

# Patch test results of the European baseline series among patients with occupational contact dermatitis across Europe – analyses of the European Surveillance System on Contact Allergy network, 2002–2010

Maria Pesonen<sup>1</sup>, Riitta Jolanki<sup>1</sup>, Francesca Larese Filon<sup>2</sup>, Mark Wilkinson<sup>3</sup>, Beata Kręciszc<sup>4</sup>, Marta Kieć-Świerczyńska<sup>4</sup>, Andrea Bauer<sup>5</sup>, Vera Mahler<sup>6</sup>, Swen M. John<sup>7</sup>, Axel Schnuch<sup>8</sup>, Wolfgang Uter<sup>9</sup> and on behalf of the ESSCA network<sup>†</sup>

<sup>1</sup>Occupational Medicine, Finnish Institute of Occupational Health, Topeliuksenkatu 41 a A, 00250 Helsinki, Finland, <sup>2</sup>Unit of Occupational Medicine, Department of Medicine and Public Health, University of Trieste, Via della Pietà 19, 34129 Trieste, Italy, <sup>3</sup>Department of Dermatology, The Leeds Teaching Hospitals NHS Trust, Harehills Lane, Leeds, LS7 4SA, UK, <sup>4</sup>Department of Allergology and Environmental Health, Nofer Institute of Occupational Medicine, 8 Teresy Street, 91-348 Lodz, Poland, <sup>5</sup>Department of Dermatology, University Allergy Centre, University Hospital Carl Gustav Carus, Technical University Dresden, Fetscherstraße 74, D-01307 Dresden, Germany, <sup>6</sup>Department of Dermatology, University Hospital Erlangen, Ulmenweg 18, D-91054 Erlangen, Germany, <sup>7</sup>Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrueck, Sedanstrasse 115, 49069 Osnabrueck, Germany, <sup>8</sup>Information Network of Departments of Dermatology (IVDK), University of Göttingen, von-Sieboldstr. 3, D-37075 Göttingen, Germany, and <sup>9</sup>Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen/Nürnberg, Waldstr. 6, D-91054 Erlangen, Germany

## Summary

**Background.** Occupational contact dermatitis is one of the most common occupational diseases in Europe. In order to develop effective preventive measures, detailed and up-to-date data on the incidence, main causes and professions at risk of occupational contact dermatitis are needed.

**Objectives.** To describe the pattern of patch test reactivity to allergens in the European baseline series of patients with occupational contact dermatitis in different occupations.

**Methods.** We analysed data collected by the European Surveillance System on Contact Allergy (ESSCA) network from 2002 to 2010, from 11 European countries.

**Results.** Allergens in the European baseline series associated with an at least doubled risk of occupational contact dermatitis include: thiuram rubber chemical accelerators, epoxy resin, and the antimicrobials methylchloroisothiazolinone/methylisothiazolinone, methylidibromo glutaronitrile, and formaldehyde. The highest risk of occupational contact dermatitis was found in occupations classified as 'other personal services workers', which includes hairdressers, nursing and other healthcare professionals, precision workers in metal and related materials, and blacksmiths, tool-makers and related trades workers.

**Conclusions.** In the planning and implementation of measures aimed at preventing occupational contact dermatitis, the focus should be on the identified high-risk occupational groups and the most common occupational allergies.

**Key words:** chromium; clinical epidemiology; cobalt; contact allergy; epoxy resins; formaldehyde; methylchloroisothiazolinone/methylisothiazolinone; methylidibromo glutaronitrile; occupational dermatitis; patch testing; *p*-phenylenediamine; thiurams.

*Correspondence:* Maria Pesonen, Finnish Institute of Occupational Health, Topeliuksenkatu 41 a A, 00250 Helsinki, Finland. Tel: +358 304741; Fax: +358 95875449. E-mail: maria.pesonen@ttl.fi

<sup>†</sup>Members of the European Surveillance System on Contact Allergy network are as follows: Austria: Werner Aberer, Graz. Switzerland: Andreas Bircher, Basel; Dagmar Simon, Bern; and Barbara Ballmer-Weber, Zürich. Germany: Peter Frosch, Dortmund; Thomas Fuchs, Göttingen; Jochen Brasch, Kiel; Andrea Bauer, Dresden; Peter Elsner, Jena; Swen Malte John, Osnabrück; Vera Mahler, Erlangen; and Elke Weisshaar, Heidelberg. Denmark: Jeanne Duus Johansen, Hellerup/Copenhagen. Spain: Ana Giménez Arnau, Barcelona; Javier Sánchez-Pérez, Madrid; Juan Fco. Silvestre, Alicante; Juan García-Gavín and Virginia Fernández-Redondo, Santiago de Compostela; José Carlos Amario-Hita and José M. Fernandez-Vozmediano (deceased), Cadiz; and Pedro Mercader, Murcia. Finland: Riitta Jolanki and Maria Pesonen, Helsinki; and Tapio Rantanen, Lahti. Italy: Fabio Ayala and Anna Balato, Napoli; Andrea Peserico, Padova; Francesca Larese Filon, Trieste; W. Wallnofer, Bolzano; Maria Teresa Corradin, Pordenone; and Rosella Gallo, Genova. Lithuania: Skaidra Valiukeviciene, Kaunas. The Netherlands: Pieter-Jan Coenraads and Marie-Louise Schuttelaar, Groningen; and Thomas Rustemeyer, Amsterdam. Poland: Beata Kręciszc and Marta Kieć-Świerczyńska, Lodz; Magdalena Czarnecka-Operacz and Anna Sadowska, Poznan. United Kingdom: David I. Orton, Amersham; Cathy M. Green, Dundee; Mark Wilkinson, Leeds; Jane E. Sansom, Bristol; Codagh M. King, Liverpool; Helen L. Horne, Middlesbrough; John S. C. English, Nottingham; Graham A. Johnston, Leicester; Barry N. Statham (deceased), Swansea; Mahbub M. U. Chowdhury, Cardiff; Natalie Stone, Newport, Gwent; Sue Cooper, Oxford; David J. Gawkrödger, Sheffield; and Anthony D. Ormerod, Aberdeen.

