

Changing delayed-type sensitizations to the baseline series allergens over a decade at the Zurich University Hospital

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Background: Patch testing detects delayed-type sensitizations and may show changes in prevalence over time.

Objectives: To compare sensitization prevalence to our baseline series allergens during the years 2000–2004 to results from 1990 to 1994.

Methods: We analysed baseline patch test series allergens from 2000 through 2004.

Results: 4094 individuals were patch tested to the baseline series (mean age 45.4 years, males 41.7%). The highest sensitization rates were found for nickel sulfate (19.3%), fragrance mix (10.4%) and *Myroxylon pereirae* (7.8%). Compared to 1990–1994, methylchloroisothiazolinone (and) methylisothiazoline (MCI/MI) and neomycin sulfate sensitization decreased and lanolin alcohol, thiuram mix and ammoniated mercury sensitization increased.

Conclusions: Current sensitization rates are similar to those across Europe. Reduced sensitizations to MCI/MI and neomycin sulfate and increased sensitizations to thiuram mix and ammoniated mercury chloride may well be because of changes in exposure. The current group comprises a higher proportion affected by leg dermatitis and may thus explain the higher sensitization to lanolin alcohol. Comparing patch results over time shows important changes in sensitization prevalence.

Key words: allergic contact dermatitis; ammoniated mercury; lanolin alcohol; methylchloroisothiazolinone; neomycin sulfate; patch test; standard series; thiuram mix. © John Wiley & Sons A/S, 2010.

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Patch testing, introduced by Jadassohn 1896 (1), is the standard procedure for detecting allergens that cause allergic contact dermatitis. A patient with suspected allergic contact dermatitis is usually tested with the baseline series, and optionally, according to the patients contact and occupational history, with additional series. The baseline series is continually adapted according to changes in the environmental and occupational exposure (2).

We expanded the previously published study (3) from our department, which covered the years 1990–1994, with patch test results of 4094 patients from our department during the years 2000–2004.

This allowed us to assess trends in sensitization rates over a decade.

Materials and Methods

Patients

Between 2000 and 2004, 4094 patients with suspected allergic contact dermatitis were patch tested with the baseline series allergens by us. All patients were informed in writing before patch testing that topical steroids on the back, phototherapy, sun or sunbed exposure or systemic immunosuppressive treatment were not compatible with patch

testing. At the time of patch test application, the skin was visually inspected for tanning and the above exclusion criteria were ascertained verbally. If any of the exclusion criteria were fulfilled, patch testing was deferred to a later time point. The study protocol was approved by the local Ethics Committee for Research (Ref. Nr. EK: Nr. 827).

Patch testing and test substances

Patch testing was performed in accordance with national and international guidelines (1, 4). Briefly, test substances were applied on the upper back of the patients for 2D, using Finn chambers® on Scanpor® tape (Hermal, Reinbek, Germany). Reactions were assessed on D2 (first reading) and D3 (second reading), in special cases again on D4 (third reading). Patch testing and the first reading of the skin reactions were carried out by the same three assistants of the patch test clinic and supervised by dermatologists. The second and the third reading of the skin reactions and the interpretation of the results were performed by dermatologists.

All substances were bought from Hermal GmbH, Reinbek, Germany.

Data analysis

Both test results and personal data of patients were entered into the ALLDAT software (5) (developed by Stüben, Erlangen, Germany). The test results were recorded as follows: – no reaction, ? doubtful reaction, +, ++, +++ weak, moderate, strong allergic reaction, irr toxic/irritant reaction. Test results '+', '++', '+++' were considered to be positive, '–', '?', and 'irr' to be negative. The personal data contained name, date of birth, sex, occupation, date of patch testing, clinical diagnosis, and localization of skin changes.

All statistic analyses were performed using the statistical package SPSS 15 (SPSS Inc., Chicago, IL, USA). Statistical significance was determined with

the Chi square test for trend, as recommended by Uter et al. (6), and the Linear-by-linear association test. The significance level according to the Bonferroni correction was set at $P < 0.005$.

