

Nickel, cobalt and chromate sensitization and occupation*

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Background: Exposure to nickel, cobalt and chromate are important causes of occupational contact dermatitis.

Objectives: To estimate the prevalence of nickel, cobalt and chromate allergy in a population of consecutive patients and to investigate the possible association with individual and occupational risk factors.

Patients/Methods: A total of 14 464 patients (67.6% women and 32.4% men) with suspected allergic dermatitis underwent patch tests. The associations between patch test results and occupations were studied by multivariate logistic regression analysis.

Results: About 24.6% of the patients reacted positively to nickel sulphate, 10.2% to cobalt chloride and 8.7% to potassium dichromate. Nickel sensitization was higher in women aged 26–35 years in comparison with the youngest group (15–25 years) and the older group (>45 years). In women, the prevalence of positive reactions to nickel was positively associated with metal and mechanical work (OR 1.54; 95% CI 1.16–2.05). Chromate sensitization was more prevalent in building trade workers for both women (OR 1.58; 95% CI 1.00–2.49) and men (OR 2.24; 95% CI 1.55–3.22). Cobalt sensitization was associated with textile and leather work in women (OR 1.52; 95% CI 1.09–2.12) and with cleaning work in men (OR 1.86; 95% CI 1.18–2.93).

Conclusions: Our study showed interesting associations between some occupations and nickel, chromate and cobalt allergy.

Key words: dermatitis; nickel; cobalt; chromate; occupation; patch test. © John Wiley & Sons A/S, 2010.

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Exposures to nickel, chromate, and cobalt are common cause of metal sensitization. The sensitization and the contact dermatitis caused by these allergens are common in the general population (1) and in some occupational groups (2–4). Contact sensitization to nickel, cobalt and chromate is influenced by age, sex, geographical and historical factors (5, 6).

Nickel is a common allergen in the general population, mainly among young women with nickel sensitization being influenced by social and

cultural factors (e.g. ear piercing, nickel-plated jewellery, etc.) (5) and by other skin contact with nickel containing objects. Recently, some authors described nickel dermatitis following skin contact with cell phones (7–9). Nickel is also an occupational allergen (10–3).

Cobalt sensitization affects both women and men and cosensitization with nickel and chromate has often been reported (14, 15).

Sensitization and the contact dermatitis from chromate are more frequent in men and can be caused by occupational cutaneous exposure to soluble compounds in cement or leather (16).

*All centres are members of the North-Eastern Italy Contact Dermatitis Group (NEICDG).

The aim of this study was to estimate the prevalence of nickel, cobalt and chromate sensitization in a population of consecutive patients who attended Units of Dermatology or Occupational Medicine in North-Eastern Italy for allergic contact dermatitis. A further aim was to investigate the association between nickel, cobalt and chromate sensitization and various individual and occupational risk factors.

Patients and Methods

Patients

From 1997 to 2004, a total of 15 217 consecutive patients with symptoms and/or signs of suspected allergic dermatitis were patch tested in eight Units of Dermatology or Occupational Medicine in North-Eastern Italy (Belluno, Bolzano, Padova, Pordenone, Rovereto, Rovigo, Trento, Trieste). A standardized questionnaire was used to collect information about individual characteristics, occupational history, personal and familiar history of atopy (asthma and/or allergic rhinoconjunctivitis with at least one positive prick test to relevant aeroallergens), and dermatitis localization (Table 1). We excluded 753 patients with missing responses to personal and occupational history or with incomplete patch testing. Finally, 14 464 consecutive patients were included in the study.

Patch tests

The patients were patch tested with the European baseline series (17) using Finn[®] chambers on Scanpor[®] tape. The tested allergens included nickel sulfate 5.0% in pet., cobalt(II)chloride 1.0% in pet. and potassium dichromate 0.5% in pet. All allergens were applied on the upper back and removed after 2 D. The sites were examined on removal and 1 D after removal, according to the International Contact Dermatitis Research Group (ICDRG) guidelines (18). Positive reactions of +, ++ and +++ grades were considered positive.

Table 1. Questions used to collect information about suspected contact allergy

Have you suffered or have you ever suffered from:		
Atopic eczema	Yes	No
Allergic rhinoconjunctivitis	Yes	No
Allergic asthma	Yes	No
Does your mother/father or sister/brother or daughter/son suffer (or has suffered) from:		
Atopic eczema	Yes	No
Allergic rhinoconjunctivitis	Yes	No
Allergic asthma	Yes	No
What is:		
Your current occupation_____	from (date)_____	
Your previous occupation_____	for years_____	
Duration of current symptoms: _____months		
Primary (initial) site _____		
Secondary spread	Yes	No

Statistical analysis

Data analysis was performed with the software Stata[®] 10.1 (Stata Corporation, 2008). Continuous variables were summarized using the median as a measure of central tendency and the range as that of dispersion.