Funding: No external funding.

Conflict of interests: The authors have declared no conflicts of interest pertinent to this analysis.

Accepted for publication 17 November 2014

Occupational skin diseases represent up to 34% of the occupational diseases recorded in Europe (1). The economic burden of occupational skin diseases exceeds €5 billion/year in the EU, which includes the costs of treatment, financial compensation, and loss of productivity (2, 3). The majority of occupational skin diseases in Europe consist of allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD). In order to plan effective preventive measures against occupational dermatitis and to target them towards high-risk occupations, detailed information on the incidence and causes of occupational contact dermatitis is needed. On the basis of the data of the European Surveillance System on Contact Allergy (ESSCA) network, we analysed the pattern of patch test reactivity of patients with and without occupational dermatitis to the allergens in the European baseline series (EBS), both globally and in different occupations and occupational groups.

## Patients and Methods

### Patient data

The ESSCA network has already been described in previous publications (4). Briefly, the clinical and demographic data, along with the patch test results of all patients patch tested in the member departments of the ESSCA, are documented electronically in local departments, by the use of diverse data capture software, and, partly, the ESSCA's multilingual software WINALLDAT/ESSCA (5). Data are pooled in the ESSCA data centre in Erlangen for further analysis with R software (version 3.0.1; [www.R-project.org](http://www.R-project.org)) (6).

The present analysis includes data from the years 2002–2010 from 11 European countries (Table 1). Only patients (i) aged 16–68 years, representing persons potentially engaged in working life, (ii) with a valid documented current occupation, and (iii) patch tested with the EBS were considered for the present analysis. In the ESSCA data, the relationship between occupational exposures and contact dermatitis leading to presentation for patch testing is documented as 'yes', 'partial', 'no', and 'unknown'. As this statement, made upon final evaluation after the patch test, refers to the contact dermatitis, it is not possible to link this information to single allergens on a case-by-case basis. For the present analysis, patients with clear or partial occupational causation were contrasted with patients for whom an occupational cause of contact dermatitis had been explicitly denied.

### Patch testing

Patch testing follows international recommendations (7). The maximum patch test reaction between D3 and

D5 (inclusive) was considered to be the outcome, and dichotomized into positive versus non-positive (thus comprising negative, irritant and doubtful reactions). The EBS is maintained by the European Environmental Contact Dermatitis Research Group for the European Society of Contact Dermatitis (ESCD). The latest version of the EBS has recently been published (8), but our study used the previous version (9).

### Statistical methods

In the ESSCA network, information on the patient's occupation is recorded according to the International Standard Classification of Occupations (ISCO-88). This enabled us to utilize European workforce statistics. The workforce (i.e. the number of employed people) varies considerably between different occupations. For the purposes of this study, the workforce in occupations at the three-digit level of the ISCO-88 classification in each of the participating countries in the year 2000 was extracted from the LABORSTA database, maintained by the International Labour Organization (<http://laborsta.ilo.org>). Newer statistics on specific occupations were not available at the time of analysis. The total workforce in Europe in 2002 and 2010 in the 15–64-year age group was extracted from Eurostat, the statistical office of the EU ([http://epp.eurostat.ec.europa.eu/statistics\\_explained/index.php/Employment\\_statistics](http://epp.eurostat.ec.europa.eu/statistics_explained/index.php/Employment_statistics)) (Table 1). The total workforce in participating countries was 136.73 million in 2000, 138.681 million in 2002, and 148.213 million in 2010. Therefore, the workforce had increased by 1.4% in 2002 and by 8.4% in 2010 from the year 2000.

Descriptive statistical analyses were performed according to pertinent guidelines (10), in particular with the use of age-standardized and sex-standardized prevalence rates with accompanying 95% confidence intervals (CIs). The association between suffering from occupational contact dermatitis and specific contact sensitization was quantified with prevalence ratios (PRs) derived from log-binomial regression analysis, adjusted for sex and (dichotomized) age, and accompanied by 95% CIs calculated with the profile likelihood method.

The risk assessment for occupational contact dermatitis in different occupations was based on the calculation of the risks of occupational contact dermatitis, defined as the share of documented cases in the ESSCA network per 10 000 employed persons in a given occupation in all of the 11 countries participating in 2000. In order to calculate this risk, the mean risk of occupational contact dermatitis in the whole patient population was set to 1 as a reference (Table 2).

