

Concurrent sensitization to metals and occupation

Francesca Rui¹, Massimo Bovenzi¹, Andrea Prodi¹, Anna Belloni Fortina², Ilaria Romano², Maria Teresa Corradin³ and Francesca Larese Filon¹

¹Clinical Unit of Occupational Medicine, Department of Medical Sciences, University of Trieste, Trieste 34129, Italy, ²Dermatology Unit, Department of Pediatrics, University of Padova, Padova 35128, Italy, and ³Dermatologic Unit, S. Maria degli Angeli Hospital, Pordenone 33170, Italy

doi:10.1111/j.1600-0536.2012.02100.x

Summary

Background. Cosensitization to nickel, cobalt and chromium occurs in the general population and in some occupational groups.

Objectives. To estimate the isolated and concurrent occurrence of nickel, cobalt and chromium contact sensitization and their association with individual and occupational risk factors.

Patients/methods. Twelve thousand four hundred and ninety-two patients were patch tested with the European baseline series between 1997 and 2004 in north-eastern Italy. The associations between patch test results and patient characteristics and occupations were investigated by means of multinomial logistic regression analysis.

Results. Of the patients, 34.7% (4334 patients) had one or more positive patch test reactions to metals. As compared with those with negative reactions to all three metals, nickel sensitization was significantly higher in females than in males, not only as monosensitization, but also as cosensitization with cobalt, with chromium, or with both metals. Building and related trades workers showed positive reactions to chromium + nickel [odds ratio (OR) 1.99; 95% confidence interval (CI) 1.05–3.76] and chromium + cobalt (OR 2.61; 95% CI 1.46–4.67). Cleaning workers showed a high prevalence of nickel, chromium, nickel + chromium and nickel + cobalt + chromium cosensitization (ORs 1.29, 1.66, 2.11, and 1.79, respectively). An excess risk for cosensitization to all three metals was found in textile and leather workers (OR 2.19; 95% CI 1.10–4.33), and in bartenders (OR 2.10; 95% CI 1.03–4.26).

Conclusions. Some occupational groups are more likely to develop nickel, cobalt and chromium cosensitization.

Key words: chromium; cobalt; cosensitization; dermatitis; nickel; occupation; patch test.

Contact allergies to nickel, cobalt and chromium are common, may cause allergic contact dermatitis, and frequently occur simultaneously in the general population (1–4) and in some occupational groups (5–9). Their prevalence and trend may be dependent on

age and sex, and influenced by social, cultural and occupational aspects (1, 10–17). Our previous study confirmed that the prevalence of metal monosensitization is significantly different between the sexes, and showed associations between some occupations and nickel, chromium and cobalt allergy (18). Concurrent nickel, cobalt and chromium sensitization is frequently seen in patients with allergic contact dermatitis (3, 4, 19). A large multifactorial analysis of concurrent patch test reactions by Hegewald et al. showed that nickel + chromium and nickel + cobalt cosensitization were overrepresented among female patients, and confirmed the occupational

Correspondence: Dr Francesca Rui, Unità Clinica Operativa di Medicina del Lavoro, Dipartimento di Scienze di Medicina Pubblica, Università degli Studi di Trieste, Centro Tumori, Via della Pietà, 19 I-34129 Trieste, Italy. Tel: +39-040-3992409; Fax: +39-040-368199. E-mail: frui@units.it

Conflicts of interest: The authors have declared no conflicts.

Accepted for publication 17 March 2012

relevance of cobalt + chromium allergy in building workers (20).

The aims of this study were:

- To estimate the prevalence of isolated and concurrent contact sensitization to nickel, cobalt and chromium in a population of consecutive patients who attended units of dermatology or occupational medicine in north-eastern Italy for allergic contact dermatitis;
- To investigate the association between isolated and concurrent nickel, cobalt and chromium 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, and Trieste). A standardized questionnaire was used to collect information about individual characteristics and occupational history. We excluded 753 patients with missing responses to personal and occupational history or with incomplete patch testing. Moreover, 1972 retired people were also excluded from data analysis, because of insufficient or lack of reliable information about their previous occupations. Finally, 12 492 consecutive patients were included in the study. Details of the surveyed population have been reported in a previous paper (18).

