The European baseline series in 10 European Countries, 2005/2006 – Results of the European Surveillance System on Contact Allergies (ESSCA)

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Background: Continual surveillance based on patch test results has proved useful for the identification of contact allergy.

Objectives: To provide a current view on the spectrum of contact allergy to important sensitizers across Europe.

Patients/Methods: Clinical and patch test data of 19 793 patients patch tested in 2005/2006 in the 31 participating departments from 10 European countries (the European Surveillance System on Contact Allergies’ (ESSCA) www.essca-dc.org) were descriptively analysed, aggregated to four European regions.

Results: Nickel sulfate remains the most common allergen with standardized prevalences ranging from 19.7% (central Europe) to 24.4% (southern Europe). While a number of allergens shows limited variation across the four regions, such as Myroxylon pereirae (5.3–6.8%), cobalt chloride (6.2–8.8%) or thiuram mix (1.7–2.4%), the differences observed with other allergens may hint on underlying differences in exposures, for example: dichromate 2.4% in the UK (west) versus 4.5–5.9% in the remaining EU regions, methylchloroisothiazolinone/methylisothiazolinone 4.1% in the South versus 2.1–2.7% in the remaining regions.

Conclusions: Notwithstanding residual methodological variation (affecting at least some ‘difficult’ allergens) tackled by ongoing efforts for standardization, a comparative analysis as presented provides (i) a broad overview on contact allergy frequencies and (ii) interesting starting points for further, in-depth investigation.

Key words: clinical epidemiology; contact allergy; patch testing. © John Wiley & Sons A/S, 2009.

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Past experience has shown that clinical surveillance of contact allergy, i.e. systematic analysis of patch test data, is a prerequisite for the identification and, ultimately, the control of contact allergy epidemics (1). As these often start locally or nationally, continual analysis should not only focus on global trends but also on possible differences between, e.g. European regions to derive valuable starting points for the in-depth investigation of possible unacceptable exposures. On a European level, the ‘European Surveillance System on Contact Allergies’ (ESSCA; www.essca-dc.org) has proved useful in providing current information on the spectrum of contact allergy across Europe in the countries participating (2, 3). The present analysis of 2005/2006 patch test data aims at providing an update.

**Methods**

Background information on the objectives and methods of the ESSCA has been reported (2). Briefly, patch test results obtained with the European Baseline Series and selected other allergens also tested in consecutive patients, e.g. in local or national adaptations of the European Baseline Series, were collected along with basic demographic and clinical data. After import from the various patch test software databases, including ‘WinAlldat/ESSCA’ (4), internal reports were delivered to each centre to be checked for completeness and plausibility. If feedback necessitated amendments, these were made before pooling data for the analyses presented. As a compromise between a global and a very detailed results presentation on the level of single departments, a regional aggregation within Europe was chosen with the ‘western’ region equivalent to the UK, but otherwise grouping several countries in one region (Table 1).

Routine patch test exposure time was 2 days, except in Kiel, Germany, where it was 1 day. Patch test results were recorded according to international guidelines (5). The standard ‘positive outcome’ (allergic reaction) of the patch test was defined as a morphologically + to +++ reaction (5) between D3 and D5 after the application of the patch test which was not, upon final evaluation, considered irritant. Descriptive analysis of data followed current guidelines as elaborated by ESSCA (6), in particular employing age- and sex-standardization of sensitization prevalences (7). For data management and descriptive analysis, the statistical software package SAS™ (version 9.1, SAS Institute, Cary, NC, USA) was used.