The difference between groups was tested by the Mann–Whitney test. The difference between categorical data cross tabulated into contingency tables was tested by the χ^2 statistic.

The associations between patch test results and occupation were investigated by means of multivariate logistic regression analysis, while controlling for age (five categories: 15–25, 26–35, 36–45, 46–55 and ≥ 56 years), and personal and familiar history of atopy. Odds ratios (OR) and 95% confidence intervals (CI) were estimated from the coefficients and the standard errors of logistic regression output, assuming office work as the reference category. We did mass analysis. Logistic analysis was conducted by sex separately.

Results

The study population included 9771 women (67.6%) and 4693 men (32.4%). Men were slightly older than women (mean difference: 0.8 year), but the difference was significant because of the large samples involved ($P < 0.01$) (Table 2). The crude prevalence of personal and family atopy and sensitization to nickel and cobalt were significantly greater in the women than in the men. In the male population, there was a greater chromate sensitization and the symptoms and/or signs of dermatitis were more frequently localized in the hands and/or forearms, while in women dermatitis was more often confined to other sites (Table 2). In case of simultaneous positive reaction to two or three metals, the subject was included in both or in all three sensitization

Table 2. Characteristics of the study population

	Women (<i>N</i> = 9771)	Men (<i>N</i> = 4693)	Total (<i>N</i> = 14 464)
Age (years)	39 (14–94)	39 (19–85)*	39 (14–94)
Personal atopy	1627 (16.7)	702 (15.0)**	2329 (16.1)
Familiar atopy	895 (9.2)	310 (6.6)***	1205 (8.3)
Hand/forearm dermatitis	2625 (26.9)	1486 (31.7)***	4111 (28.4)
Nickel sensitization	3087 (31.6)	469 (10.0)***	3556 (24.6)
Cobalt sensitization	1090 (11.2)	392 (8.4)***	1482 (10.2)
Chromate sensitization	776 (7.9)	476 (10.1)***	1252 (8.7)

Age is given as median (range). The other variables are given as numbers (%). Mann–Whitney test: * $P < 0.01$.

χ^2 statistic: ** $P < 0.05$; *** $P < 0.001$.

Table 3. Occupations in the study population by sex

Occupation	N (%)		
	Women	Men	Total
Office workers	2206 (22.6)	1024 (21.8)	3230 (22.3)
Others	1648 (16.9)	699 (14.9)	2347 (16.2)
Pensioners	1084 (11.1)	888 (18.9)	1972 (13.6)
Household workers	1641 (16.8)	18 (0.4)	1659 (11.5)
Cleaners	932 (9.5)	239 (5.1)	1171 (8.1)
Personal health care workers	719 (7.4)	187 (4.0)	906 (6.3)
Metal and mechanical workers	216 (2.2)	436 (9.3)	652 (4.5)
Building and related trades workers	214 (2.2)	331 (7.1)	545 (3.8)
Textile and leather workers	291 (3.0)	108 (2.3)	399 (2.8)
Bartenders	252 (2.6)	108 (2.3)	360 (2.5)
Chemical processing plant workers	97 (1.0)	114 (2.4)	211 (1.5)
Car, bus and truck drivers	31 (0.3)	146 (3.1)	177 (1.2)
Hairdressers, beauticians	136 (1.4)	13 (0.3)	149 (1.0)
Food processing workers	96 (1.0)	52 (1.1)	148 (1.0)
Electrical and electronic workers	34 (0.3)	113 (2.4)	147 (1.0)
Agricultural workers	62 (0.6)	78 (1.7)	140 (1.0)
Wood processing workers	57 (0.6)	75 (1.6)	132 (0.9)
Printing trades workers	44 (0.4)	39 (0.8)	83 (0.6)
Glass plant workers	11 (0.1)	25 (0.5)	36 (0.2)
Total	9771 (100)	4693 (100)	14 464 (100)

categories. Table 3 reports the occupations in the study population by sex.

