

# Contact allergy trends in Sweden – a retrospective comparison of patch test data from 1992, 2000, and 2009

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doi:10.1111/cod.12346

## Summary

**Background.** Contact allergy prevalence rates change over time as a result of variations in allergen exposure. Data from patch test clinics are often used as markers for allergy trends.

**Objectives.** The aim of the present retrospective study was to describe trends in rates of sensitization to allergens in the Swedish baseline series.

**Patients/materials/methods.** Prevalence rates are described by comparing consecutive patch test data from 1992, 2000 and 2009 in Swedish patch test clinics. In total, 3680 patients were included in 1992, 3825 in 2000, and 3112 in 2009.

**Results.** Among test substances with a sensitization rate above 2% in 2009, significant decreases were noted for nickel sulfate, cobalt chloride, colophonium, and methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI), and a significant increase for *p*-phenylenediamine, as compared with 1992. Potassium dichromate reactions had increased among younger women, whereas reactions to nickel and cobalt had decreased in this group. Sensitization to chromium, cobalt and fragrance mix I had decreased among older men, and sensitization to nickel had decreased among younger men.

**Conclusions.** It is probable that these changes in 1992–2009 reflect both changes in regulations for nickel, lower levels of chromium in cement and of MCI/MI in cosmetics, and increasing use of hair dyes.

**Key words:** contact allergy; contact dermatitis; epidemiology; patch testing; prevalence; trends.

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*Funding:* The project was funded by the Edvard Wellander foundation, Sweden and the County Council in Örebro, Sweden.

*Conflicts of interest:* The authors do not have any conflicts of interests to declare.

Accepted for publication 6 December 2014

Contact allergy is common, and its possible consequence, allergic contact dermatitis, decreases the quality of life for the individual and has negative socio-economic effects in the form of sick leave and healthcare expenses. This calls for measures to prevent both sensitization and elicitation (1) The prevalence of contact allergy changes over time, as a result of variations in allergen exposure (1, 2). Such variations might be caused by fashion trends or changes in industrial technologies and regulations (2). Monitoring these contact allergy trends is important in order to detect the need for preventive measures and to

evaluate the effects of previously implemented measures (1). Monitoring studies are difficult to perform in the general population, owing to logistic problems. Therefore, most studies are based on data from consecutively patch tested dermatitis patients (3). The aim of this study was to report trends in the rates of sensitization to allergens in the Swedish baseline series by comparing consecutive patch test data obtained in 1992, 2000 and 2009 at Swedish patch test clinics.

## Materials and Methods

A retrospective analysis was performed on consecutive patch test data collected during three 18-month periods (1991–1993, 1999–2001, and 2008–2010), including patients tested with the Swedish baseline series because of suspicion of contact allergy. The three subgroups are referred to as the 1992, 2000 and 2009 subgroups, respectively. The sites of data collection were 14 departments of dermatology or occupational and environmental dermatology in Sweden, situated in Eskilstuna (one department), Gothenburg (one department), Jönköping (one department), Linköping (one department), Lund (one department), Malmö (one department), Stockholm (two departments), Umeå (one department), Uppsala (one department), and Örebro (four departments). The subgroups comprised 3662 patients in 1992, 3825 in 2000, and 3112 in 2009. In 1992, 76% of the patients were tested with materials from Chemotechnique Diagnostics AB (Tygelsjö, Sweden) applied with Finn Chambers® (Epitest Oy, Helsinki, Finland), and 24% were tested with TRUE Test™ (Mekos AS, Hillerød, Denmark), baseline panels I and II, and additional materials, tested as above with Finn Chambers® to meet the Swedish baseline series criteria of that period. The corresponding figures for 2000 were 86% and 14%, and those for 2009 were 96% and 2%, respectively. In 2009, 2% were tested with test substances from Chemotechnique Diagnostics AB applied with IQ® chambers from the same manufacturer. Tests were applied on the back and occluded for 2 days. Readings were performed on two occasions (D3 and D6–D7) for the 2000 and 2009 subgroups. For the 1992 subgroup, readings were performed only on D3. If readings of patch tests are performed only on D3 we will miss 10–15% of the positive reactions as compared with two readings (D2 and D7) (3). This applied for all test substances in the Swedish baseline series. Results were recorded according to ICDRG criteria (4). A +, ++ or +++ reaction at either reading or both readings was recorded as a positive patch test reaction in the present study. An irritant response, a doubtful response or a negative reading was recorded as a negative result. For

each test substance and subgroup, crude prevalence and prevalence stratified by sex and age (<40 or ≥40 years) were calculated. For statistical analyses, chi-square tests were used. The crude prevalence rates from the D3 readings in the three subgroups were compared to determine trends. Differences in prevalence between the 1992 and 2009 subgroups and between women and men after two readings (D3 and D6–D7) in the 2000 and 2009 subgroups were also analysed. Finally, chi-square analyses were used to compare prevalence stratified by sex or age (<40 or ≥40 years) for the test substances with a crude prevalence of >2% in 1992 and 2009 (one reading, D3), and to compare the number of positive test reactions per positively tested patient and the number of positively tested persons in each subgroup. The age and sex subgroups contained few patients, and test substances with crude prevalence rates of <2% were not analysed further. The significance level was set at  $p < 0.05$ . All calculations were performed with STATISTICA 12 for Windows™ (StatSoft®, Tulsa, Oklahoma, USA). Data from 1992 and 2000 have been published previously (3). These data are now compared with unpublished results from 2009. The study was based on the Swedish patch test register, EpiReg, which does not contain personal information other than age and sex. The use of this register was approved by the Research Ethical Committee in Uppsala.