**Results**

In the 31 participating departments 9695 patients were patch tested in the year 2005 in the course of 9767 consultations, and 10 293 patients were tested in 2006, in the course of 10 366 consultations (Table 1), i.e. a small proportion of patients was seen and patch tested more than once. In these cases, the most current consultation was chosen for analysis. In the following analyses, the 2 years are aggregated. The median number of patients per clinic was 608 in the 2 years. With 240 and 110 patients, respectively, Middlesbrough, UK and Bern, Switzerland contributed the lowest number of patients (in 2006 only). The largest number of patients consulted the departments in Amsterdam, The Netherlands and Leeds, UK (1558 and 1537 patients, respectively). Among the 31 departments, one department is specialized in paediatric dermatology (Padova ‘Pedia-

tra’, Italy). Because of its restricted age range (all patients less than 18 years old, see Ref. (3)), and in view of the fact that many allergens exhibit a strong association with age, the results of this specialized department are not included in the further analyses presented in this paper but will be reported elsewhere.

The distribution of important demographic variables according to the MOAHlFA index in the four regions is shown in Table 2. While the proportion of male patients is relatively similar, other patient characteristics differ more – most markedly the proportion of patients with occupational dermatitis, diagnosed upon final evaluation (see Discussion). The age distribution showed some differences, with the youngest patients tested in the south (median age 39, inter-quartile range [IQR] 26–56) and the oldest in central Europe (median age 45 years, IQR 32–58), the western (median 43 years, IQR 29–58) and north-eastern (median 42 years, IQR 30–52) regions occupying an intermediate rank.

In 25 of the 31 centres at least 95% of the patients were tested with the European Baseline Series (8), as locally or nationally adapted, in five centres between 90% and 95%. In one centre only (Erlangen, Germany) slightly fewer than 90% of the patients were tested to this series. The proportion of patients with positive reactions to at least one allergen of the European Baseline Series among those tested with this series as used in the respective department displayed considerable variability between centres, but was very similar across regions (Table 1). The patch test results with the European Baseline Series in the 30 departments, aggregated to four regions, are shown in Table 3, the allergens grouped into different classes (fragrances, metals, preservatives, rubber allergens, a few ‘diverse’ allergens and topical agents). The number of patients
Table 1. Participating ESSCA departments in 2005/2006 with patient numbers

<table>
<thead>
<tr>
<th>Region</th>
<th>Department</th>
<th>Shorthand</th>
<th>Allergen supplier(s)(^{#})</th>
<th>Number of patients</th>
<th>Number of consultations(^{$})</th>
<th>Percentage positive to ESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergen supplier(s)(^{#})</td>
<td>Number of patients</td>
<td>Number of consultations(^{$})</td>
<td>Percentage positive to ESS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Amersham UK-01 HT, CH 1038 1061 41.6
- Nottingham UK-02 HT, CH 926 926 45.2
- Oxford* UK-04 HT, CH 372 372 45.2
- Sheffield UK-05 HT, CH 808 808 40.0
- Dundee UK-07 HT, CH 919 919 35.9
- Leeds UK-08 HT, CH 1537 1537 36.8
- Aberdeen UK-09 HT, CH 605 605 62.5
- Liverpool UK-10 HT, CH 613 613 42.0
- Dundee UK-11 HT, CH 618 618 49.5
- Middlesbrough* UK-12 HT, CH 240 240 59.6
- Swansea UK-30 HT, CH 344 344 44.5
- Cardiff UK-31 HT, CH 584 584 36.8

**West**
- Barcelona ES-01 HT, CH 751 755 43.5
- Napoli IT-01 CH 708 708 36.1
- Padova IT-02 CH 895 895 52.7
- Padova Ped. IT-03 CH 648 648 30.6
- Pordenone IT-06 CH 431 431 41.1

**South**
- Groningen NL-01 TT 784 793 41.8
- Amsterdam-VU NL-02 HT, CH 1558 1582 42.7
- Basel CH-42 TT, HT 517 535 47.3
- Bern* CH-56 HT 110 112 56.5
- Graz AT-25 HT 660 660 50.9
- Dortmund DE-01 HT 593 602 31.1
- Göttingen DE-03 HT 258 261 37.1
- Kiel DE-06 HT 470 472 48.8
- Jena DE-12 HT 672 696 40.4
- Erlangen DE-24 HT 683 744 50.1