**Table 1.** Characteristics of patients and frequency of occupational contact dermatitis (OCD) in participating countries

Country	Workforce (millions)	n (total)	No. with OCD	% with OCD	OCD			
					% male	% with AD	Mean age (years)	% positive EBS
Austria	3.684	1525	407	26.7	42.5	17.6	33.4	58.7
Switzerland	3.789	3420	870	25.4	55.1	17.3	36.5	59.1
Germany	36.324	6477	2191	33.8	56.6	26.8	39.8	57.3
Denmark	2.716	1244	169	13.6	39.6	18.9	38.3	29.6
Spain	15.306	1999	380	19.0	43.7	14.8	40.1	55.3
Finland	2.367	2523	1198	47.5	47.8	27.7	40.7	63.6
Italy	20.930	6538	482	7.4	45.9	6.5	35.5	54.0
Lithuania	1.525	679	230	33.9	30.4	15.3	41.4	38.7
The Netherlands	7.860	3832	1206	31.5	51.2	28.3	35.8	52.7
Poland	14.518	1942	678	34.9	37.0	16.1	40.4	66.5
United Kingdom	27.711	14 098	2806	19.9	39.4	33.7	37.1	48.1
<b>Total</b>	<b>136.730</b>	<b>44 277</b>	<b>10 617</b>	<b>24.0</b>	<b>46.7</b>	<b>21.6</b>	<b>38.1</b>	<b>54.6</b>

AD, atopic dermatitis; EBS, European baseline series.

n (total), number of patients aged 16–68 years patch tested in the European Surveillance System on Contact Allergy network in 2002–2010; % positive EBS, proportion of patients with OCD with at least one positive reaction to allergens in the EBS.

## Results

### Characteristics of patients

In the study period, the participating departments recorded consultations with 44 277 patients in the selected age group (16–68 years), with documented current occupation and a patch test including the EBS. In cases of multiple consultations with one patient, the most current case was selected for analysis. The number of female patients was 27 309 (61.7%). The age distribution in this age-restricted clinical sample was as follows: first quartile, 30 years; median, 41 years; third quartile, 50 years; mean age, 40.5 years.

Altogether, 10 617 patients with occupational contact dermatitis were identified, including mainly ( $n = 9309$ ) those for whom this was regarded as a clear relationship, and those with at least partial occupational causation of contact dermatitis ( $n = 1308$ ), in the ESSCA data from 2002 to 2010. These were compared with patients with no occupational causation of dermatitis ( $n = 24 177$ ). Patients for whom the role of occupational exposures could not be determined with certainty were excluded from the comparative analyses. The distribution of patients with occupational contact dermatitis across the participating countries is shown in Table 1, together with the basic characteristics of these patients, and the total number of employed persons, that is, the workforce, aged  $\geq 15$  years in each country.

The patients with occupational contact dermatitis were significantly younger than those with non-occupational contact dermatitis (38.1 versus 41.8 years,  $p < 0.0001$ ) in our age-restricted sample, and males were more prominent in the group of patients with

occupational contact dermatitis (46.7% versus 33.5%,  $p < 0.0001$ ). Atopic dermatitis was slightly more prominent in patients with non-occupational dermatitis (21.6% versus 23.3%), but there was marked variation in atopic dermatitis proportions between countries. In Germany, atopic dermatitis was significantly more common in patients with than in patients without occupational contact dermatitis (26.8% versus 19.3%,  $p < 0.0001$ ).

### Occupations associated with a high risk of occupational contact dermatitis

The spectrum of occupations of the patients with occupational contact dermatitis and the calculated risk of occupational contact dermatitis by occupation are shown in Table 2. The average 9-year (from 2000 to 2010) risk of occupational contact dermatitis, as defined here, for all occupations in the present data was 7.8 per 100 000 employed persons. The highest risk of occupational contact dermatitis was found in occupations classified as ‘other personal services workers’, which includes hairdressers as a large group. A high risk was also seen in nursing and other health professionals, precision workers in metal and related materials, and blacksmiths, tool-makers and related trades workers.

Table 3 shows the occupations with a high risk of occupational contact dermatitis and the percentages of patients with ACD, ICD and combination of ACD and ICD in each of the occupations. The highest frequencies of ACD were found in hairdressers and beauticians, bricklayers and stonemasons, and dental assistants. ICD was most commonly found in waiters and bartenders, housekeepers, and nursing and midwifery associate professionals. The percentages of ACD, ICD and combined ACD and

**Table 2.** Risk of occupational contact dermatitis (OCD) in different occupational groups according to the ISCO-88 classification

Occupational group	No. with OCD	Risk
Other personal services workers*	941	10.58
Nursing and midwifery professionals	374	5.86
Nursing and midwifery associate professionals	817	5.34
Precision workers in metal and related materials	133	4.57
Health associate professionals (except nursing)	338	3.93
Health professionals (except nursing)	426	3.74
Blacksmiths, tool-makers, and related trades	370	3.52
Rubber and plastic products machine operators	114	3.49
Food processing and related trades	278	3.08
Painters, building structure cleaners, and related trades	240	2.74
Housekeeping and restaurant services	740	2.38
Other machine operators and assemblers	77	2.37
Metal and mineral products machine operators	131	2.06
Assemblers	166	2.00
Machinery mechanics and fitters	453	1.89
Domestic and related helpers, cleaners, and launderers	501	1.48
Textile, garment and related trades	123	1.35
Building frame and related trades	335	1.22
Physical and engineering science technicians	272	1.16
Building finishers and related trades	281	1.13

The mean risk of occupational dermatitis in the whole patient population was set as 1.00 in order to calculate the risk of occupational dermatitis in each occupational group. Occupational groups with a risk of occupational dermatitis of  $> 1$  and number of cases of  $\geq 75$  are shown.