Results

Patients

Of the 4094 patients tested, 2388 (58.3%) were female and 1706 (41.7%) were male. The mean age was 45.4 (± 17.9) years. The four age groups A, B, C, D (<30, 30–44, 45–59, ≥ 60 years of age) consisted of the following percentages: 22.7%, 28.2%, 26.2%, 22.9%.

Demographic characteristics of the study population according to the MOAHLFA index (7) are presented in Table 1. About 10.6% of the patients suffered from atopic dermatitis. The percentage of patients with the hand, the leg, and the face as primary site of dermatitis was 36%, 6.5%, and 19.8%, respectively.

Eighteen percent of the patients were housekeeping and cleaning professionals. Other common occupations included 'office work' (16.8%), 'retired or unemployed' (13.5%), 'nursing' (7.4%), and 'metal working' (6.5%). The 'food industry and gastronomy' were represented less (5.7%), as were the occupations 'construction' (2.7%), 'hairstressing and cosmetic industry' (2.6%), and 'painting' (1.4%)

Sensitizations

Table 2 summarizes the 13 most common sensitizers of the baseline series during the years 2000–2004. The most common allergen causing positive patch tests was nickel sulfate with a sensitization rate of 19.3%, followed by fragrance mix and *Myroxylon pereirae* with 10.4% and 7.8%, respectively.

Nickel allergy was found to be almost four times more frequent among women than men. In women, the most common sensitizers following nickel sulfate in females were fragrance mix,

Table 1. The MOAHLFA index (4), summarizing important characteristics of the study population

Year of test	2000	2001	2002	2003	2004	2000–2004
Number of tested patients	1046	923	813	669	643	4094
MOAHLFA (%)						
M Male	41.8	40.7	43.8	38.4	43.5	41.7
O Occupational dermatitis	n.d. ^a	n.d. ^a	n.d. ^a	n.d. ^a	n.d. ^a	n.d. ^a
A Atopic dermatitis	16	9.5	7.5	8.5	9.3	10.6
H Primary site: hand	37.5	33.2	36	37	36.7	36
L Primary site: leg	16.8	12.8	17	16.3	20.8	16.5
F Primary site: face	21	22.5	19.3	17.6	16.6	19.8
A Age, ≥ 4	57.9	57.5	60.1	58.1	62.4	59

^aNot determined.

Table 2. Frequencies of the 13 most common contact allergens of the baseline series in Zurich during 2000–2004

Sex	Male + female				Female				Male			
	2000–2004 (n = 4094)				2000–2004 (n = 2388)				2000–2004 (n = 1706)			
	+/+/+/+	(%)	Min	Max	+/+/+/+	(%)	Min	Max	+/+/+/+	(%)	Min	Max
Substances												
1. Nickel sulfate	792	(19.3)	17.3	23.0	669	(28.0)	24.8	34.1	123	(7.2)	5.7	8.7
2. Fragrance mix I	427	(10.4)	8.2	13.5	285	(11.9)	8.0	16.4	142	(8.3)	5.9	9.4
3. <i>Myroxylon pereirae</i>	318	(7.8)	6.7	9.6	204	(8.5)	7.2	12.3	114	(6.7)	6.1	7.7
4. Cobalt (II) chloride	297	(7.3)	4.7	10.0	227	(9.5)	5.5	13.6	70	(4.1)	2.8	5.7
5. Potassium dichromate	201	(4.9)	2.7	7.6	121	(5.1)	2.2	8.8	80	(4.7)	3.4	7.1
6. <i>p</i> -Phenylenediamine	171	(4.2)	3.7	4.8	122	(5.1)	4.4	6.2	49	(2.9)	2.1	3.5
7. Lanolin alcohol	147	(3.6)	2.2	4.3	104	(4.4)	3.0	5.7	43	(2.5)	1.1	4.0
8. Ammoniated mercury	146	(3.6)	2.5	5.4	101	(4.2)	2.8	7.0	45	(2.6)	1.4	3.4
9. Colophonium	120	(2.9)	2.6	3.6	85	(3.6)	3.0	3.9	35	(2.1)	1.1	3.5
10. Thiuram mix	100	(2.4)	1.9	2.8	56	(2.3)	1.9	2.9	44	(2.6)	1.4	3.6
11. Methylchloroisothiazolinone (and) methylisothiazolinone	88	(2.1)	1.4	3.4	51	(2.1)	1.4	3.7	37	(2.2)	1.4	3.1
12. Neomycin sulfate	81	(2.0)	1.3	2.7	59	(2.5)	1.6	2.8	22	(1.3)	0.6	2.5
13. Propolis	81	(2.0)	1.4	2.3	47	(2.0)	1.5	2.6	34	(2.0)	1.1	2.9