## Results

The age and sex distributions of the subgroups are shown in Table 1. The median age was 39 years in 1992, 40 years in 2000, and 43 years in 2009. Crude and age-stratified and sex-stratified prevalence rates for one reading (D3) in the 1992, 2000 and 2009 subgroups are shown in Table 2. The test substances with significant prevalence variations from 1992 to 2009 are shown in Fig. 1. Figure 2 shows the sex-stratified prevalence after reading at D3 for the allergens with prevalence rates of >2.0%. Table 3 shows the prevalence rates for two readings (D3 and D6–D7) for 2000 and 2009. Comparison of reactions on D3 showed a significant difference, with at least one positive patch test reaction being observed in 47.8% of patients and an average of 1.5 positive reactions per positive patient in 1992 (only one reading at D3). Corresponding rates in 2000 and 2009 were 42.9% and 1.8 reactions, and 37.5% and 1.7 reactions, respectively. The ratio of positive test reactions to number of persons tested is shown in Table 4. A significantly ( $p < 0.05$ ) lower ratio was found in 2009 than in 1992. Allergens with sensitization rates of >2% in 2009 (with two readings, on D3 and D6–D7) were nickel, cobalt,

**Table 1.** Age and sex distributions in the 1992, 2000 and 2009 subgroups

| Subgroup | <40 years | ≥40 years | Total | F/M  |
|----------|-----------|-----------|-------|------|
| 1992     |           |           |       |      |
| Females  | 1209      | 1162      | 2371  | –    |
| Males    | 682       | 609       | 1291  | –    |
| Total    | 1891      | 1771      | 3662  | 1.84 |
| 2000     |           |           |       |      |
| Females  | 1169      | 1248      | 2417  | –    |
| Males    | 695       | 713       | 1408  | –    |
| Total    | 1864      | 1961      | 3825  | 1.75 |
| 2009     |           |           |       |      |
| Females  | 889       | 1104      | 1993  | –    |
| Males    | 507       | 612       | 1119  | –    |
| Total    | 1396      | 1716      | 3112  | 1.78 |

F, female; M, male.

fragrance mix I, *Myroxylon pereirae*, chromium, colophonium, formaldehyde, methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI), methyldibromo glutaronitrile (MDBGN), *p*-phenylenediamine, and fragrance mix II. For these most frequent sensitizers, statistically significant decreases in crude prevalence were found for nickel, cobalt, MCI/MI, fragrance mix I and colophonium between 1992 and 2009 (D3 reading) (Table 2, Fig. 1). MDBGN and fragrance mix II were not included in the baseline series in 1992. For *p*-phenylenediamine, there was a significant increase in crude prevalence during the same period. The crude prevalence for chromium did not change between 1992 and 2009. However, there was a significant increase among younger women and a decrease among older men. MDBGN was introduced into the baseline series after 1992, and fragrance mix II was introduced after 2000. They emerged as two of the most frequent sensitizers in 2009, with a rate of >2%. Between 1992 and 2009 (D3 readings), there were significantly decreased prevalence rates for Amerchol™ L 101, ethylenediamine dihydrochloride, neomycin sulfate, diazolidinyl urea, tosylamide/formaldehyde resin, and black rubber mix, all of which had sensitization rates of <2% (Table 2, Fig. 1).

Regarding nickel, the data showed (Table 2) that the decrease in the crude prevalence of contact allergy was attributable to a decrease among women, with the major contribution from younger women, in whom the prevalence had decreased by ~10 percentage points. For cobalt, there were significant decreases among younger women and among older men. The results of the comparison between women and men in 2000 and 2009 (D3 and D6–D7 readings) are shown in Table 3. Statistically significant differences, with a higher prevalence of contact allergy among women, were

found for nickel, cobalt, fragrance mix I, neomycin sulfate, MCI/MI, *p*-phenylenediamine, tixocortol pivalate, epoxy resin, ethylenediamine dihydrochloride, quaternium-15, primin, sesquiterpene lactone mix and tosylamide/formaldehyde resin in the 2000 subgroup. For nickel, cobalt, *p*-phenylenediamine, and epoxy resin, these differences remained in 2009, whereas the differences for the other substances were eliminated. For formaldehyde, there was a statistically significant difference between women and men in 2009, but not in 2000.

## Discussion

In the present study, we report contact allergy trends among patients seen at Swedish patch test clinics. Twenty-four allergens were followed over the period 1992–2009. The crude prevalence had decreased for 10 allergens, was unchanged for 13 allergens, and had increased for 1 allergen.

We have to point out two erroneous statements on patch test concentrations in our previous publication (3). In Sweden, we have tested cobalt chloride at 0.5% and MCI/MI at 0.02%, and not, as stated in the paper, at 1% and 0.01%, respectively.