Patch tests

The patients were patch tested with the European baseline series (21), using Finn Chambers® on Scanpor® tape. The tested allergens included nickel sulfate 5.0% in petrolatum, cobalt(II) chloride 1.0% pet., and potassium dichromate 0.5% pet. All allergens were applied on the upper back and removed after 48 hr. The sites were examined on removal and 24 hr after removal, according to the International Contact Dermatitis Research Group guidelines (22). Positive reactions of +, ++ and +++ grades were considered to be positive.

Statistical analysis

Data analysis was performed with SPSS™ (version 13.0). Continuous variables were summarized by using the mean as a measure of central tendency and the standard

deviation (SD) as a measure of dispersion. Categorical data were tabulated into $2 \times k$ or $k \times k$ contingency tables. The associations between patch test results and individual characteristics and occupations were investigated by means of multinomial logistic regression analysis. The dependent variable included positive reactions to the three metals considered (isolated or concurrent sensitization to nickel, cobalt and chromate, mutually exclusive) as previously described by Hegewald et al. (20). The independent variables included in the logistic models were age (four categories: ≤ 27 , 28–37, 38–47 and >47 years), sex, number of positive reactions to other allergens (apart from the three metals), and occupations. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from the coefficients and the standard errors of logistic regression output, assuming negative reactions to all three metals as the reference category. Trend across categories was assessed by means of the likelihood-ratio test. A p -value of <0.05 was established as the limit of statistical significance.

Results

The study population included 8687 women (69.5%) and 3805 men (30.5%). The mean age was 38 years (SD 13.7 years). Of the patients, 65.3% ($n = 8158$) had negative patch test reactions to metals (nickel, cobalt, and chromium), 18.5% ($n = 2314$) reacted positively only to nickel, 2.7% ($n = 342$) reacted positively only to cobalt, 4.1% ($n = 516$) reacted positively only to chromium, 4.7% ($n = 593$) reacted positively to nickel and cobalt, 1.7% ($n = 209$) reacted positively to nickel and chromium, 1.4% ($n = 171$) reacted positively to cobalt and chromium, and 1.5% ($n = 189$) reacted positively to nickel, cobalt and chromium simultaneously. Tables 1 and 2 show the characteristics and the occupations of the study population by metal sensitization, respectively.

Sex

The prevalence of nickel sensitization was higher in females than in males, either as isolated allergen (OR 6.06; 95% CI 5.20–7.07), in association with cobalt (OR 4.10; 95% CI 3.18–5.29), in association with chromium (OR 2.02; 95% CI 1.43–2.86), or in association with both metals (OR 2.35; 95% CI 1.61–3.45). Conversely, chromate sensitization and chromium + cobalt cosensitization were more prevalent in males (Table 3).

Age

Nickel and chromate sensitization alone and nickel + chromium sensitization were significantly more frequent in patients aged 28–37 years than in the younger

Table 1. Characteristics of the study population

Variables	Patch test-negative to metals* n = 8158 (65.3%)	Nickel n = 2314 (18.5%)	Cobalt n = 342 (2.7%)	Chromium n = 516 (4.1%)	Ni + Co n = 593 (4.7%)	Ni + Cr n = 209 (1.7%)	Co + Cr n = 171 (1.4%)	Ni + Co + Cr n = 189 (1.5%)	Total n = 12492 (100%)
Sex									
Females	5174 (59.6)	2090 (24.1)	223 (2.6)	290 (3.3)	514 (5.9)	159 (1.8)	86 (1.0)	151 (1.7)	8687
Males	2984 (78.4)	224 (5.9)	119 (3.1)	226 (5.9)	79 (2.1)	50 (1.3)	85 (2.2)	38 (1.0)	3805
Age (years)									
≤27	2021 (63.7)	664 (20.9)	95 (3.0)	95 (3.0)	176 (5.5)	48 (1.5)	35 (1.1)	40 (1.3)	3174
28–37	1963 (59.3)	784 (23.7)	82 (2.5)	137 (4.1)	190 (5.7)	70 (2.1)	33 (1.0)	54 (1.6)	3313
38–47	1809 (66.1)	507 (18.5)	64 (2.3)	107 (3.9)	120 (4.4)	40 (1.5)	47 (1.7)	41 (1.5)	2735
>47	2365 (72.3)	359 (11.0)	101 (3.1)	177 (5.4)	107 (3.3)	51 (1.6)	56 (1.7)	54 (1.7)	3270
Other sensitization [†] (n)									
0	5218 (69.6)	1363 (18.2)	167 (2.2)	207 (2.8)	316 (4.2)	77 (1.0)	69 (0.9)	79 (1.1)	7496
1	1822 (61.5)	586 (19.8)	95 (3.2)	143 (4.8)	165 (5.6)	62 (2.1)	47 (1.6)	45 (1.5)	2965
2	750 (55.7)	254 (18.9)	51 (3.8)	115 (8.5)	62 (4.6)	46 (3.4)	30 (2.2)	39 (2.9)	1347
≥3	368 (53.8)	111 (16.2)	29 (4.2)	51 (7.5)	50 (7.3)	24 (3.5)	25 (3.7)	26 (3.8)	684