\*Includes hairdressers.

ICD do not add up to 100% (Table 3), because, for some patients, skin conditions other than ACD and ICD, such as endogenous eczema or psoriasis, were considered to be aggravated by occupational factors.

#### **Patch test positivity to allergens in the EBS among patients with and without occupational contact dermatitis**

The results obtained with the EBS, stratified for patients with versus without occupational contact dermatitis, are shown in Table 4. The allergens with the strongest association with occupational contact dermatitis, that is, those with a  $\geq 1.75$  risk of occupational contact dermatitis, were thiurams, epoxy resin, mercapto rubber chemicals, and *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine (IPPD), followed by a number of antimicrobials. These were defined as allergens associated with a markedly increased risk of occupational contact dermatitis.

Allergy to nickel was only slightly more common among patients with occupational contact dermatitis (8% increase in risk, according to the adjusted PR). Similarly,

the frequency of allergy to fragrance mix did not differ greatly between patients with and without occupational contact dermatitis at this general level (7.3% and 7.1%, respectively). Of the EBS allergens, only balsam of Peru (*Myroxylon pereirae*) and *p*-tert-butylphenol formaldehyde resin were more frequently positive in patients without than in those with occupational contact dermatitis.

#### **Occupations with a high frequency of patch test positivity to the allergens in the EBS associated with a markedly increased risk of occupational contact dermatitis**

Of the allergens associated with markedly increased risk of occupational contact dermatitis, thiurams, epoxy resin and methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) were chosen for a more detailed analysis of allergy frequency in different occupations (Table 5), because there was a sufficiently high frequency of contact allergy to these among patients with occupational contact dermatitis, that is, number of cases  $\geq 300$ , and a PR of occupational contact dermatitis of at least 1.5 (that is, the risk was increased by at least 50%), which was also significant [lower limit of 95% CI of  $> 1$  (Table 4)].

Contact allergy to epoxy resin was most commonly found among floor-layers and tile-setters, 23.8% of whom were patch test positive for epoxy resin. Epoxy allergy was also common among carpenters and joiners, and painters (Table 5). The highest frequencies of thiuram mix positivity were observed in medical assistants (19.4%) and food preparers, including butchers and fishmongers (18.3%). Other occupations with a high frequency of thiuram mix positivity included housekeeping and restaurant workers, cooks, domestic helpers, cleaners and launderers, dental assistants, bricklayers and stonemasons, and nursing and midwifery associate professionals (Table 5). MCI/MI contact allergy was most frequently found in floor-layers and tile-setters, in chemical-processing plant operators, and in precision workers in metal and related material, 11.6%, 9.6% and 9.5% of whom, respectively, were patch test-positive for MCI/MI (Table 5).

Among the allergens associated with a markedly increased risk of occupational contact dermatitis (Table 4) with a case frequency of  $< 300$ , contact allergy to mercapto rubber chemicals, that is, patch test positivity for mercapto mix or to 2-mercaptobenzothiazole, was most often found in housekeepers and related workers (4.6%, 95% CI 1.27–11.36), followed by dental assistants (3.6%, 95% CI 1.05–9.47). Contact allergy to formaldehyde was most commonly found in personal care and related workers (5.7%, 95% CI 3.08–9.59) and machine tool setters and setter-operators (4.2%, 95% CI 1.95–7.87).

**Table 3.** Characteristics of patients with occupational contact dermatitis in occupational subgroups with a high level of occurrence of occupational contact dermatitis classified in detail (i.e. ISCO-88 codes at the four-digit level)