Nickel is known to be the allergen with the highest sensitization rates, and nickel allergy is more common in women than in men, facts that are once again confirmed in our recent Swedish data (5). We found that nickel sensitization is decreasing among young women, a finding consistent with results previously documented by others in countries where legislative measures have been taken to limit nickel exposure (6). The EU nickel limitation (the former Nickel Directive, which, since 2009, has been part of the EU chemicals regulation REACH) entered into force in 2000. However, before that, there was already a decrease in nickel allergy among younger women, as shown in a previous study comparing Swedish patch test data from 1992 to 2000 (3). This was thought to be attributable to gradual adaptation to the forthcoming entry into force of the nickel regulation, which had been adopted in 1994 (3, 7). Similar effects on the prevalence of nickel allergy among younger females have been seen in Denmark, Germany, and Italy (8).

Between 1992 and 2000, the prevalence of cobalt allergy remained stable in Swedish dermatitis patients (3), but has now, when we compare 17 years from 1992, decreased significantly among younger females and older men (Table 2). In Denmark, contrasting results have been obtained. One study reported an unchanged prevalence in female dermatitis patients between 1985 and 2007, whereas another showed that the overall prevalence of cobalt allergy had increased from 1992 to 2009

**Table 2.** Crude and age-stratified prevalence (%) of positive reactions to allergens in the Swedish baseline series in 1992, 2000, and 2009; results of reading at D3

