practice in Iranian women, but a very rare fashion trend in men, may explain this difference.

In this study, sensitivity to cobalt ranked second with a frequency of 12.8%. There was a significant association between positive reactions to cobalt and positive reactions to nickel and potassium dichromate ($P < 0.00001$), which has also been observed in the past (2, 25, 26). These relationships are thought to be related to the fact that the metals are usually associated with one another (27). We did not find any association between cobalt allergy and probability of occupational dermatitis in this study. Most non-occupational exposure is through metal objects, especially costume jewellery (24).

It is a considerable fact that PTBP is a relatively common allergen in Middle East. Parateritarybutyl phenol formaldehyde resin was the third most common allergen in Iran, UAE (15) and Pakistan (16) with sensitivity rates of 8.0%, 7.5% and 9.7%, respectively. Sensitivity to PTBP

was significantly more common in patients with foot and leg involvement. We suggest that frequent use of glued leather products such as shoes could be the main cause. Specifically, this high rate of PTBP sensitization may be because of wearing tight and fully covered shoes and as some studies showed high incidence of sensitivity to PTBP in shoe dermatitis (28, 29). Hence, we recommend further investigations to evaluate suspected shoe dermatitis in our community with standard and specific allergens.

Chromate allergy has a relatively similar frequency rate among Middle East countries except in Saudi Arabia with a high rate of 32.9% (30). It is the second leading cause of contact allergy in Pakistan (16), Turkey (18) and Saudi Arabia. It was the fourth common allergen in this study, and low rates of suspected occupational dermatitis in this sample of patients could be the cause. Despite some reports (12), chromate sensitivity was not occupational in these patients, and we did not find frequent cement exposure in them; hence, exposure to other products such as leather tanned with chromium salts, soil, matches, paper, etc. may explain the sensitivity to chromate.

In the United States, a concentration of 0.25% of potassium dichromate is used for patch testing, but all other main patch test series contain 0.5% concentration; hence, sensitivity rate to this allergen is commonly lower in reports from USA than those from other parts of the world (31–33).

In a Danish study, fragrance mix was the only allergen to which sensitivity increased significantly during 2 separate periods in 80s and 90s (1). It seems that usage of perfumes has increased globally in recent years. It is worthy to mention that 90% of our fragrance-sensitive patients were older than 40 years, which was the case in other reports (34).

The sensitivity rate of colophony in this study was similar to reports from other countries of the region, except Turkish study. Major sources of colophony were found to be adhesives and cosmetics in this study.

Paraphenylenediamine was not a common allergen in this study, although it is not an ignorable allergen at least in this region. Most of our patients were young, and this could be the cause, as they do not need to colour their grey or white hair or beard with black dye.

Balsam of Peru is a common allergen in many countries (10, 31), but the sensitivity to it was observed in only 2.4% of our patients. Preservatives used in various products may be responsible for allergy to it, and preservative containing products seems to be less commonly used in Iran.

Allergy to neomycin in USA has increased by 2% every 2 years from 1990 to 1998 (31). This is because of widespread use of neomycin as an over-the-counter medicament. Contact allergy to neomycin was found in only 0.8% of patients in this study. Very few neomycin-containing medications are available in Iran, and none of them are over-the-counter. In addition, most dermatologists are reluctant to prescribe them because of numerous reports of contact allergy. Also, as we did not perform late readings beyond 72 hr, some positive reactions to neomycin may be missed.

In this study, reactions to more than 2 allergens were more common in patients who had acute vesiculobullous dermatitis at the time of testing. This could suggest a relationship between presence of acute dermatitis and multiple positive reactions in the same patient, the so-called excited skin (angry back) phenomenon (35).

We did not find even a single positive reaction to 5 tested allergens which is far different from other studies (10, 31, 32). They include benzocaine, *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine, cetyl stearyl alcohol, Bufexamac and mercapto mix. Further studies are required to evaluate the suitability of these allergens for screening patients for ACD in Iran.

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