Nickel sensitization

In the female group, nickel sensitization was significantly associated with metal and mechanical work (OR 1.54; 95% CI 1.16–2.05) (Table 4). In men, nickel sensitization was significantly higher in farmers (OR 1.94; 95% CI 1.02–3.67), and in health service workers (OR 1.59; 95% CI 1.00–2.54) when compared with office workers. The association with domestic cleaning in women (OR 1.12; 95% CI 0.95–1.32) and textile and leather workers in men

(OR 1.70; 95% CI 0.97–2.99) were increased but not statistically significant.

Nickel sensitization was higher in women of 26–35 years and lower in younger (15–25 years) and older women (>45 years). In men, there was no association between nickel sensitization and age (Table 7).

Personal and familiar atopy and dermatitis site (hand/forearm versus other sites) were not associated with nickel sensitization in both men and women (data not shown).

Cobalt sensitization

Cobalt sensitization was significantly associated with textile and leather work (OR 1.52; 95% CI 1.09–2.12) and retirement condition (OR 1.36; 95% CI 1.00–1.85) in women, and with cleaning work (OR 1.86; 95% CI 1.18–2.93) in men (Table 5).

Cobalt sensitization prevalence increases with age in men and decreases in women (Table 7). Only in men, dermatitis was more frequently localized in hands and forearms than in other sites (OR 1.30; 95% CI 1.02–1.66). Personal and familiar atopy was not associated with cobalt sensitization in either sex (data not shown).

Chromate sensitization

Chromate sensitization was significantly associated with construction work in both sexes (women: OR 1.58, 95% CI 1.00–2.49; men: OR 2.24, 95% CI 1.55–3.22) (Table 6). Moreover, significant associations were found with cleaning work in the female group (OR 1.48; 95% CI 1.12–1.96). The association with driving occupation in men group (OR 1.65; 95% CI 0.98–2.77) was increased but not statistically significant.

The prevalence of chromate sensitization was found to increase with age in both sexes (Table 7), even though the trend was more evident in men.

In the male group, dermatitis was more frequent in hands and/or forearms than in other sites (OR 1.58; 95% CI 1.26–1.97), while the opposite was observed in the women (OR 0.73; 95% CI 0.60–0.87).

Table 4. Prevalence of nickel sensitization (number and percentage) in the occupational groups and associations between nickel sensitization and occupation by sex

Occupation	Women			Men		
	N (%)	OR	95% CI	N (%)	OR	95% CI
Office workers	798 (36.2)	1.0	–	96 (9.4)	1.0	–
Personal health-care workers	267 (37.1)	0.96	0.80–1.15	27 (14.4)	1.59	1.00–2.54
Metal and mechanical workers	107 (49.5)	1.54	1.16–2.05	36 (8.3)	0.81	0.54–1.22
Agricultural workers	20 (32.3)	0.93	0.54–1.61	13 (16.7)	1.94	1.02–3.67

The odds ratios (OR) and 95% confidence intervals (CI) are adjusted by age and personal and family history of atopy, assuming the office workers as the reference category. In **bold** we have highlighted statistically significant results.

Table 5. Prevalence of **cobalt** sensitization (number and percentage) in the occupational groups and associations between cobalt sensitization and occupation by sex

Occupation	Women			Men		
	N (%)	OR	95% CI	N (%)	OR	95% CI
Office workers	265 (12.0)	1.0	–	80 (7.8)	1.0	–
Pensioners	116 (10.7)	1.36	1.00–1.85	71 (8.0)	0.78	0.50–1.22
Cleaners	107 (11.5)	0.97	0.76–1.25	32 (13.4)	1.86	1.18–2.93
Textile and leather workers	51 (17.5)	1.52	1.09–2.12	9 (8.3)	1.01	0.49–2.09

The odds ratios (OR) and the 95% confidence intervals (CI) are adjusted by age and personal and family history of atopy, assuming the office workers as the reference category. Highlighted in **bold** are statistically significant results.

Table 6. Prevalence of **chromate** sensitization (number and percentage) in the occupational groups and associations between chromate sensitization and occupation by sex

Occupation	Women			Men		
	N (%)	OR	95% CI	N (%)	OR	95% CI
Office workers	144 (6.5)	1.0	–	82 (8.0)	1.0	–
Cleaners	98 (10.5)	1.48	1.12–1.96	32 (13.4)	1.47	0.94–2.31
Building and related trades workers	25 (11.7)	1.58	1.00–2.49	63 (19.0)	2.24	1.55–3.22

The odds ratios (OR) and the 95% confidence intervals (CI) are adjusted by age and personal and family history of atopy, assuming the office workers as the reference category. Highlighted in **bold** are statistically significant results.