| Allergen                                         | Test concentration<br>2009 (%) | Crude prevalence |      |             | Prevalence in those<br>aged <40 years |      |             |      |      |            | Prevalence in those<br>aged age ≥40 years |      |             |      |      |            |
|--------------------------------------------------|--------------------------------|------------------|------|-------------|---------------------------------------|------|-------------|------|------|------------|-------------------------------------------|------|-------------|------|------|------------|
|                                                  |                                | 1992             | 2000 | 2009        | Women                                 |      |             | Men  |      |            | Women                                     |      |             | Men  |      |            |
|                                                  |                                |                  |      |             | 1992                                  | 2000 | 2009        | 1992 | 2000 | 2009       | 1992                                      | 2000 | 2009        | 1992 | 2000 | 2009       |
| Nickel sulfate                                   | 5.0                            | 21.4             | 19.8 | <b>17.6</b> | 33.8                                  | 29.4 | <b>23.3</b> | 7.3  | 6.4  | 6.1        | 25.2                                      | 26.3 | <b>24.7</b> | 5.4  | 6.2  | 6          |
| Fragrance mix I                                  | 8.0                            | 6.3              | 6.9  | 5.2         | 4.6                                   | 6    | 3.7         | 4.3  | 2.3  | 4.1        | 8.1                                       | 6    | 7.1         | 8.8  | 5.8  | <b>4.9</b> |
| <i>Myroxylon pereirae</i>                        | 25.0                           | 4.9              | 6.5  | 4.8         | 3.1                                   | 3.3  | 2.8         | 2.9  | 3.8  | 2.6        | 7.4                                       | 9.9  | 6.7         | 6.2  | 8.3  | 6.2        |
| Cobalt chloride                                  | 0.5                            | 6.6              | 6.4  | <b>4.5</b>  | 9.7                                   | 8.1  | <b>6.4</b>  | 4    | 3.8  | 2.6        | 6.9                                       | 8    | 5.2         | 2.5  | 3.1  | <b>2</b>   |
| Potassium dichromate                             | 0.5                            | 3.7              | 4.2  | 4.4         | 2.4                                   | 3.3  | <b>4.5</b>  | 2.8  | 2.5  | 3.9        | 4                                         | 5    | 4.8         | 6.7  | 5.7  | <b>4.1</b> |
| Formaldehyde                                     | 1.0                            | 2.5              | 2.6  | 2.5         | 2.5                                   | 2.8  | 2.7         | 1.5  | 1.5  | 1          | 2.8                                       | 3.2  | 3.1         | 3.3  | 2.6  | 2.3        |
| Colophonium                                      | 20.0                           | 5.4              | 3.4  | <b>2.4</b>  | 3.2                                   | 2    | <b>1.1</b>  | 2.5  | 2    | <b>0.8</b> | 8.8                                       | 5.4  | <b>3.8</b>  | 6.2  | 3.4  | <b>3.3</b> |
| <i>p</i> -Phenylenediamine                       | 1.0                            | 1.4              | 2    | <b>2.1</b>  | 1.2                                   | 1.6  | 2.4         | 0.4  | 0.9  | 0.4        | 2                                         | 3.2  | 3.3         | 1.6  | 1.7  | 1          |
| MCI/MI                                           | 0.02                           | 3.1              | 2.4  | <b>2</b>    | 2.5                                   | 2.1  | 1.7         | 1.6  | 0.9  | <b>0.4</b> | 4.2                                       | 3.6  | 2.8         | 4.1  | 2.1  | 2.3        |
| Thiuram mix                                      | 1.0                            | 2                | 1.2  | 1.6         | 1.3                                   | 0.5  | 1.2         | 1.3  | 1.7  | 1.4        | 2.7                                       | 1.8  | 2           | 2.9  | 1    | 1.6        |
| Quaternium-15                                    | 1.0                            | 1.1              | 1.2  | 1.4         | 1.3                                   | 1.5  | 1.8         | 0.4  | 0.3  | 0.6        | 0.8                                       | 1.4  | 1.4         | 1.8  | 1.1  | 1.3        |
| Tixocortol pivalate                              | 0.1                            | 1.7              | 1.6  | 1.2         | 1.3                                   | 2.2  | 1.6         | 1.3  | 0.9  | 1          | 2.7                                       | 1.7  | 1.3         | 1.3  | 1    | 0.8        |
| Epoxy resin                                      | 1.0                            | 1.3              | 1.2  | 1.2         | 0.7                                   | 0.7  | 1.1         | 1.5  | 0.7  | 0.9        | 1.1                                       | 1    | 1           | 2.3  | 3    | 2.1        |
| Amerchol™ L 101                                  | 50.0                           | 2.9              | 1.1  | <b>0.7</b>  | 2.6                                   | 0.8  | 1           | 1.2  | 0.6  | 0.2        | 4.3                                       | 1.4  | 0.6         | 2.6  | 1.7  | 0.8        |
| Caine mix                                        | 10.0                           | 1.1              | 1.2  | 0.7         | 0.5                                   | 0.4  | 0.1         | 0.7  | 0.7  | 1.1        | 1.3                                       | 1.8  | 0           | 2.3  | 2.1  | 1.5        |
| <i>p</i> -tert-Butylphenol<br>formaldehyde resin | 1.0                            | 0.8              | 1    | 0.7         | 1                                     | 0.9  | 0.7         | 0.9  | 0.3  | 1          | 0.8                                       | 1.1  | 0.6         | 0.5  | 1.7  | 0.8        |
| Diazolidinyl urea                                | 2.0                            | 1.9              | 1.4  | <b>0.5</b>  | 1.4                                   | 0.8  | 0.8         | 0.7  | 0.9  | 0.2        | 2.7                                       | 1.8  | 0.4         | 2.5  | 2.1  | 0.8        |
| Black rubber mix                                 | 0.6                            | 0.9              | 0.6  | <b>0.5</b>  | 0.6                                   | 0.4  | 0.3         | 0.6  | 0.3  | 0.6        | 1.1                                       | 0.8  | 0.5         | 1.5  | 1    | 0.5        |
| Neomycin sulfate                                 | 20.0                           | 1.9              | 1.2  | <b>0.4</b>  | 1.2                                   | 1    | 0.3         | 1    | 0.4  | 0.4        | 2.7                                       | 2    | 0.4         | 2.6  | 0.8  | 0.3        |
| Mercaptobenzothiazole                            | 2.0                            | 0.6              | 0.4  | 0.4         | 0.4                                   | 0.4  | 0.7         | 0.2  | 0.6  | 0.8        | 0.9                                       | 0.2  | 0.2         | 0.8  | 0.4  | 0.3        |
| Tosylamide/formaldehyde<br>resin                 | 10.0                           | 1                | 0.7  | <b>0.3</b>  | 1.2                                   | 0.8  | 0.1         | 0.2  | 0.2  | 0          | 1.6                                       | 1.3  | 0.5         | 0.5  | 0.3  | 0.5        |
| Paraben mix                                      | 16.0                           | 0.5              | 0.4  | 0.3         | 0.4                                   | 0.3  | 0.3         | 0.4  | 0.2  | 0.2        | 0.3                                       | 0.6  | 0           | 1.1  | 0.8  | 0.7        |
| Ethylenediamine<br>dihydrochloride               | 1.0                            | 1.9              | 1.4  | <b>0.2</b>  | 1.2                                   | 1    | 0.6         | 1.6  | 1.2  | 0.6        | 2.4                                       | 2.2  | 0.8         | 2.1  | 0.7  | 0          |
| Quinoline mix                                    | 6.0                            | 0.5              | 0.5  | 0.2         | 0.2                                   | 0.4  | 0.1         | 0.2  | 0.7  | 0.4        | 0.9                                       | 0.6  | 0.2         | 1    | 0.6  | 0.3        |

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone.

Allergens: bold type denotes allergens with significant changes/variations between 1992, 2000, and 2009 ( $p < 0.05$ ; chi-square).Crude prevalence: bold type denotes significant changes in crude prevalences between 2009 and 1992 ( $p < 0.05$ ; chi square).Age-stratified and sex-stratified prevalence: bold type denotes significant changes between 2009 and 1992 ( $p < 0.05$ ; chi-square). Allergens with a crude prevalence of  $> 2\%$  were analysed.

(9, 10). In a recent German study (11) covering the period 1992–2012, the overall prevalence of cobalt allergy was 5.23%, with increases for males aged  $< 45$  years and females aged  $\geq 45$  years during the period. The cause of these discrepancies between different studies is not known. A positive patch test reaction to cobalt is often, but not always, associated with a positive reaction to nickel (11). This has been suggested to be attributable to co-exposure and co-sensitization to these metals (3, 12), especially in females (13). Co-occurrence of cobalt and nickel in alloys is, however, considered to be less likely than formerly, owing to an increase in the price of cobalt and a higher degree of metal refining (14). Further studies on the relationship between exposure and sensitization are needed.