Occupation	No. with OCD	Mean age (years)	% males	% with ACD	% with ICD	% with ACD and ICD
Medical doctors	176	37.4	42.6	33.6	30.1	9.7
Dentists	90	38.9	33.3	47.4	22.8	10.5
Nursing and midwifery professionals	374	36.4	9.4	28.9	38.9	17.9
Chemical and physical science technicians	100	36.6	34.0	25.5	25.5	9.1
Dental assistants	110	31.8	0.9	51.9	19.0	2.5
Physiotherapists and related associate professionals	99	36.3	12.1	40.3	27.8	13.9
Nursing and midwifery associate professionals	817	37.4	7.5	26.3	34.9	10.4
Housekeepers and related workers	88	41.4	14.8	29.3	29.3	12.1
Cooks	421	33.7	53.4	20.3	37	13.4
Waiters, waitresses, and bartenders	150	31.5	29.3	22.0	47.6	13.4
Hairdressers, barbers, beauticians, and related workers	919	27.9	6.9	45.0	23.5	17.4
Gardeners, horticulturists, and nursery growers	124	39.9	36.3	33.7	20.7	9.8
Bricklayers and stonemasons	100	39.1	97.0	60.3	15.9	4.8
Carpenters and joiners	82	40.5	93.9	48.1	17.3	7.7
Plumbers and pipe-fitters	80	39.0	93.8	37.0	30.4	8.7
Painters, varnishers, and related workers	181	38.6	87.3	48.6	16.2	6.3
Machine tool setters and setter-operators	241	40.8	92.1	32.5	32.5	12.9
Precision workers in metal and related materials	133	38.8	70.3	35.6	21.1	11.1
Bakers, pastry cooks, and confectionery makers	175	33.6	53.1	18.3	40.5	8.7
Plastic products machine operators	87	41.4	74.7	40.8	22.4	8.2
Domestic and related helpers, cleaners, and laundresses	495	43.4	13.9	31.7	34.9	11.4
<b>All occupations</b>	<b>10617</b>	<b>38.1</b>	<b>46.7</b>	<b>35.3</b>	<b>28.7</b>	<b>10.7</b>

ACD, allergic contact dermatitis; ICD, irritant contact dermatitis; OCD, occupational contact dermatitis.

Only occupations with at least 75 cases of occupational contact dermatitis are shown. Percentages refer to non-missing diagnoses. Other diagnoses account for the remainder.

The highest frequencies of methyl dibromo glutaronitrile (MDBGN) contact allergy were found in blacksmiths and tool-makers (23.8%, 95% CI 8.22–47.17), and welders and flame-cutters (13.6%, 95% CI 5.17–27.35).

We also analysed the occupational distribution of some of the less prominent occupational allergens, that is, those with a < 1.5-fold increased risk of occupational dermatitis (Table 4). Among patients with occupational contact dermatitis, hairdressers, barbers, beauticians and related workers had a high frequency of *p*-phenylenediamine (PPD) allergy (19.6%). PPD allergy also occurred in occupations not directly associated with PPD exposure, such as waiters and bakers, although with much lower frequencies (5.3% and 4.2%, respectively).

Cobalt allergy was most prevalent in bricklayers and stonemasons with occupational contact dermatitis (25.3%), but was also frequent in occupations without any obvious occupational exposure to cobalt, for example waiters (16.0%), office clerks (12.4%), medical doctors (11.8%), and physiotherapists (10.4%). Chromium allergy was most commonly found in bricklayers and stonemasons (31.9%), and was also frequent in metal and mineral products machine operators (10.3%), transport labourers and freight handlers (9.1%) and plumbers and pipe-fitters (9.1%) with occupational contact dermatitis.

Regarding patients with occupational contact dermatitis, allergy to colophonium was found in gardeners, horticulturists and nursery growers, and physiotherapists, with frequencies of 8.5% and 8.3%, respectively. Colophonium allergy was also frequent in carpenters and joiners (7.8%), in precision workers in metal and related materials (7.4%) and in machine tool setters and setter-operators (7.3%) with occupational contact dermatitis.

## Discussion

The EBS, which is widely used for patch testing in European dermatology units, includes contact allergens that are predominantly occupational, allergens encountered in both the work environment and in a non-occupational context, and allergens that are occupationally relevant in only exceptional cases. On the basis of the patient data collected by the ESSCA network, the allergens in the EBS associated with a markedly increased risk of occupational contact dermatitis include rubber chemicals, that is, thiurams, mercapto compounds, and IPPD, epoxy resin, and the antimicrobials MI, MCI/MI, MDBGN, and formaldehyde. Contact allergies to PPD, cobalt and chromium were common both in patients with and

**Table 4.** Risk of occupational contact dermatitis (OCD) associated with allergy to test substances of the European baseline series