Table 7. Nickel, cobalt, and chromate sensitization by age and sex

Age (years)	Women							Men						
	N	Nickel		Cobalt		Chromate		N	Nickel		Cobalt		Chromate	
		OR	95% CI	OR	95% CI	OR	95% CI		OR	95% CI	OR	95% CI	OR	95% CI
15–25	1730	1.0	–	1.0	–	1.0	–	776	1.0	–	1.0	–	1.0	–
26–35	2320	1.43	1.25–1.63	1.02	0.84–1.24	1.13	0.88–1.45	1083	1.26	0.92–1.72	1.28	0.87–1.87	1.58	1.11–2.26
36–45	2172	0.94	0.82–1.09	0.82	0.67–1.02	1.21	0.93–1.58	1003	1.10	0.79–1.52	1.52	1.04–2.22	1.77	1.24–2.54
46–55	1368	0.64	0.54–0.76	0.93	0.73–1.17	1.44	1.09–1.91	734	0.87	0.61–1.26	1.75	1.17–2.60	2.29	1.58–3.31
≥56	2181	0.40	0.33–0.48	0.61	0.46–0.80	1.59	1.16–2.17	1097	0.96	0.62–1.49	1.87	1.18–2.99	2.34	1.52–3.61

The odds ratios (OR) and 95% confidence intervals (CI) are adjusted by personal and family history of atopy. Significant associations are marked in **bold**.

Personal and familiar atopy was not associated with chromate sensitization in either sex (data not shown).

Discussion

This study of a large group of Italian patients confirmed that the prevalence of nickel sensitization is considerably different between the two sexes: 31.6% of women *versus* 10.0% of men were sensitized to nickel. This finding is consistent with other investigations (3, 6, 19, 20). It has been reported that the use of jewellery and earring may account for the predominant occurrence of nickel sensitization in females (3). In our study, the overall prevalence of nickel sensitization was 24.6%. In 1997, Schnuch et al. (5), studying 40 000 subjects from 24 German Allergology Departments, found that 15.7% of them were sensitized to nickel. Two European Surveillance System of Contact Allergies (ESSCA) studies reported nickel allergy of 18.0 and 20.1% in the study populations (4, 21). In a

group of 1000 patients (566 men and 434 women) patch tested in an Indian Dermatology Centre, the percentage of nickel sensitization was 12.9% (22). One reason for the greater prevalence of nickel sensitization in our population could be related to a wide diffusion of cheap jewellery and to the delay of the “Nickel Directive” (Council Directive 94/27/EC) application in Italy compared with other European Countries (4, 21).

The role of nickel as an occupational allergen is still unclear (23) and, according to some authors, up to 12% of the total estimated cases of occupational contact dermatitis are thought to be due, at least partially, to nickel (10). In this study, nickel sensitization was found to be associated with metal/mechanical work among women. An increased risk for nickel contact allergy has been already described in metal finishers (6). Nickel cutaneous allergy in metalworkers has been attributed to the content of this allergen in work tools (24). In our study there were significant associations between nickel sensitization and occupations in agriculture,

and health care services among men. It has been reported that the simultaneous exposure to irritant chemical agents occurring in such jobs might influence the onset and the course of dermatitis caused by nickel (25). It is not completely clear why we found an association with nickel sensitization and occupation in agriculture, but we can suppose that the frequent contact with metal objects in a condition of dry and damaged skin (by chemical and physical factors) can increase nickel permeation and cause an increase of sensitization to that metal.

In our study, cobalt sensitization was a little more frequent, although significantly, in the female group (11.2%) than in the male group (8.4%). The overall prevalence of cobalt sensitization in our sample (10.2%) was higher than in other studies carried out in some European centres (5, 20, 21), but it was similar to the prevalence reported in a retrospective study of 3854 subjects at the Mayo Clinic (10.3%) (26). In our investigation, cobalt sensitization was associated with textile/leather work among women, and with cleaning work among men. Cobalt sensitization is believed to be involved in the onset of allergic contact dermatitis in several occupations: hairdressing, building, hygiene and cleaning works (16). It has been suggested that the contamination of household products with cobalt may have some role in the development of hand eczema, although Basketter et al. excluded a role of cobalt contamination of household products in the sensitization and elicitation of allergic contact dermatitis (27). However, cobalt rarely is a unique sensitizer; more frequently this allergen is found to be associated with either nickel (among women) or chromate (among men) sensitization (15, 16, 28, 29).