A decrease in the rate of contact allergy to fragrance mix I and *M. pereirae* has been reported by several investigators in Europe (15, 16). A possible cause of this is shift in the composition of fragrances. We could not confirm a decrease for *M. pereirae* in our study population, but found a tendency for there to be a decrease for fragrance mix I ( $p = 0.05$ ). Fragrance allergy has often been associated with female sex and older age (16, 17). A sex difference was found for fragrance mix I in the 2000 subgroup, but not in the 2009 subgroup. As fragrance mix II was included in the Swedish baseline series after the year 2000, no comparison between years is possible. The results from 2009 show that fragrance mix II is among the top allergens/mixes, with a crude prevalence of 2.3% and with no difference between sexes. Data from Germany,

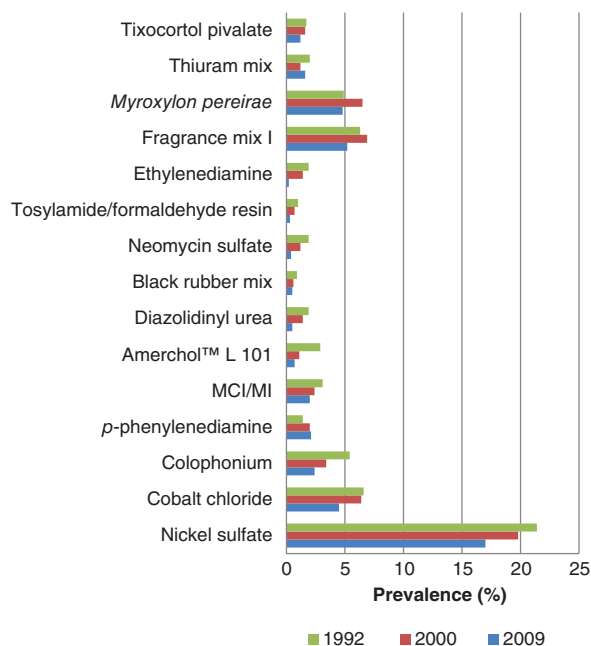


**Fig. 1.** The figure presents the allergens with significant variations ( $p < 0.05$ ) in prevalence rates during the period 1992–2000–2009. Crude prevalence rates for readings at D3 are shown. MCI/MI = Methylchloroisothiazolinone/Methylisothiazolinone.

Switzerland and Austria showed a prevalence of 4.9% in dermatitis patients in 2005–2008 (18).

Chromium allergy has been shown to have increased in Denmark with a prevalence of 3.3% in 2007 in consecutive dermatitis patients (the increase being attributed to leather exposure) (5). We found no statistically significant change in the crude prevalence over time (1992–2009). However, there was a significant increase among young females, and a decrease among older men; the latter is attributed to the restriction of chromium in cement.

Contact allergy to colophonium decreased in Sweden between 1992 and 2000, as previously reported (3). We found that there has been a further decrease in the 2009 subgroup.

The prevalence of contact allergy to formaldehyde has been reported to be 1.5% and 2.5% in European multicentre studies, with no statistically proven changes for the periods 1996–2009 and 2001–2008, respectively (19, 20). In our neighbouring country, Denmark, formaldehyde allergy remained relatively stable, at a level of approximately 2–4%, in 1985–2008. We found crude prevalence rates in line with previous data. Danish researchers found a higher prevalence in females, a finding only reproduced once, by us, in 2009 (21). We saw no changes over time (1992–2009).

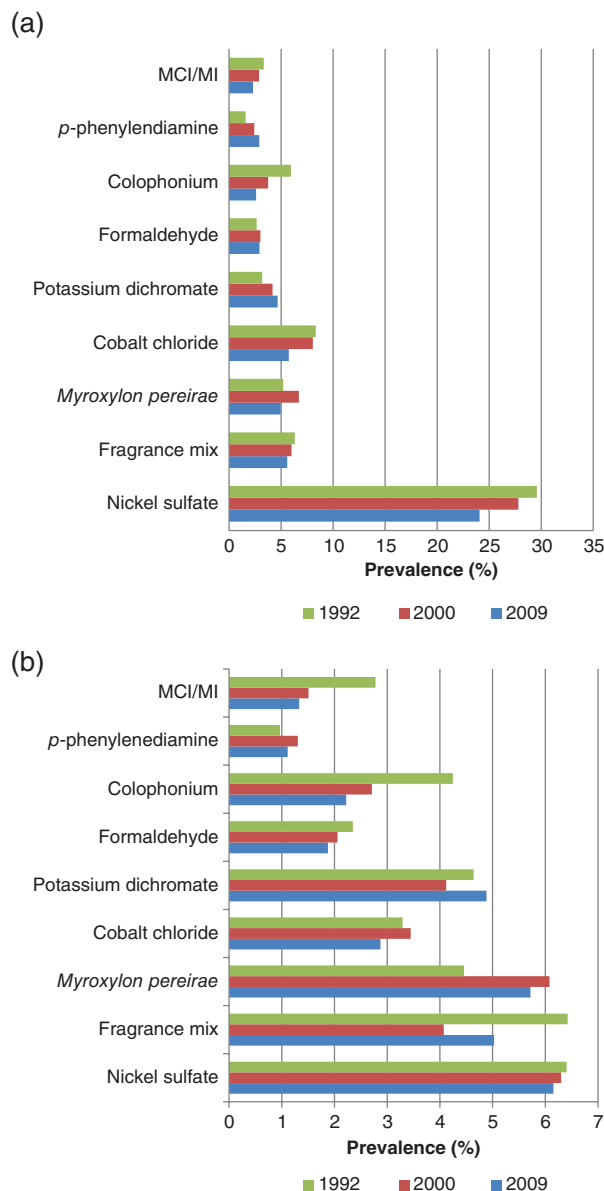


**Fig. 2.** Gender stratified variations in crude prevalence for allergens with a prevalence > 2.0% in 2009. Readings at D3. Figure 2 a = females; Figure 2 b = males. MCI/MI = Methylchloroisothiazolinone/Methylisothiazolinone.