The variables are given as numbers (%).

*As determined by patch testing with nickel sulfate, cobalt(II) chloride and potassium dichromate in the European baseline series.

[†]Number of positive patch test reactions to other allergens (apart from nickel, cobalt, and chromium).

group (≤27 years) (ORs 1.28, 1.40, and 1.49, respectively) (Table 3). The older patients (>47 years) showed a reduced risk for nickel sensitization alone and nickel + cobalt sensitization (ORs 0.46 and 0.52, respectively), but an increased risk for chromium sensitization alone (OR 1.40; 95% CI 1.06–1.85).

Other sensitizations

The frequency of isolated nickel sensitization was significantly increased in patients who had positive patch test reactions to one (OR 1.28; 95% CI 1.14–1.44) or two (OR 1.32; 95% CI 1.13–1.56) allergens other than metals. Significant positive trends for nickel, cobalt and chromium sensitization (either isolated or concurrent sensitization) were observed in patients with positive patch test reactions to one or more non-metal allergens (Table 3).

Occupations

Nickel sensitization was significantly associated with metal and mechanical work (OR 1.42; 95% CI 1.11–1.82) and cleaning work (OR 1.29; 95% CI 1.08–1.53) (Table 4). A significant association was found between isolated cobalt sensitization and textile and leather work (OR 1.85; 95% CI 1.10–3.09). The frequency of chromium allergy was found to be significantly increased in building workers (OR 2.51; 95% CI 1.74–3.63), metal workers (OR 1.76; 95% CI 1.20–2.59), bartenders (OR 1.67; 95% CI 1.00–2.80), and cleaners (OR 1.66; 95% CI 1.17–2.34). Building and related trades work was significantly

associated with positive reactions to nickel + chromium (OR 1.99, 95% CI 1.05–3.76) and chromium + cobalt (OR 2.61, 95% CI 1.46–4.67). Patients allergic to nickel + chromium were overrepresented (OR 2.11, 95% CI 1.33–3.34) among cleaners. Finally, textile and leather workers (OR 2.19; 95% CI 1.10–4.33), cleaners (OR 1.79; 95% CI 1.09–2.94) and bartenders (OR 2.10; 95% CI 1.03–4.26) showed an increased risk for concurrent sensitization to all three metals.

Discussion

Sex and cosensitization

This study confirmed the importance of sex in the prevalence of nickel and chromium sensitization. The frequency of monosensitization to nickel was significantly higher in females, probably because of the use of jewellery and ear piercing by women (12, 23–25). Nickel + cobalt and nickel + chromium cosensitization and multi-metal sensitization were also more prevalent in the female group, as reported by Hegewald et al. (20).

Consistent with the findings of other investigators, chromium allergy by itself, or in association with cobalt sensitization, affected males more frequently (4, 13, 25), whereas cobalt monosensitization by itself did not show a sex preference (4).