Allergen	OCD <sup>+</sup>		OCD <sup>-</sup>		PR (95% CI)
	OCD <sup>+</sup> : tested	OCD <sup>+</sup> : % positive (std) (95% CI)	OCD <sup>-</sup> : tested	OCD <sup>-</sup> : % positive (std) (95% CI)	
Thiuram mix (PTD, TETD, TMTD, and TMTM)	10 036	5.63 (5.15–6.1)	23 688	1.35 (1.21–1.5)	4.23 (3.69–4.87)
Epoxy resin	9969	3.06 (2.73–3.4)	23 736	0.82 (0.71–0.94)	4.02 (3.37–4.81)
2-MBT	10 036	1.42 (1.18–1.67)	23 669	0.52 (0.43–0.61)	2.91 (2.28–3.73)
<i>N</i> -isopropyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine	8016	1.05 (0.82–1.28)	20 231	0.41 (0.32–0.49)	2.62 (1.94–3.54)
Mercapto mix (CBS, MBTS, and MOR)	5242	1.32 (1–1.64)	10 430	0.62 (0.47–0.78)	2.46 (1.73–3.52)
MI	1966	1.42 (0.88–1.96)	6033	0.5 (0.32–0.67)	2.36 (1.74–3.22)
Formaldehyde	9986	3.04 (2.69–3.4)	23 564	1.82 (1.65–1.99)	1.75 (1.50–2.02)
Methyldibromo glutaronitrile	8465	3.33 (2.94–3.73)	19 248	2.07 (1.87–2.27)	1.66 (1.43–1.93)
MCI/MI	9967	4.02 (3.63–4.42)	23 510	2.49 (2.29–2.68)	1.65 (1.46–1.87)
Clioquinol	2332	0.36 (0.12–0.6)	4974	0.24 (0.11–0.38)	1.64 (0.70–3.74)
Potassium dichromate	9924	5.58 (5.12–6.03)	23 180	3.89 (3.64–4.13)	1.48 (1.34–1.64)
Sesquiterpene lactone mix	6550	0.83 (0.6–1.06)	15 988	0.59 (0.47–0.7)	1.45 (1.07–1.96)
<i>p</i> -Phenylenediamine	7909	5.43 (4.91–5.95)	20 071	3.99 (3.72–4.26)	1.43 (1.28–1.59)
Cobalt(II) chloride	9737	9.29 (8.69–9.89)	22 972	6.77 (6.45–7.09)	1.39 (1.28–1.50)
Colophonium	10 078	4.02 (3.62–4.42)	23 674	3.14 (2.91–3.36)	1.34 (1.18–1.51)
Benzocaine	2611	0.92 (0.54–1.3)	6853	0.71 (0.51–0.91)	1.32 (0.81–2.11)
Primin	6385	0.29 (0.14–0.43)	16 147	0.25 (0.17–0.32)	1.28 (0.74–2.13)
Methyldibromo glutaronitrile + 2-phenoxyethanol (e.g. Euxyl™ K 400)	1539	4.62 (3.51–5.74)	3534	3.56 (2.96–4.16)	1.24 (0.94–1.64)
Quaternium-15	7264	1.67 (1.37–1.97)	17 807	1.36 (1.19–1.53)	1.23 (1.01–1.50)
Paraben mix	9134	0.92 (0.72–1.12)	22 506	0.82 (0.7–0.94)	1.10 (0.85–1.50)
Nickel(II) sulfate	9807	23.44 (22.57–24.3)	23 031	21.83 (21.31–22.34)	1.08 (1.03–1.12)
Lanolin alcohols	9881	1.68 (1.41–1.95)	23 464	1.55 (1.4–1.71)	1.06 (0.88–1.27)
Fragrance mix I	9941	7.28 (6.73–7.82)	23 340	7.11 (6.79–7.44)	1.01 (0.93–1.10)
Fragrance mix II	6415	4.4 (3.87–4.93)	15 894	4.23 (3.92–4.55)	1.01 (0.87–1.16)
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	7822	2.12 (1.77–2.47)	18 917	2.09 (1.89–2.3)	0.97 (0.80–1.16)
Neomycin sulfate	7673	1.58 (1.28–1.87)	19 551	1.68 (1.51–1.86)	0.90 (0.72–1.10)
Balsam of Peru ( <i>Myroxylon pereirae</i> )	9955	4.92 (4.47–5.37)	23 406	5.46 (5.18–5.75)	0.88 (0.72–0.98)
Tixocortol pivalate	6136	0.94 (0.68–1.20)	15 052	1.05 (0.88–1.21)	0.85 (0.62–1.15)
<i>p</i> -tert-Butylphenol formaldehyde resin	10 072	0.91 (0.72–1.11)	23 721	1.2 (1.06–1.34)	0.78 (0.61–0.99)
Budesonide	6409	0.55 (0.36–0.74)	15 232	0.71 (0.58–0.85)	0.77 (0.54–1.08)

CBS, *N*-cyclohexyl-2-benzothiazyl sulfonamide; CI, confidence interval; MBTS, dibenzothiazyl disulfide; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone; MOR, 2-(4-morpholinylmercapto)benzothiazole; OCD<sup>+</sup>, patients with OCD; OCD<sup>-</sup>, patients without OCD; % positive (std), proportions standardized for age and sex; PR, adjusted prevalence ratio; PTD, dipentamethylenethiuram disulfide; TETD, tetraethylthiuram disulfide; TMTD, tetramethylthiuram disulfide; TMTM, tetramethylthiuram monosulfide; 2-MBT, mercaptobenzothiazole. Ordering according to PR (decreasing): PTD; TETD; TMTD; TMTM; 2-MBT; CBS; MBTS; MOR; methyldibromo glutaronitrile; MCI/MI.

patients without occupational contact dermatitis, but had the highest prevalence in professions with known occupational exposure to these allergens. The highest risk of occupational contact dermatitis was seen in occupations classified as ‘other personal services workers’, which includes hairdressers as a large group, nursing and other health professionals, precision workers in metal and related materials, blacksmiths, tool-makers, and workers in related trades. Our results closely resemble

those of a recent French study, in which the occupations with the highest frequency of occupational allergic contact dermatitis were hairdressers, healthcare workers, cleaning staff, and masons (11).