**Central**
- Helsinki FI-01 HT, CH 296 297 42.1
- Lahti FI-02 CH 465 465 50.3
- Kaunas LT-01 HT 242 242 46.3
- Lodz PL-01 CH 608 608 39.1

**Northeast**
- 1611 1612 44.0

\(^{\#}\)HT = Trolab\(^{\text{TM}}\) (Almirall-Hermal, Reinbek, Germany), CH = Chemotechnique Diagnostics\(^{\text{TM}}\) (Malmo, Sweden), TT = True test\(^{\text{®}}\).

\(^{\$}\)Consultation is the presentation of a patient for patch testing, possibly multiply during a period.

*2006 only.

tested varies within regions, because of different compositions of the local standard series in the departments aggregated, or because allergens have been withdrawn or added to the series during the study period, such as hydroxyisohexyl 3-cyclohexene carboxaldehyde (e.g. Lyral\(^{\text{®}}\)) or the fragrance mix II. Regarding methyldibromo glutaronitrile, a subset of ‘central’ patients had initially (also) been tested with 0.2% in petrolatum, yielding 3.0% [95% confidence interval (CI): 2.3–3.7%] standardized positive reactions.

The temporary addition of allergens to a Baseline series (locally or in a contact allergy network) can give clues on its potential to become a permanent part of the Baseline series. Among those allergens tested in consecutive patients in more than one region, 2-bromo-2-nitropropane-1,3-diol (bronopol) yielded 1.1% and 1.2% positive reactions in the ‘West’ (tested 0.25% in pet.) and the ‘Central’ region (tested 0.5% in pet.), respectively appears to be a candidate for inclusion.

**Discussion**

The present descriptive analysis of contact allergy prevalences in patients patch tested for suspected allergic contact dermatitis throughout many, albeit not all, European countries differs from the preceding report, which contrasted global contact allergy prevalences (and MOAHFLA characteristics) with local minima and maxima (3): In an attempt to reduce the impact of inter-departmental variation in patient characteristics and the potential for variation in interpretation of positive reactions several centres have now been aggregated to regions. This reduced the amount of variation and yielded a more stable picture. As a trade-off, local clustering of contact allergy to specific allergens cannot be recognized. However, supplementary centre-wise reports from
the contributing national contact dermatitis groups can compensate for this (e.g. Ref. (9)).

Still, focussing first on the patient characteristics according to the MOAHLFA index, remarkable differences persisted. As mentioned above, the specialization of two of four ‘north-eastern’ departments in occupational dermatology [Finnish Institute of Occupational Health (FIOH), Helsinki, Finland and Nofer Institute, Lodz, Poland] has a strong impact on the MOAHLFA index, with a very high proportion of occupational dermatitis (2004 average: 14.3%) and hand dermatitis (2004 average: 32.9%), see Table 2. In the UK patients with facial dermatitis are over-represented compared with the remaining regions, while the proportion of patients with dermatitis affecting the leg and hand and male patients is very similar. The proportion of patients aged 40 and above is high among the ‘central’ European patients, mostly due to the German patients (10). As many allergens exhibit an age gradient – positive, e.g., the fragrance mix (11, 12), or negative, as in case of nickel (13) – an age distribution differing across space (as here) or over time may confound comparisons. Hence, the contact allergy prevalences have been standardized for age and sex in this analysis, following pertinent guidelines (6).