A European multicentre study reported MCI/MI contact allergy to be stable at ~2.2% in 1996–2009 (19). The corresponding Danish level was 2% in 1985–2008 (21), and the German level for MCI/MI allergy for the period 1992–2010 was stable, at ~2.33% (22). However, in this study, there was an increase in MCI/MI allergy over time for younger persons with occupational dermatitis. In contrast, we found a decrease in the crude prevalence from 3.1% in 1992 to 2.0% in 2009. This trend

**Table 3.** Sex-stratified prevalence (%) of positive patch test reactions to allergens in the Swedish baseline series in 2000 and 2009; pooled results of two readings

|                                               | 2000  |            | 2009  |            |
|-----------------------------------------------|-------|------------|-------|------------|
|                                               | Women | Men        | Women | Men        |
| Nickel sulfate                                | 31.1  | <b>6.7</b> | 26.7  | <b>7.0</b> |
| Cobalt chloride                               | 10.0  | <b>4.5</b> | 7.3   | <b>3.0</b> |
| Fragrance mix I                               | 9.1   | <b>5.1</b> | 6.1   | 4.6        |
| <i>Myroxylon pereirae</i>                     | 6.9   | 6.3        | 5.2   | 4.7        |
| Potassium dichromate                          | 5.2   | 4.8        | 5.4   | 4.6        |
| Colophonium                                   | 4.2   | 3.2        | 3.4   | 2.2        |
| Formaldehyde                                  | 3.2   | 2.4        | 3.2   | <b>1.9</b> |
| Neomycin sulfate                              | 3.3   | <b>1.9</b> | 1.2   | 0.6        |
| MCI/MI                                        | 3.3   | <b>1.6</b> | 2.4   | 1.6        |
| MDBGN                                         | 2.4   | 1.8        | 2.2   | 1.8        |
| <i>p</i> -Phenylenediamine                    | 2.6   | <b>1.5</b> | 3.0   | <b>1.0</b> |
| Tixocortol pivalate                           | 2.4   | <b>1.3</b> | 1.9   | 1.3        |
| Diazolidinyl urea                             | 1.5   | 1.6        | 0.7   | 0.6        |
| Epoxy resin                                   | 1.1   | <b>2.1</b> | 0.7   | <b>1.8</b> |
| Ethylenediamine dihydrochloride               | 1.8   | <b>0.9</b> | 0.9   | 0.4        |
| Lichen acid mix                               | 1.6   | 1.1        | 0.8   | 0.8        |
| Caine mix                                     | 1.3   | 1.4        | 0.7   | 0.8        |
| Thiuram mix                                   | 1.3   | 1.3        | 1.8   | 1.6        |
| Quaternium-15                                 | 1.7   | <b>0.7</b> | 1.8   | 1.3        |
| Budesonide                                    | 1.1   | 1.6        | 0.9   | 0.6        |
| Amerchol™ L 101                               | 1.1   | 1.2        | 0.8   | 0.5        |
| <i>p</i> -tert-Butylphenol formaldehyde resin | 1.2   | 1.1        | 0.7   | 1.0        |
| Primin                                        | 1.7   | <b>0.1</b> | –     | –          |
| Sesquiterpene lactone mix                     | 1.3   | <b>0.4</b> | 0.5   | 0.4        |
| Tosylamide/formaldehyde resin                 | 1.2   | <b>0.2</b> | 0.4   | 0.4        |
| Black rubber mix                              | 0.7   | 0.7        | 0.6   | 0.5        |
| Quinoline mix                                 | 0.5   | 0.8        | 0.2   | 0.3        |
| Paraben mix                                   | 0.5   | 0.6        | 0.3   | 0.4        |
| Mercaptobenzothiazole                         | 0.4   | 0.5        | 0.5   | 0.6        |
| Fragrance mix II                              | –     | –          | 2.4   | 2.0        |
| HICC                                          | –     | –          | 1.1   | 1.2        |

HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; MDBGN, methylidibromo glutaronitrile. Values in bold denote  $p < 0.05$ .

was already evident in 2000. Earlier European patch test data for MCI/MI are based on testing with a concentration of 100 ppm. It has recently been reported that testing with MCI/MI 200 ppm gives more positive test reactions without irritation (23). In Sweden, we have tested with 200 ppm since the late 1980s. Just after the end of our study, a large number of reports started to appear concerning an alarming increase in the frequency of sensitization to MCI/MI and, particularly, to MI separately (24). Concerning contact allergy to MDBGN, prevalence rates of 2.5–4.5% have been reported for 2008–2009 (19–21). MDBGN has not been permitted in leave-on