M. pereirae, cobalt (II) chloride, potassium dichromate, and *p*-phenylenediamine (in descending order) (Table 2).

In the male group, the most common patch test allergen was fragrance mix, followed closely by nickel sulfate, *M. pereirae*, potassium dichromate, and cobalt (II) chloride (in descending order) (Table 2).

Table 3 shows subgroup sensitization rates for sex and age, respectively. Both nickel sulfate and cobalt (II) chloride allergies were predominantly present in young women (A, B). In the male proportion of the study population, they were most common with men aged 30–44 (B). Positive patch test results to fragrance mix both in women and men were increasing in frequency with age. Almost half of the patient population with sensitization to *M. pereirae* were older people (D). Positive patch test results to potassium dichromate were predominantly seen in women aged 30–44 years (B). *p*-phenylenediamine causes contact allergy primarily in young women (A). Sensitizations to lanolin alcohol were mainly seen in women aged 45–59 (C). Ammoniated mercury induced sensitization predominantly in young females and males (A). Positive patch test results to neomycin sulfate were most prevalent in aged women (D).

Discussion

We evaluated the frequencies of allergic reactions to the allergens of the baseline series to show trends of contact allergy to those substances. Knowledge of changes in frequencies is essential for introducing preventive measures. Comparing our test results with the data from Bangha and Elsner (3) distinctive trends became apparent. It is important to keep in mind, that although the evaluated trends of frequencies of some sensitization rates may show true changes of exposure to those allergens, we cannot rule out that these changes may actually be because of a different composition of the two compared study populations.

While the sex distribution in the two study populations is similar, the age distribution shows a difference. Interestingly, contrary to observations which found an increase of age over time in patch test population (8) (The increase of age over time in patch test populations seems to be a general phenomenon), the percentage of young patients aged below 45 years was slightly higher in our study.

Nickel sulfate was the leading allergen in our study (19.3%), with especially high sensitization rates among young women. Bangha and Elsner (3) reported a declining trend of nickel sulfate. However, compared over a decade, such trend was no