The European Baseline Series is continually being adapted by a working group of the European Society of Contact Dermatitis (ESCD). During the study period, the latest addition had been methylidibromo glutaronitrile, recommended to be tested at 0.5% in pet. (14). While this allergen had indeed been included by most ESSCA participants, the most common test concentration was 0.3%. About 3 years later, the fragrance mix II (14% pet.) and hydroxyisohexyl 3-cyclohexene carboxaldehyde (5% pet.) have been included in the recommendation (8). As these allergens, in particular hydroxyisohexyl 3-cyclohexene carboxaldehyde, have been tested by several groups starting in 2005 or 2006 (earlier in some centres) already, the present analysis is able to confirm the necessity to include these important fragrance allergens in the European Baseline Series in terms of a high contact allergy prevalence. With respect to the metal allergens the regionally aggregated prevalences of contact allergy to nickel appear remarkably similar, and to average out between-centre differences (even within regions) previously noted (3). In contrast, patch test results with cobalt and particularly with chromate diverge more, with the contact allergy prevalence to chromate being significantly lower in the UK (‘western’ region) than in each of the other three regions. This observation may warrant further investigation.

Some allergens such as p-phenylenediamine, *Myroxylon pereirae* resin, thiuram mix or budesonide yielded very similar contact allergy frequencies, which may illustrate fairly homogenous exposure across Europe. In case of other allergens outliers are observed:

- Contact allergy to lanolin (wool alcohol) is significantly more common in ‘central’ Europe than in the remaining regions – be it due residual...
### Table 3. Test results with the European Baseline Series (EBS) (8) in the four regions