The present study focused on EBS patch test results. However, when patients with suspected occupational dermatitis are examined, patch testing limited to the EBS is inadequate in most cases. Instead, it is necessary to expand the patch testing to specialized series of allergens,

**Table 5.** Occupations with a high frequency of thiuram mix, epoxy resin and methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) allergy among patients with occupational contact dermatitis

	No. tested	No. positive	% positive	95% CI
<b>Thiuram mix</b>				
<b>Total</b>	<b>10036</b>	<b>537</b>	<b>5.35</b>	<b>4.92–5.81</b>
Medical assistants	31	6	19.40	7.45–37.47
Butchers, fishmongers, and related food preparers	60	11	18.30	9.52–30.44
Housekeeping and restaurant services workers	75	9	12.00	5.64–21.56
Builders, traditional materials	67	8	11.90	5.3–22.18
Domestic and related helpers, cleaners, and launderers	475	51	10.70	8.1–13.87
Cooks	411	38	9.20	6.63–12.47
Dental assistants	104	9	8.70	4.03–15.79
Bricklayers and stonemasons	95	8	8.40	3.71–15.92
Medical doctors	170	12	7.1	3.7–12.0
Nursing and midwifery associate professionals	801	52	6.50	4.89–8.43
<b>Epoxy resin</b>				
<b>Total</b>	<b>9969</b>	<b>341</b>	<b>3.42</b>	<b>3.07–3.80</b>
Floor-layers and tile-setters	42	10	23.8	12.05–39.45
Carpenters and joiners	77	13	16.9	9.31–27.14
Painters, varnishers, and related workers	170	28	16.5	11.23–22.92
Plastic products machine operators	83	12	14.5	7.7–23.89
Electrical and electronic equipment mechanics and fitters	75	10	13.3	6.58–23.16
Bricklayers and stonemasons	97	9	9.3	4.33–16.88
Precision workers in metal and related materials	92	8	8.7	3.83–16.42
Wood treaters, cabinet-makers, and related trades workers	70	6	8.6	3.21–17.73
Plumbers and pipe-fitters	79	6	7.6	2.84–15.8
Machinery mechanics and fitters	436	22	5.0	3.19–7.54
<b>MCI/MI</b>				
<b>Total</b>	<b>9967</b>	<b>408</b>	<b>4.09</b>	<b>3.71–4.50</b>
Floor-layers and tile-setters	43	5	11.6	3.89–25.08
Chemical-processing plant operators	52	5	9.6	3.2–21.03
Precision workers in metal and related materials	95	9	9.5	4.42–17.22
Painters, varnishers, and related workers	165	14	8.5	4.72–13.83
Physiotherapists and related associate professionals	96	8	8.3	3.67–15.76
Machinery mechanics and fitters	425	30	7.1	4.81–9.92
Transport labourers and freight handlers	80	5	6.2	2.06–13.99
Nursing and midwifery professionals	368	22	6.0	3.78–8.91
Other associate professionals	121	7	5.8	2.36–11.56
Dental assistants	105	5	4.8	1.6–10.8

Occupations with < 30 tested patients and/or < 5 positive reactions have been omitted. Total: all patients with occupational contact dermatitis tested with the given allergen

which are chosen according to the occupation and exposure of the patient.

Departments contributing to the ESSCA data vary greatly. This is true both at a national level (e.g. regarding the health system and referral mechanism) and – if there are several departments in one country – in terms of between-department differences, for example regarding institutional background and research interests. Most of the departments are general dermatological clinics, and their dermatologists see patients with contact dermatitis mostly of non-occupational origin, whereas two centres (in Finland and in Poland) are specialized in investigating only suspected occupational skin diseases. In view of such presumptive heterogeneity of representativeness

(selection) and quantitative contribution in each of the countries considered, we refrained from making comparisons between countries concerning morbidity. Furthermore, the number of consultations with patients from certain occupational groups, related to the workforce in the given occupational group, cannot be regarded as a measure of morbidity, as coverage will differ between countries, and will, most importantly, be generally very partial. However, on a general, European level, we consider the case mix of occupational patients to be fairly representative, owing to the broad scope of participating departments. Some variation may be expected at the methodological level of patch testing, despite the fact that ESSCA members are members of the

ESCD, adhere to common patch testing guidelines (7), and utilize, for example, online training tools for patch test reading. However, we conclude that the ESSCA data represent the characteristics of the occupational contact dermatitis cases in Europe relatively well.

Among our patients, positive patch test reactions to thiuram mix, which includes thiuram rubber chemicals, were most commonly found in domestic helpers, cleaners and laundry workers, healthcare workers, and housekeeping and restaurant workers, that is, in occupations that frequently need to use water impermeable protective gloves. Thiuram allergy was also commonly found in bricklayers and stonemasons with occupational contact dermatitis. The occupations associated with a high risk of thiuram allergy in our data correspond well with those previously reported in Germany, Switzerland, and Austria (12). According to the literature, occupational thiuram allergy is likely to develop because of rubber glove usage (12–14). Even though the use of thiurams as vulcanization accelerators in rubber glove production has been reduced, and dithiocarbamates and mercaptobenzothiazole derivatives are now more commonly used (15, 16), positive patch test reactions to thiurams are still more common than positive reactions to dithiocarbamates. A possible explanation for this is that thiurams and dithiocarbamates constitute a redox pair in which a dithiocarbamate may be oxidized to the corresponding thiuram disulfide, and the thiuram may be reduced to reform the dithiocarbamate (16, 17). Thiurams are considered to be better markers of sensitization to the dithiocarbamate /thiuram redox pair than dithiocarbamates (16). Allergy to another class of vulcanization accelerators, mercapto rubber chemicals, was also associated with a markedly increased risk of occupational contact dermatitis in our patient population. However, contact allergy to mercapto rubber chemicals was less frequent than allergy to thiurams.