Table 3. Sensitization rates categorized according to sex and age 2000–2004

Age group	A: <30 years				B: 30–44 years				C: 45–59 years				D: ≥60 years			
	Women (n = 581)		Men (n = 350)		Women (n = 602)		Men (n = 551)		Women (n = 633)		Men (n = 440)		Women (n = 572)		Men (n = 365)	
Substances	AR ^a (%)	95% CI	AR ^a (%)	95% CI	AR ^a (%)	95% CI	AR ^a (%)	95% CI	AR ^a (%)	95% CI	AR ^a (%)	95% CI	AR ^a (%)	95% CI	AR ^a (%)	95% CI
Nickel sulfate	211 (36.3)	32.5–40.3	24 (6.9)	4.7–10.0	228 (37.9)	34.1–41.8	46 (8.3)	6.3–11.0	157 (24.8)	21.6–28.3	32 (7.3)	5.2–10.1	73 (12.8)	10.3–15.7	21 (5.8)	3.8–8.6
Fragrance mix I	35 (6.0)	4.4–8.3	15 (4.3)	2.6–6.9	78 (13.0)	10.5–15.1	31 (5.6)	4.0–7.9	90 (14.2)	11.7–17.1	48 (10.9)	8.3–14.2	82 (14.3)	11.7–17.4	48 (13.2)	10.1–17.0
<i>Myroxylon peretiae</i>	26 (4.5)	3.1–6.5	11 (3.1)	1.8–5.5	40 (6.6)	4.9–8.9	27 (4.9)	3.4–7.0	50 (7.9)	6.0–10.2	30 (6.8)	4.8–9.6	88 (15.4)	12.7–18.6	46 (12.6)	9.6–16.4
Cobalt (II) chloride	83 (14.3)	11.7–17.4	15 (4.3)	2.6–6.9	70 (11.6)	9.3–14.4	30 (5.4)	3.8–7.7	43 (6.8)	5.1–9.0	18 (4.1)	2.6–6.4	31 (5.4)	3.8–7.6	7 (1.9)	0.9–3.9
Potassium dichromate	23 (4.0)	2.7–5.9	17 (4.9)	3.1–7.6	37 (6.1)	4.5–8.4	27 (4.9)	3.4–7.0	37 (5.8)	4.3–8.0	21 (4.8)	3.1–7.2	24 (4.2)	2.8–6.2	15 (4.1)	2.5–6.7
<i>p</i> -Phenylenediamine	42 (7.2)	5.4–9.6	10 (2.9)	1.6–5.2	28 (4.7)	3.2–6.6	7 (1.3)	0.6–2.6	36 (5.7)	4.1–7.8	18 (4.1)	2.6–6.4	16 (2.8)	1.7–4.5	14 (3.8)	2.3–6.3
Lanolin alcohol	19 (3.3)	2.1–5.1	7 (2.0)	1.0–4.1	22 (3.7)	2.4–5.5	9 (1.6)	0.9–3.1	35 (5.5)	4.0–7.6	12 (2.7)	1.6–4.7	28 (4.9)	3.4–7.0	11 (3.0)	1.7–5.3
Ammoniated mercury	54 (9.3)	7.2–11.9	17 (4.9)	3.1–7.6	18 (3.0)	1.9–4.7	17 (3.1)	1.9–4.9	11 (1.7)	1.0–3.1	7 (1.6)	0.8–3.2	18 (3.1)	2.0–4.9	4 (1.1)	0.4–2.8
Colophonium	18 (3.1)	2.0–4.8	5 (1.4)	0.6–3.3	20 (3.3)	2.2–5.1	9 (1.6)	0.9–3.1	26 (4.1)	2.8–5.6	11 (2.5)	1.4–4.4	21 (3.7)	2.4–5.5	10 (2.7)	1.5–5.0
Thiuram mix	13 (2.2)	1.3–3.8	3 (0.9)	0.3–2.5	19 (3.2)	2.0–4.9	16 (2.9)	1.8–4.7	12 (1.9)	1.1–3.3	15 (3.4)	2.1–5.5	12 (2.1)	1.2–3–6	10 (2.7)	1.5–5.0
Methylchloroisothiazolinone (and methylisothiazolinone)	13 (2.2)	1.3–3.8	2 (0.6)	0.2–2.1	10 (1.7)	0.9–3.0	13 (2.4)	1.4–4.0	12 (1.9)	1.1–3.3	14 (3.2)	1.9–5.3	16 (2.8)	1.7–4.5	8 (2.2)	1.1–4.3
Neomycin sulfate	8 (1.4)	0.7–2.7	3 (0.9)	0.3–2.5	9 (1.5)	0.8–2.8	8 (1.5)	0.7–2.8	17 (2.7)	1.7–4.3	3 (0.7)	0.2–2.0	25 (4.4)	3.0–6.4	8 (2.2)	1.1–4.3
Propolis	1 (0.2)	0.0–1.0	3 (0.9)	0.3–2.5	11 (1.8)	1.0–3.2	4 (0.7)	0.3–1.9	17 (2.7)	1.7–4.3	10 (2.3)	1.2–4.1	18 (3.1)	2.0–4.9	17 (4.7)	2.9–7.3

^aAR, allergic reactions (+/+ +/+ +/+ +/+).

longer detectable. A nickel directive was issued by the Swiss government in 1995 (9), similar to the EU Nickel Directive from 1994 (10). One explanation for the static sensitization rates to nickel sulfate could be a slow enforcement of the nickel directive; another reason could be that sensitization occurred prior to the directive. However, with these regulations in action, we expect a decrease in nickel sulfate sensitizations within the next decade, especially in the group of young women.