Age

Nickel sensitization has changed over time because of the effect of the EU nickel regulation, especially in countries

Table 2. Occupations in the study population

Occupations	Patch test-negative to metals n = 8158 (65.3%)	Nickel n = 2314 (18.5%)	Cobalt n = 342 (2.7%)	Chromium n = 516 (4.1%)	Ni + Co n = 593 (4.7%)	Ni + Cr n = 209 (1.7%)	Co + Cr n = 171 (1.4%)	Ni + Co + Cr n = 189 (1.5%)	Total n = 12 492 (100%)
Office workers	2104 (65.1)	633 (19.6)	94 (2.9)	102 (3.2)	173 (5.4)	46 (1.4)	36 (1.1)	42 (1.3)	3230
Agricultural workers	95 (67.9)	24 (17.1)	3 (2.1)	4 (2.9)	3 (2.1)	3 (2.1)	5 (3.6)	3 (2.1)	140
Chemical processing plant workers	151 (71.6)	30 (14.2)	10 (4.7)	6 (2.8)	6 (2.8)	2 (0.9)	3 (1.4)	3 (1.4)	211
Textile and leather workers	232 (58.1)	83 (20.8)	19 (4.8)	15 (3.8)	25 (6.3)	9 (2.3)	5 (1.3)	11 (2.8)	399
Wood processing workers	90 (68.2)	23 (17.4)	5 (3.8)	4 (3.0)	5 (3.8)	2 (1.5)	1 (0.8)	2 (1.5)	132
Metal and mechanical workers	444 (68.1)	106 (16.3)	10 (1.5)	42 (6.4)	26 (4.0)	6 (0.9)	13 (2.0)	5 (0.8)	652
Building and related trades workers	357 (65.5)	71 (13.0)	10 (1.8)	50 (9.2)	19 (3.5)	13 (2.4)	19 (3.5)	6 (1.1)	545
Electrical and electronic workers	118 (80.3)	11 (7.5)	4 (2.7)	5 (3.4)	1 (0.7)	3 (2.0)	3 (2.0)	2 (1.4)	147
Household workers	1135 (68.4)	275 (16.6)	47 (2.8)	76 (4.6)	67 (4.0)	20 (1.2)	15 (0.9)	24 (1.4)	1659
Cleaners	654 (55.8)	289 (24.7)	35 (3.0)	55 (4.7)	63 (5.4)	34 (2.9)	14 (1.2)	27 (2.3)	1171
Personal healthcare workers	555 (61.3)	214 (23.6)	20 (2.2)	26 (2.9)	50 (5.5)	13 (1.4)	11 (1.2)	17 (1.9)	906
Hairdressers, beauticians	96 (64.4)	34 (22.8)	2 (1.3)	2 (1.3)	11 (7.4)	3 (2.0)	1 (0.7)	0	149
Car, bus and truck drivers	124 (70.1)	18 (10.2)	5 (2.8)	12 (6.8)	7 (4.0)	3 (1.7)	6 (3.4)	2 (1.1)	177
Bartenders	217 (60.3)	84 (23.3)	9 (2.5)	19 (5.3)	13 (3.6)	5 (1.4)	3 (0.8)	10 (2.8)	360
Others	1786 (68.3)	419 (16.0)	69 (2.6)	98 (3.7)	124 (4.7)	47 (1.8)	36 (1.4)	35 (1.3)	2614

Co, Cobalt(II) chloride; Cr, potassium dichromate; Ni, nickel sulfate.

Data are given as numbers (%).

Table 3. Multinomial logistic regression [odds ratios (ORs)] and 95% confidence intervals (CIs)] between some variables and nickel, cobalt and chromium sensitization versus negative patch test reactions to metals