**Table 4.** The number of positive test reactions per patch tested patient

| Group | Total | Females | Males |
|-------|-------|---------|-------|
| 1992  | 0.84  | 0.82    | 0.86  |
| 2000  | 0.75  | 0.89    | 0.52  |
| 2009  | 0.63  | 0.73    | 0.45  |

Chi-square analysis showed a significant difference ( $p < 0.05$ ) between 1992 and 2009.

cosmetic products since 2005 (25), and it has not been permitted in any cosmetic products since 2008 (26). MDBGN is, however, allowed in other types of products, without limitation. A decline in contact allergy to this allergen has been shown since 2008 by others, a finding that was not reproduced in the current data (19). Future analyses of data from our database (EpiReg) will show whether the same trends for MCI/MI, MI and MDBGN found in other countries can be seen in Sweden.

Previous studies have shown differing results regarding trends in sensitization to *p*-phenylenediamine. In two different studies, the sensitization rate in Sweden was shown to increase in 1992–2000 (3) and to remain stable in 1993–2000 (27). In Denmark, an overall proportion of 2% positive patients was found in 1985–2007, with a statistically non-significant increase during the study period (28). We found the crude prevalence to be 2.1% in the 2009 subgroup, an increase from 1.4% in 1992. Contact allergy to *p*-phenylenediamine was more frequent in women [with increases from 1.2% to 2.4% among younger women (<40 years) and from 2% to 3.3% among older women]. This is probably attributable to more widespread use of hair dye products among women.

We found a decline in the prevalence of sensitization to neomycin sulfate. This has previously been observed in Germany, and is thought to be the result of decreased use of this substance as a topical agent (29). Neomycin has not been available as a topical medicament in Sweden for several years.

Finally, the prevalence of contact allergy to tosylamide/formaldehyde resin has decreased since 1992. Exposure to the resin has decreased, as it has been replaced by acrylates in modern nail lacquers.

In this study, data reported as subgroups 1992, 2000 and 2009 were collected during comparable time periods, and the participating sites were the same (apart from some minor differences), which is a strength. The study is, however, retrospective in nature, which means that we have no control over changes in referral patterns or indications for patch testing over time. However, the inclusion criterion for patch testing in Sweden is contact dermatitis with a suspicion of contact allergy.

A higher percentage of patients with positive patch test results in 1992 than in 2009, and fewer positive test reactions per tested patient in 2009, might indicate that the indication for testing has widened. However, it could also be a sign of decreasing rates of sensitization to the tested allergens. During the period 1992–2009, nickel, chromium and MCI/MI were subjected to regulations, and exposure to some allergens (e.g. neomycin, ethylenediamine, and tosylamide/formaldehyde resin) decreased in Sweden; for some allergens (e.g. colophonium, rubber chemicals, and some perfumes) the actual exposure situation is more uncertain. The reactivity among patch test-positive patients appears not to have changed, as the average number of positive test reactions per positively tested patient remains stable.

Although we have identified significant changes in prevalence, the study used three measuring points, and variations could have occurred between these points. The analysis was also performed on a selected population in

which contact allergy prevalence rates can be expected to exceed those of the general population, meaning that no valid assumptions about the latter can be made. Thus, future studies should ideally be population-based.

## Acknowledgements

This study was performed on behalf of the Swedish Contact Dermatitis Research Group. The following departments of dermatology in Sweden provided test results: Unit of Occupational and Environmental Dermatology, Centre for Occupational and Environmental Medicine, Stockholm County Council (and previous organizations); Malmö University Hospital; Lund University Hospital; Sahlgrenska University Hospital, Göteborg; Karolinska University Hospital, Stockholm; Linköping University Hospital; Norrland University Hospital, Umeå; Örebro University Hospital; Eskilstuna, Mälars Hospital; Huddoktorn, private practice in Örebro; Karlskoga lasarett; Lindesberg lasarett; Ryhov Hospital, Jönköping; Uppsala University Hospital.