<table>
<thead>
<tr>
<th></th>
<th>Western</th>
<th>Southern</th>
<th>Central</th>
<th>Northeast</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>nr(t)</td>
<td>%p 95% CI</td>
<td>%</td>
</tr>
<tr>
<td><strong>Fragrance mix I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.0</td>
<td>8539</td>
<td>614</td>
<td><strong>6.8</strong></td>
</tr>
<tr>
<td><strong>Fragrance mix II</strong></td>
<td>14</td>
<td>782</td>
<td>19</td>
<td><strong>2.5</strong></td>
</tr>
<tr>
<td>Hydroxyisohexyl 3-cyclohexene carboxaldehyde (LYRAL™)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0</td>
<td>4787</td>
<td>89</td>
<td><strong>1.8</strong></td>
<td>1 (1.4–2.2)</td>
</tr>
<tr>
<td><strong>Hydroxyisohexyl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myroxylon pereirae</td>
<td>25</td>
<td>8537</td>
<td>488</td>
<td><strong>5.4</strong></td>
</tr>
<tr>
<td>Nickel sulfate</td>
<td>5.0</td>
<td>8468</td>
<td>1752</td>
<td><strong>20.8</strong></td>
</tr>
<tr>
<td>Cobalt(II) chloride</td>
<td>1.0</td>
<td>8498</td>
<td>522</td>
<td><strong>6.2</strong></td>
</tr>
<tr>
<td>Potassium dichromate</td>
<td>0.5</td>
<td>8537</td>
<td>211</td>
<td><strong>2.4</strong></td>
</tr>
<tr>
<td>Colophonium</td>
<td>20</td>
<td>8529</td>
<td>333</td>
<td><strong>3.8</strong></td>
</tr>
<tr>
<td>p-Phenylenediamine</td>
<td>1.0</td>
<td>8535</td>
<td>313</td>
<td><strong>3.6</strong></td>
</tr>
<tr>
<td>Lanolin alcohol</td>
<td>30</td>
<td>8543</td>
<td>125</td>
<td><strong>1.4</strong></td>
</tr>
<tr>
<td>Methylidibromo glutaraldehyde + 2-phenoxethanol</td>
<td>1.0</td>
<td>8549</td>
<td>109</td>
<td><strong>1.2</strong></td>
</tr>
<tr>
<td>Methylidibromo glutaraldehyde</td>
<td>0.3</td>
<td>8549</td>
<td>109</td>
<td><strong>1.2</strong></td>
</tr>
<tr>
<td>Methylchloroisothiazolinone/Methylhylisothiazolinone*</td>
<td>0.01</td>
<td>7504</td>
<td>159</td>
<td><strong>2.1</strong></td>
</tr>
<tr>
<td>Formaldehyde*</td>
<td>1.0</td>
<td>8541</td>
<td>179</td>
<td><strong>2.0</strong></td>
</tr>
<tr>
<td>Quaternium-15</td>
<td>1.0</td>
<td>8550</td>
<td>158</td>
<td><strong>1.8</strong></td>
</tr>
<tr>
<td>Paraben mix</td>
<td>16</td>
<td>8552</td>
<td>60</td>
<td><strong>0.7</strong></td>
</tr>
<tr>
<td>Thiuram mix</td>
<td>1.0</td>
<td>8540</td>
<td>199</td>
<td><strong>2.2</strong></td>
</tr>
<tr>
<td>2-Mercaptobenzothiazole</td>
<td>2.0</td>
<td>8546</td>
<td>84</td>
<td><strong>1.0</strong></td>
</tr>
<tr>
<td>Mercapto mix</td>
<td>2.0</td>
<td>8535</td>
<td>60</td>
<td><strong>0.7</strong></td>
</tr>
<tr>
<td>Allergen</td>
<td>Western</td>
<td>Southern</td>
<td>Central</td>
<td>Northeast</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------</td>
<td>----------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td></td>
<td>% nr(t)</td>
<td>nr(p) %p</td>
<td>95% CI</td>
<td>nr(t) nr(p) %p 95% CI</td>
</tr>
<tr>
<td>Mercapto mix (only CBS, MBTS, MOR)</td>
<td>1.0</td>
<td>473 0 0</td>
<td></td>
<td>3414 31 1.0 (0.6–1.4)</td>
</tr>
<tr>
<td>N-isopropyl-N′-phenyl-p-phenylene diamine (IPPD)</td>
<td>0.1 8528 27 0.3 (0.2–0.5)</td>
<td>2666 24 0.9 (0.5–1.2)</td>
<td>4790 51 1.1 (0.8–1.4)</td>
<td>849 5 0.7 (0.1–1.3)</td>
</tr>
<tr>
<td>Epoxy resin</td>
<td>1.0 8544 81 0.9 (0.7–1.1)</td>
<td>2665 23 0.9 (0.5–1.2)</td>
<td>5741 118 2.0 (1.7–2.4)</td>
<td>1603 24 1.6 (0.9–2.2)</td>
</tr>
<tr>
<td>4-tert-butylphenol formaldehyde resin</td>
<td>1.0 8551 55 0.6 (0.5–0.8)</td>
<td>1942 26 1.4 (0.8–1.9)</td>
<td>5740 72 1.3 (1.0–1.6)</td>
<td>1606 12 0.8 (0.3–1.3)</td>
</tr>
<tr>
<td>Sesquiterpene lactone mix</td>
<td>0.1 8547 100 1.1 (0.9–1.3)</td>
<td>1904 10 0.5 (0.2–0.8)</td>
<td>2610 19 0.7 (0.4–1.0)</td>
<td>1144 9 0.8 (0.3–1.3)</td>
</tr>
<tr>
<td>Primin</td>
<td>0.01 8552 23 0.2 (0.1–0.3)</td>
<td>1987 22 1.1 (0.6–1.5)</td>
<td>1904 9 0.5 (0.2–0.8)</td>
<td>1606 3 0.2 (0.0–0.3)</td>
</tr>
<tr>
<td>Neomycin sulfate</td>
<td>20 8544 170 1.9 (1.6–2.2)</td>
<td>2666 39 1.4 (1.0–1.9)</td>
<td>3239 39 1.1 (0.8–1.5)</td>
<td>1598 64 3.8 (2.9–4.7)</td>
</tr>
<tr>
<td>Benzocaine</td>
<td>5.0</td>
<td>2665 28 1.0 (0.7–1.4)</td>
<td>890 13 1.3 (0.6–2.1)</td>
<td>849 10 1.3 (0.5–2.1)</td>
</tr>
<tr>
<td>Chloquinol</td>
<td>5.0</td>
<td>1574 3 0.2 (0.0–0.4)</td>
<td>1377 1 0.1 (0.0–0.2)</td>
<td>1490 8 0.5 (0.2–0.9)</td>
</tr>
<tr>
<td>Budesonide§</td>
<td>0.01 8547 56 0.6 (0.5–0.8)</td>
<td>1302 9 0.7 (0.3–1.2)</td>
<td>1376 10 0.7 (0.3–1.1)</td>
<td>1512 9 0.6 (0.2–0.9)</td>
</tr>
<tr>
<td>Tixocortol-21-pivalate§</td>
<td>0.1 6211 85 1.3 (1.1–1.6)</td>
<td>1311 1 0.1 (0.0–0.3)</td>
<td>2083 18 0.9 (0.5–1.2)</td>
<td>1364 24 1.7 (1.0–2.4)</td>
</tr>
</tbody>
</table>