	Nickel OR (95% CI)	Cobalt OR (95% CI)	Chromium OR (95% CI)	Ni + Co OR (95% CI)	Ni + Cr OR (95% CI)	Co + Cr OR (95% CI)	Ni + Co + Cr OR (95% CI)
Sex							
Males	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)
Females	6.06 (5.20–7.07)	1.02 (0.80–1.31)	0.78 (0.63–0.95)	4.10 (3.18–5.29)	2.02 (1.43–2.86)	0.71 (0.50–0.99)	2.35 (1.61–3.45)
Age (years)							
≤27	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)
28–37	1.28 (1.13–1.46)	0.88 (0.65–1.20)	1.40 (1.06–1.84)	1.18 (0.95–1.47)	1.49 (1.02–2.18)	0.92 (0.57–1.50)	1.36 (0.89–2.07)
38–47	0.90 (0.78–1.04)	0.74 (0.53–1.04)	1.20 (0.89–1.60)	0.77 (0.60–1.00)	0.89 (0.57–1.38)	1.43 (0.90–2.25)	1.12 (0.71–1.76)
>47	0.46 (0.40–0.55)	0.87 (0.63–1.19)	1.40 (1.06–1.85)	0.52 (0.40–0.69)	0.87 (0.57–1.34)	1.35 (0.86–2.11)	1.11 (0.71–1.74)
Other sensitization†							
0	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)
1	1.28 (1.14–1.44)	1.63 (1.26–2.11)	1.99 (1.59–2.48)	1.55 (1.27–1.89)	2.36 (1.68–3.32)	1.96 (1.35–2.86)	1.65 (1.14–2.39)
2	1.32 (1.13–1.56)	2.13 (1.54–2.95)	3.83 (3.00–4.88)	1.41 (1.06–1.88)	4.18 (2.87–6.09)	2.96 (1.91–4.59)	3.35 (2.26–4.96)
≥3	1.21 (0.96–1.52)*	2.47 (1.64–3.72)**	3.39 (2.45–4.71)**	2.36 (1.71–3.26)**	4.44 (2.76–7.12)**	4.97 (3.09–7.99)**	4.54 (2.87–7.19)**

Co, cobalt(II) chloride; Cr, potassium dichromate; Ni, nickel sulfate.

Likelihood-ratio test for trend: * $p < 0.001$; ** $p < 0.0001$.

Significant associations are marked in bold.

†Numbers of positive patch test reactions to other haptens (apart from nickel, cobalt, and chromium).

Table 4. Multinomial logistic regression [odds ratios (ORs) and 95% confidence intervals (CIs)] between occupations and nickel, cobalt and chromium sensitization versus negative patch test reactions to metals

Occupations	Nickel OR (95% CI)	Cobalt OR (95% CI)	Chromium OR (95% CI)	Ni + Co OR (95% CI)	Ni + Cr OR (95% CI)	Co + Cr OR (95% CI)	Ni + Co + Cr OR (95% CI)
Textile and leather workers	1.11 (0.84–1.46)	1.85 (1.10–3.09)	1.26 (0.72–2.22)	1.25 (0.80–1.95)	1.65 (0.79–3.43)	1.20 (0.46–3.11)	2.19 (1.10–4.33)
Metal and mechanical workers	1.42 (1.11–1.82)	0.53 (0.27–1.03)	1.76 (1.20–2.59)	1.18 (0.76–1.82)	0.82 (0.34–1.95)	1.55 (0.81–2.99)	0.79 (0.31–2.04)
Building and related trades workers	1.07 (0.80–1.42)	0.64 (0.33–1.25)	2.51 (1.74–3.63)	0.97 (0.59–1.59)	1.99 (1.05–3.76)	2.61 (1.46–4.67)	1.01 (0.42–2.41)
Cleaners	1.29 (1.08–1.53)	1.21 (0.81–1.82)	1.66 (1.17–2.34)	1.05 (0.77–1.43)	2.11 (1.33–3.34)	1.22 (0.65–2.30)	1.79 (1.09–2.94)
Bartenders	1.24 (0.93–1.63)	0.90 (0.45–1.81)	1.67 (1.00–2.80)	0.70 (0.39–1.25)	0.95 (0.37–2.44)	0.75 (0.23–2.48)	2.10 (1.03–4.26)

Co, cobalt(II) chloride; Cr, potassium dichromate; Ni, nickel sulfate.
Significant associations are marked in bold.

where the EU provisions have been adopted (26–28). In our study, nickel sensitization was more frequent among patients aged 28–37 years than in the youngest group. As reported previously (18), this finding may be explained by the delayed introduction of the EU Nickel Directive in Italy. People older than 47 years showed a lower frequency of sensitization to nickel, owing to reduced contact with metals and jewellery, as reported by other authors (20, 23).

Concomitant nickel and cobalt allergy is generally explained by cosensitization (29), owing to the presence of cobalt as an impurity in the nickel alloys used in jewellery (30). Nevertheless, in our study, cobalt monosensitization and cosensitization with other metals did not show any significant association with age. Chromium allergy was more frequent in the 28–37-year-old and >47-year-old groups than in the youngest group: it is known that the prevalence of chromium sensitization increases with age (9, 11) and can be related to cement or leather exposure (31, 32).