Epoxy resin is a well-known occupational contact allergen (18). In the present data, epoxy resin allergy was most common among patients in male-dominated occupations who may utilize epoxy products such as epoxy glues and paints in their work, especially floor-layers and other construction workers, painters, plastic product machine operators, precision workers in metal and related materials, and electrical workers. This is in line with previous investigations on epoxy resin allergy (19). The high frequency of epoxy allergy among plumbers and pipe-fitters (7.6%) might be attributable to the fact that those working in sewer pipe repair and using epoxy injection casting or pipe liner techniques may be highly exposed to epoxy products (20); these techniques have

been increasingly popular since the beginning of this century.

Regarding the antimicrobial allergens, contact allergy, especially to MI and, to a lesser extent, to MCI/MI, was most common among precision workers in metal and related materials, and among painters and varnishers, who may handle paints that commonly contain MI and MCI/MI as a preservative. MI was shown to be present in multiple products registered for use at workplaces in concentrations of 0.01 ppm to 10% (21). Recently, new sensitization has increasingly been found, especially to MI. The increase in MCI/MI sensitization is considered to be mainly attributable to primary MI sensitization (22). The European Scientific Committee on Consumer Safety has recently adopted the opinion that 100 ppm in cosmetic products is not safe for the consumer, and that, for leave-on products, no safe MI concentrations regarding the induction of contact allergy or elicitation have been adequately demonstrated. Moreover, the Committee stated that, for rinse-off cosmetic products, a concentration of 15 ppm (0.0015%) MI is considered to be safe for the consumer with regard to induction of contact allergy, whereas no information is available on elicitation (23). Among our patients with occupational contact dermatitis, contact allergy to MDBGN was most common in bricklayers and stonemasons. Within the EU, MDBGN has not been permitted in cosmetics since 2008 (24). Our data show that contact allergy to MDBGN still occurs among patients with occupational contact dermatitis. Formaldehyde allergy was frequent in plastic product machine operators, presumably because of contact with formaldehyde resins, in machine tool setters and setter-operators, who may handle metal-working fluids that contain formaldehyde releasers, in personal care and related workers, and in physiotherapists, who handle skin cleansers and skin care products, as well as massage creams, that may contain formaldehyde releasers as preservatives.

Of the EBS metal allergens, cobalt and chromium most commonly caused allergies in bricklayers and stonemasons. Some possible sources of chromium and cobalt exposure in these professions are cement products, which contain both of these metals. EU-wide efforts to reduce the amount of hexavalent chromium in cement by adding ferrous sulfate (25) are, in some countries, still relatively recent, and are thus not reflected in our data. Chromium allergy might also be attributable to the use of protective gloves made of chromium-tanned leather. Cobalt allergy was also common in some occupations for which occupational cobalt exposure seems unlikely, for example waiters and bartenders, and office clerks. Cobalt allergy in these patients might represent cross-exposure to nickel, as,



according to animal experiments, cross-sensitization is not likely (26).

The observed frequency of PPD allergy among patients in occupations with no occupational source of PPD exposure, 5.3–4.2%, is consistent with previously reported PPD allergy frequencies in non-occupational patch tested patients (27). This implies that PPD allergy in these patients is caused by non-occupational PPD exposure, possibly by dyeing one's own hair or by unintentional skin contact with PPD resulting from the use of temporary black henna tattoos (28). However, the hairdressers and beauticians with occupational contact dermatitis had a high frequency of PPD allergy (19.6%) in our patient population. Their excess PPD sensitization prevalence is likely to be occupationally acquired, because of exposure to permanent hair, eyelash and eyebrow dyes, which contain PPD and related *para*-amino compounds, even though some hairdressers may also experience elicitation as a result of dyeing their own hair.

## Conclusions

According to the ESSCA data for 2002–2010, the allergens associated with a markedly increased risk of

occupational contact dermatitis in the EBS include thiuram rubber chemical accelerators, epoxy resin, and the antimicrobials MCI/MI, MDBGN, and formaldehyde. Thiuram allergy was most frequent in occupations that require the frequent use of watertight protective gloves. Epoxy allergy was found among, for example, construction workers, painters, and plumbers, who may utilize epoxy paints, adhesives and coatings in their work. The highest risk of occupational contact dermatitis was found in occupations classified as other personal services workers, which include hairdressers, nurses and other healthcare professionals, precision workers in metal and related materials, blacksmiths, tool-makers, and related trades workers. Preventive measures against occupational contact dermatitis should be targeted towards the identified high-risk occupational groups and allergies identified as predominantly occupational.

## Acknowledgements

We appreciate the support of the Horizon 2020 COST Action TD1206 ('Development and Implementation of European Standards on Prevention of Occupational Skin Diseases'; StanDerm).

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