*Budesonide tested 0.1% and tixocortol-21-pivalate 1% by the UK departments (‘western’). Methyldibromo glutaronitrile 0.5% in pet. had not been tested in the period. Allergens were tested in pet., except where otherwise indicated (*water). nr(t): number tested; nr(p): number positive; %p: percent positive (standardized for age and sex); 95% CI: accompanying 95% confidence interval. IT-03 not included.
confounding by higher age, or differing specific reading standards (which may, of course, explain some amount of variation in case of other allergens as well).

- The prevalence of contact allergy to methyl dibromo glutaronitrile (tested 0.3%) showed marked variation across Europe, but also nationally (9) which seems hard to explain, assuming that the main exposure via leave-on and rinse-off cosmetics is fairly homogenous due to a European market of these products. However, methyl dibromo glutaronitrile can probably be regarded a declining allergen (15).
- Methylchloroisothiazolinone/methylisothiazolinone has achieved a relatively stable contact allergy prevalence of around 2%, notwithstanding some between-centre variation (3, 9) or decreases noted in some parts of Europe (16). However, in the ‘south’ contact allergy to this preservative is still significantly more common, which may warrant investigation of possible sensitizing exposures.
- Neomycin sulfate is still (slightly) above 1% positive patch test reactions in consecutively tested patients and thus qualifies as part of the European Baseline Series. However, at least in Germany, it is not available as over-the-counter drug, prescriptions decrease and, accordingly, contact allergy prevalence decreases (17).
- In contrast to budesonide, contact allergy frequencies to tixocortol-21-pivalate varied significantly as has also been found in previous studies (reviewed in Ref. (18)). It has been pointed out that the corticosteroids should best be read at D7 of the test, so with the presently employed reading frame (D3–D5) some false-negative results may be expected (18). Moreover, the issue of the ideal test concentration does not seem to be settled: regarding tixocortol-21-pivalate, the British Contact Dermatitis Society recommends (19) and uses 1% instead of 0.1%.

It has been stated that the contact allergy prevalence in consecutively tested patients should normally exceed 0.5–1% for an allergen to be eligible for inclusion in the Baseline series (20). From this background and other considerations as well, cloquinal could be removed from this [also (3, 16)], while other, overall rare, sensitizers are at least regionally more important, such as primin or N-isopropyl-N'-phenyl-p-phenylenediamine (IPPD).

**Conclusion**

The 2005/2006 results provide an up-to-date view on the prevalence of contact allergy to allergens of the (European) Baseline Series across Europe. Methodological differences may contribute to between-centre, possibly also to between-country, variation. Hence, methods to standardize application and reading, and to monitor the reproducibility of reading and interpretation of patch test results within national and international contributors to contact dermatitis databases should be (further) developed. Still, the comparison potentially offers starting points for the in-depth investigation of possible causes of contact allergy in those areas particularly affected.

**References**


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