Monosensitization and polysensitization

The simultaneous sensitization to more than one allergen is not necessarily associated with clinical manifestations of allergic contact dermatitis (33), and sometimes patients are polysensitized (34). Several factors may contribute to this phenomenon: simultaneous or successive exposure to multiple allergens, cross-reactivity because of structural similarity, or possible false-positive reactions in the patch tests (34). In this study, nickel sensitivity was associated with sensitization to haptens other than metals; similar findings have been obtained for cobalt and chromium, as reported by Hegewald et al. (20). The simultaneous sensitization to cobalt and chromium was associated with a higher probability of having sensitization to haptens other than metals. Triplet cluster associations involving nickel, cobalt and chromium allergy could be related to occupational exposure (4, 20), and are associated with severe and chronic form of dermatitis (34). For this reason, it is important to minimize the development of multiple sensitization, especially in the workplace, by means of individual protection measures or the adoption of strict exposure regulations (35).

Occupational exposures

Isolated nickel or chromium sensitization was found to be associated with metal/mechanical work, in accord with other studies (23, 36). It is well known that nickel and chromium released from metal objects are sufficient to induce sensitization and to cause occupational allergic dermatitis (8, 36).

The frequency of chromium sensitization was significantly higher in workers engaged in building and related trades, because of the presence of hexavalent chromium in cements (20, 37, 38). Currently, sensitization to chromium is showing a decreasing trend in younger people, because of the introduction of ferrous sulfate in cement to convert hexavalent chromium to the trivalent state, which reduces its skin penetration and sensitization potential (32). In Denmark, where the addition of ferrous sulfate to cement has been compulsory since 1983, the epidemiology of chromium allergy has drastically changed, and its frequency is currently increasing in consumers exposed to leather (31, 32).

Isolated cobalt allergy induced by cement is uncommon, and is considered to be secondary to pre-existing chromium dermatitis (38), whereas concurrent chromium + cobalt allergy is significantly overrepresented among building and related trades workers, as reported by Hegewald et al. (20). In this study, isolated cobalt sensitization and concurrent nickel + cobalt + chromium sensitization were significantly more frequent in textile and leather workers, because of the use of mordants (containing metals) and of chromium in leather working processes (39–41).

The frequency of metal sensitization was significantly higher in wet workers (cleaners and bartenders), who have an increased risk of developing occupational contact dermatitis (42, 43). Exposure to water and irritants can impair the skin protective barrier, causing higher permeation of metals present in objects commonly used in workplaces (44) or in detergents (45). The role of metals in detergents as triggers for allergic sensitization is still debated, but some authors deny their role in contact dermatitis (46).

The results of this study conducted in a group of patients from north-eastern Italy confirm previous findings on concurrent nickel, chromium and cobalt allergy (20), and may contribute to our understanding of the possible association between concurrent metal sensitization and some occupations. The high rate of metal sensitivity found in our database, and the high number of people with multiple metal sensitization, tend to validate the impact of these haptens in some occupations and their possible role in the onset and the development of occupational dermatitis.

Our findings suggest the need to increase preventive measures to avoid single or multiple metal sensitization that can lead to contact dermatitis.