In our study, chromate sensitization was more frequent in men (10.1%) than in women (7.9%) and this finding is consistent with previous reports (5, 20, 30). It is well known that allergic contact dermatitis from chromate tends to affect workers exposed to chromate compounds found in materials, which are used in some jobs such as cement in building trade, tanning in leather industry, and chrome plating (5, 6, 21).

We found an overall prevalence of chromate sensitization of 8.7%, a percentage slightly higher than those reported by Schnuch et al. (5) (4.6%) and by Uter et al. (21) (5.3%), but slightly lower than those found by Akasya-Hillenbrand and Ozkaya-Bayazit (20) in a study conducted in Turkey (11.8%) and by Bajaj et al. (22) in India (11.1%). In the latter studies, the higher prevalence of chromate sensitization was attributed to the wide expansion of building trade with no personal protective equipment in Turkey and to the usual habit of the workers wearing leather shoes without any socks in India.

In our study, chromate sensitization was associated with cleaning work in women and building trade work in both sexes. As expected and in accord with the findings of other authors (15), a twofold excess risk for chromate sensitization was found in male workers engaged in building and related trades. Chromate as a salt in cement is one of the most important allergens causing occupational contact dermatitis among construction workers and is still an important allergen in the building industry (31). The EU directive 2003/53/EC requires the addition of ferrous sulfate to cement to reduce the level of hexavalent chromium to trivalent state (which has a lower degree of skin penetration). Decreased rates of chromate allergy have been found in countries where restrictions for the content of hexavalent chromium in cement have been included in the national legislation (32, 33).

Age was a significant predictor for metal sensitization, although with a different trend between sexes and in the different age categories. Nickel sensitization was more frequent among women aged 26–35 years in comparison with the youngest group aged 15–25 years (assumed as reference). Our data trend could be explained by a decrease of prevalence of nickel sensitization among youngest women caused by a delayed first effect of the EU nickel regulation in Italy. A decreasing trend in prevalence of nickel allergy was found by other authors in countries where the EU nickel regulation has been followed for a long time (34). In Denmark the government has regulated the release of nickel from metal objects since 1990 (35) and two recent Danish papers showed a decrease in the prevalence of nickel allergy among young Danish women after the introduction of nickel regulation (36, 37). Thyssen et al demonstrated that this decrement was more pronounced among women of 18–35 years (36). However, nickel sensitization appeared to decrease in the higher ages (>45 years); and this finding is consistent with those observed by other authors (6, 15, 20). Differences in exposure pattern, social and cultural factors and the effect of regulatory control of nickel exposure could explain the different significant association between the nickel sensitization and age categories. However, cobalt and chromate sensitizations were positively associated with age in men. It has been reported that the occurrence of chromate allergic dermatitis tends to increase with increasing age, mainly above 40 years, and that an early diagnosis of chromate induced dermatitis may improve the prognosis of the disease (3, 16). Furthermore, it can be assumed that chromate allergy may be higher in older patients as exposure was more prevalent decades ago due to poorer work hygiene conditions. In the male population of this investigation, chromate and cobalt allergic contact

dermatitis was more frequently localized in the hands and forearms than in other sites, supporting the hypothesis of an occupational origin of the disorder in workers involved in tasks/jobs at risk (5, 38).

This study investigated the prevalence and the possible association between metal sensitization and occupation in Italy using one of the largest databases on patch test results in Europe. Nevertheless, there are some limitations of this study that deserve attention. Although based on a large sample of individuals, the study population included patients who attended health services for suspected allergic dermatitis, and for that reason our results may be affected with selection bias. Job classification was a difficult task in this study: 16.2% of the subjects were classified as 'others' and 13.6% as 'retired' because of either insufficient or lack of reliable information about current or previous occupations, respectively. However, except for an increase prevalence of cobalt sensitization in retired women, there was no evidence for an excess risk for other metal sensitizations in these categories of subjects. The high percentage of retired people is probably due to the increasing age of the patients for demographic changes in the Western countries, Italy included, and to the reported finding that there is a tendency for older people to be more frequently patch tested for allergic contact dermatitis caused by many substances (39). Finally, the prevalence of either isolated or simultaneous metal sensitizations in our study population and their possible association with occupations are currently under investigation.

Despite these limitations, this study showed interesting association between some occupations and nickel, chromate and cobalt allergy.

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