## References

- 1 Schnuch A, Geier J, Lessmann H, Arnold R, Uter W. Surveillance of contact allergies: methods and results of the Information Network of Departments of Dermatology (IVDK). *Allergy* 2012; **67**: 847–857.
- 2 Johansen J, Menné T, Christophersen J, Kaaber K, Veien N. Changes in the pattern of sensitization to common contact allergens in Denmark between 1985–1986 and 1997–1998, with a special view to the effect of preventive strategies. *Br J Dermatol* 2000; **142**: 490–495.
- 3 Lindberg M, Edman B, Fischer T, Stenberg B. Time trends in Swedish patch test data from 1992 to 2000. A multi-centre study based on age- and sex-adjusted results of the Swedish standard series. *Contact Dermatitis* 2007; **56**: 205–210.
- 4 Lindberg M, Matura M. Patch testing. In: *Contact Dermatitis*, 5th edition, (Duus Johansen J, Frosch P J, Lepoittevin J P, Eds); Berlin, Heidelberg, Springer-Verlag, 2011: 439–464.
- 5 Thyssen J P. The epidemiology of contact allergy. Allergen exposure and recent trends. *G Ital Dermatol Venereol* 2009; **144**: 507–514.
- 6 Thyssen J P, Johansen J D, Menné T. Contact allergy epidemics and their controls. *Contact Dermatitis* 2007; **56**: 185–195.
- 7 Thyssen J P, Uter W, McFadden J, Menné T, Spiewak R, Vigan M, Gimenez-Arnau A, Lidén C. The EU Nickel directive revisited – future steps towards better protection against nickel allergy. *Contact Dermatitis* 2011; **64**: 121–125.
- 8 Garg S, Thyssen J P, Uter W et al. Nickel allergy following EU regulation in Denmark, Germany, Italy, and the United Kingdom. *Br J Dermatol* 2013; **169**: 854–858.
- 9 Carøe C, Andersen K E, Mortz C G. Fluctuations in the prevalence of nickel and cobalt allergy in eczema patients patch tested after implementation of the nickel regulation in Denmark. *Contact Dermatitis* 2011; **64**: 126–131.
- 10 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.
- 11 Uter W, Gefeller O, Geier J, Schnuch A. Contact sensitization to cobalt – multifactorial analysis of risk factors based on long-term data of the Information Network of Departments of Dermatology. *Contact Dermatitis* 2014; **71**: 326–337.
- 12 Garner L A. Contact dermatitis to metals. *Dermatol Ther* 2004; **17**: 321–327.
- 13 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.
- 14 Thyssen J P, Menné T, Lidén C et al. Cobalt release from implants and consumer items and characteristics of cobalt sensitized patients with dermatitis. *Contact Dermatitis* 2012; **66**: 113–122.
- 15 Schnuch A, Lessmann H, Geier J, Frosch P J, Uter W. Contact allergy to fragrances: frequencies of sensitization from 1996 to 2002. Results of the IVDK\*. *Contact Dermatitis* 2004; **50**: 65–76.
- 16 Thyssen J P, Carlsen B C, Menné T, Johansen J D. Trends of contact allergy to fragrance mix I and Myroxylon pereirae among Danish eczema patients tested between 1985 and 2007. *Contact Dermatitis* 2008; **59**: 238–244.
- 17 Thyssen J P, Menné T, Linneberg A, Johansen J D. Contact sensitization to fragrances in the general population: a Koch's approach may reveal the burden of disease. *Br J Dermatol* 2009; **160**: 729–735.
- 18 Krauthaim A, Uter W, Frosch P, Schnuch A, Geier J. Patch testing with fragrance mix II: results of the IVDK 2005–2008. *Contact Dermatitis* 2010; **63**: 262–269.
- 19 Schnuch A, Lessmann H, Geier J, Uter W. Contact allergy to preservatives. Analysis of IVDK data 1996–2009. *Br J Dermatol* 2011; **164**: 1316–1325.
- 20 Svedman C, Andersen K E, Brandão F M et al. Follow-up of the monitored levels of preservative sensitivity in Europe: overview of the years 2001–2008. *Contact Dermatitis* 2012; **67**: 312–314.
- 21 Thyssen J P, Engkilde K, Lundov M D, Carlsen B C, Menné T, Johansen J D.

- Temporal trends of preservative allergy in Denmark (1985–2008). *Contact Dermatitis* 2010; **62**: 102–108.
- 22 Uter W, Gefeller O, Geier J, Schnuch A. Methylchloroisothiazolinone/methylisothiazolinone contact sensitization: diverging trends in subgroups of IVDK patients in a period of 19 years. *Contact Dermatitis* 2012; **67**: 125–129.
  - 23 Bruze M, Isaksson M, Gruvberger B et al. Patch testing with methylchloroisothiazolinone/methylisothiazolinone 200 ppm aq. detects significantly more contact allergy than 100 ppm. A multicentre study within the European Environmental and Contact Dermatitis Research Group. *Contact Dermatitis* 2014; **71**: 31–34.
  - 24 Geier J, Lessmann H, Schnuch A, Uter W. Recent increase in allergic reactions to methylchloroisothiazolinone/methylisothiazolinone: is methylisothiazolinone the culprit? *Contact Dermatitis* 2012; **67**: 334–341.
  - 25 European Commission, Scientific Committee on Consumer Products. Commission Directive 2003/83/EC, 0000. Available at: [http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=ref\\_data.directives](http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=ref_data.directives) (last accessed 23 December 2014).
  - 26 European Commission, Scientific Committee on Consumer Products. Commission Directive 2007/17/EC, 0000. Available at: [http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=ref\\_data.directives](http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=ref_data.directives) (last accessed 23 December 2014).
  - 27 Wahlberg J, Tammela M, Anderson C et al. Contact allergy to p-phenylenediamine in Sweden. *Occup Environ Dermatol* 2002; **50**: 51–54.
  - 28 Thyssen J P, Carlsen B C, Søsted H, Menné T, Johansen J D. Frequency of p-phenylenediamine sensitization among Danish eczema patients tested between 1985 and 2007. *Contact Dermatitis* 2008; **59**: 184–185.
  - 29 Menezes de Pádua C A, Schnuch A, Lessmann H, Geier J, Pfahlberg A, Uter W. Contact allergy to neomycin sulfate: results of a multifactorial analysis. *Pharmacoepidemiol Drug Saf* 2005; **14**: 725–733.