References

- Thyssen J P, Linneberg A, Menné T, Johansen J D. The epidemiology of contact allergy in the general population – prevalence and main findings. *Contact Dermatitis* 2007; **57**: 287–299.
- Kränke B, Aberer W. Multiple sensitivities to metals. *Contact Dermatitis* 1996; **34**: 225.
- Bordel-Gómez M T, Miranda-Romero A, Castrodeza-Sanz J. Isolated and concurrent prevalence of sensitization to transition metals in a Spanish population. *J Eur Acad Dermatol Venereol* 2008; **22**: 1452–1457.
- Ruff C A, Belsito D V. The impact of various patient factors on contact allergy to nickel, cobalt, and chromate. *J Am Acad Dermatol* 2006; **55**: 32–39.
- Shum K W, Meyer J D, Chen Y, Cherry N, Gawkrödger D J. Occupational contact dermatitis to nickel: experience of the British dermatologist (EPIDERM) and occupational physicians (OPRA) surveillance schemes. *Occup Environ Med* 2003; **60**: 954–957.
- Cherry N, Meyer J D, Adishes A, Brooke R, Owen-Smith V, Swales C, Beck M H. Surveillance of occupational skin disease: EPIDERM and OPRA. *Br J Dermatol* 2000; **142**: 1128–1134.
- Nettis E, Marcandrea M, Colanardi M C, Paradiso M T, Ferrannini A, Tursi A. Results of standard series patch testing in patients with occupational allergic contact dermatitis. *Allergy* 2003; **58**: 1304–1307.
- Lidén C, Skare L, Nise G, Vahter M. Deposition of nickel, chromium, and cobalt on the skin in some occupations – assessment by acid wipe sampling. *Contact Dermatitis* 2008; **58**: 347–354.
- Athavale P, Shum K W, Chen Y et al. Occupational dermatitis related to chromium and cobalt: experience of dermatologist (EPIDERM) and occupational physicians (OPRA) in the UK over an 11-year period (1993–2004). *Br J Dermatol* 2007; **157**: 518–522.
- Garner L A. Contact dermatitis to metals. *Dermatol Ther* 2004; **17**: 321–327.
- Modjtahedi B S, Modjtahedi S P, Maibach H I. The sex of the individual as a factor in allergic contact dermatitis. *Contact Dermatitis* 2004; **50**: 53–59.
- ESSCA Writing Group. The European Surveillance System of Contact Allergies (ESSCA): results of patch testing the standard series, 2004. *J Eur Acad Dermatol Venereol* 2008; **22**: 174–181.
- Schnuch A, Geier J, Uter W et al. National rates and regional differences in sensitization to allergens of the standard series. *Contact Dermatitis* 1997; **37**: 200–209.
- Wöhrl S, Jandl T, Stingl G, Kinaciyan T. Mobile telephone as new source for nickel dermatitis. *Contact Dermatitis* 2007; **56**: 113.
- Livideanu C, Giordano-Labadie F, Paul C. Cellular phone addiction and allergic contact dermatitis to nickel. *Contact Dermatitis* 2007; **57**: 130–131.
- Thyssen J P, Johansen J D, Zachariae C, Menné T. The outcome of dimethylglyoxime testing in a sample of cell phones in Denmark. *Contact Dermatitis* 2008; **59**: 38–42.
- Cheng T Y, Tseng Y H, Sun C C, Chu C Y. Contact sensitization to metals in Taiwan. *Contact Dermatitis* 2008; **59**: 353–360.
- Rui F, Bovenzi M, Prodi A et al. Nickel, cobalt and chromate sensitization and occupation. *Contact Dermatitis* 2010; **62**: 225–231.
- Brasch J, Uter W, Geier J et al. Associated positive patch test reactions to standard

- contact allergens. *Am J Contact Dermat* 2001; **12**: 197–202.
- 20 Hegewald J, Uter W, Pfahlberg A et al. A multifactorial analysis of concurrent patch test reactions to nickel, cobalt, and chromate. *Allergy* 2005; **60**: 372–378.
 - 21 Isaksson M, Brandão F M, Bruze M, Goossens A. Recommendation to include budesonide and tixocortol pivalate in the European standard series. *Contact Dermatitis* 2000; **43**: 41–42.
 - 22 Wilkinson D S, Fregert S, Magnussen B, Bandmann H J, Calnan C D, Cronin E. Terminology of contact dermatitis. *Acta Derm Venereol* 1970; **50**: 287–292.
 - 23 Uter W, Pfahlberg A, Gefeller O et al. Risk factors for contact allergy to nickel – results of a multifactorial analysis. *Contact Dermatitis* 2003; **48**: 33–38.
 - 24 Lantinga H, Nater J P, Coenraads P J. Prevalence, incidence and course of eczema on the hand and forearm in a sample population. *Contact Dermatitis* 1984; **10**: 135–139.
 - 25 Akasya-Hillenbrand E, Ozkaya-Bayazit E. Patch test result in 542 patients with suspected contact dermatitis in Turkey. *Contact Dermatitis* 2002; **46**: 17–23.
 - 26 Thyssen J P, Menné T. Metal allergy – a review on exposures, penetration, genetics, prevalence, and clinical implications. *Chem Res Toxicol* 2010; **23**: 309–318.
 - 27 Thyssen J P, Johansen J D, Carlsen B C, Menné T. Prevalence of nickel and cobalt allergy among female patients with dermatitis before and after Danish government regulation: a 23-year retrospective study. *J Am Acad Dermatol* 2009; **61**: 799–805.
 - 28 Thyssen J P, Johansen J D, Menné T, Nielsen N H, Linneberg A. Nickel allergy in Danish Women before and after nickel regulation. *N Engl J Med* 2009; **360**: 2259–2260.
 - 29 Wahleberg J E, Lidén C. Cross-reactivity patterns of cobalt and nickel studied with repeated open applications (ROATs) of the skin of guinea pigs. *Am J Contact Dermat* 2000; **11**: 42–48.
 - 30 Nielsen N H, Menné T. Allergic contact sensitization in an unselected Danish population. The Glostrup Allergy Study, Denmark. *Acta Derm Venereol* 1992; **72**: 456–460.
 - 31 Thyssen J P, Jensen P, Carlsen B C, Engkilde K, Menné T, Johansen D. The prevalence of chromium allergy in Denmark is currently increasing as a result of leather exposure. *Br J Dermatol* 2009; **161**: 1288–1293.
 - 32 Zachariae C O C, Agner T, Menné T. Chromium allergy in consecutive patients in a country where ferrous sulphate has been added to cement since 1981. *Contact Dermatitis* 1996; **35**: 83–85.
 - 33 Mangelsdorf H C, Fleisher A B, Sherertz E F. Patch testing in an aged population without dermatitis: high prevalence of patch test positivity. *Am J Contact Dermat* 1996; **7**: 155–157.
 - 34 Schnuch A, Brasch J, Uter W. Polysensitization and increased susceptibility in contact allergy: a review. *Allergy* 2008; **63**: 156–167.
 - 35 Carlsen B C, Andersen K E, Menné T, Johansen J D. Patients with multiple contact allergies: a review. *Contact Dermatitis* 2008; **58**: 1–8.
 - 36 Geier J, Lessmann H, Hellweg B et al. Chromate metal products may be hazardous to patients with chromate allergy. *Contact Dermatitis* 2009; **60**: 199–202.
 - 37 Bock M, Schmidt A, Bruckner T, Diepgen T L. Occupational skin disease in the construction industry. *Br J Dermatol* 2003; **149**: 1165–1171.
 - 38 Uter W, Rühl R, Pfahlberg A, Geier J, Schnuch A, Gefeller O. Contact allergy in construction workers: result of a multifactorial analysis. *Ann Occup Hyg* 2004; **48**: 21–27.
 - 39 Adams R M. Metals. In: *Occupational Skin Disease*, Adams R M (ed.): New York, Grune & Stratton, 1983; pp. 204–237.
 - 40 Kanerva L, Jolanki R, Estlander T et al. Incidence rates of occupational allergic contact dermatitis caused by metals. *Am J Contact Dermat* 2000; **11**: 155–160.
 - 41 Warshaw E M, Schram S E, Belsito D V et al. Shoe allergens: retrospective analysis of cross-sectional data from the North American contact dermatitis group, 2001–2004. *Dermatitis* 2007; **18**: 191–202.
 - 42 Duarte I, Rotter A, Lazzarini R. Frequency of occupational contact dermatitis in an ambulatory of dermatologic allergy. *An Bras Dermatol* 2010; **85**: 455–459.
 - 43 Smith H R, Basketter D A, McFadden J P. Irritant dermatitis, irritancy and its role in allergic contact dermatitis. *Clin Exp Dermatol* 2002; **27**: 138–146.
 - 44 Ingber A, Gammelgaard B, David M. Detergents and bleaches are sources of chromium contact dermatitis in Israel. *Contact Dermatitis* 1998; **38**: 101–104.
 - 45 Kokelj F, Daris F, Lutmann A, Braidà N, Flego R. Nickel, chromate and cobalt in toilet soaps analyzed by inductively coupled plasma mass spectrometry. *Contact Dermatitis* 1994; **31**: 270.
 - 46 Basketter D A, Angelini G, Ingber A, Kern P S, Menné T. Nickel, chromium and cobalt in consumer products: revisiting safe levels in the new millennium. *Contact Dermatitis* 2003; **49**: 1–7.