Potassium dichromate used to be a common sensitizer in the male population, particularly among construction workers. As preventive measures were introduced, the frequency of sensitization to potassium dichromate in males dropped (11, 12). The declining trend observed by Bangha and Elsner (3) was no longer evident after a decade. We see a balance of frequencies in the male and female populations. This observation was also made by the Network of Departments of Dermatology (IVDK) (13). Interestingly there were especially high sensitization rates among women aged 30–44 (6.1%; Table 3). This could be explained by a particular exposure to leather (14, 15).

Bangha and Elsner (3) reported a declining trend of nickel sulfate and potassium dichromate sensitizations; however, compared over a decade, such trend was no longer detectable.

The trend of sensitizations to lanolin alcohol (wool alcohols): a common ingredient in many ointments, rose from 1.7% in 1990–1994 to 3.6% in 2000–2004 ($P < 0.001$) because of increased sensitizations in the female pool (from 2.0% to 4.4%, $P < 0.001$). Our sensitization rates are slightly higher than the ones reported by the European Surveillance System on Contact Allergies (ESSCA) (16). As the risk factors for developing allergy to lanolin alcohols are female sex, advanced age, and lower leg dermatitis (17), the reasons for the higher sensitization rates could partly lie in the increased number of individuals with leg dermatitis in our study population (1990–1994: 10%, 2000–2004: 16.5%). It should be mentioned that while positive reactions to lanolin alcohol are often highly represented in patch test populations, these reactions are often clinically irrelevant being irritations (i.e. in the setting of a so-called angry back syndrome (18)). As studies showed, sensitization to lanolin alcohol (i) is extremely low in the normal population (19), and (ii) continued use of products containing lanolin did not impair healing in leg ulcer patients sensitized to lanolin alcohol (20). Balancing adverse events and limited clinical relevance on the one hand and increasing sensitization rates on the other hand, the continued inclusion of lanolin in the standard series should be critically reviewed.

We observed a decrease in methylchloroisothiazolinone (MCI) (and) methylisothiazoline (MI) sensitization from 3.2% in 1990–1994 to 2.1% in 2000–2004 ($P < 0.001$). The decrease was apparent only in the female part of the study population (from 3.9% to 2.1%, $P < 0.001$). Similar findings were described in other European countries (7, 21–23). The diminished number of individuals with sensitization to (MCI/MI) could be explained by a lower exposure because of its substitution with methyldibromo glutaronitrile and a restriction of MCI/MI use in cosmetics, regulated by the European legislation (22, 24). Preservatives are relevant allergens in daily practice. As such substances are rotated in everyday products (22, 25), our findings corroborate the recommendation to closely track the changing use of preservatives (26, 27).

Neomycin, a topical agent against infections of the skin and mucous membranes and systemically for gastrointestinal bacterial decontamination, caused less positive patch test reactions 2000–2004 (2.0%) than 1990–1994 (4.0%) ($P < 0.001$). The decrease in sensitization rates to neomycin sulfate was seen both in the female and male population (female: from 4.9% to 2.5%, $P < 0.001$, male: from 2.7% to 1.3%, $P < 0.002$). The declining trend as well as similar sensitization rates were observed by the ESSCA and the IVDK as well (16, 28). The declining trend could be because of the fact that neomycin was more popular in the treatment of eczema and contact dermatitis a few decades ago, and that prescription rates have dropped significantly (29).

Positive reactions to thiuram mix, a marker for rubber allergy, have increased from <1.4% (1990–1994) to 2.4% (2000–2004) ($P < 0.0001$). ESSCA reported similar sensitization rates (16). The rising trend in our study could be because of an increased exposure to rubber, i.e. latex gloves, as the awareness of occupational hazards of human immunodeficiency virus infection and hepatitis has increased (30). A rise in sensitivity to thiuram mix until 1994 has been reported by the North American Contact Dermatitis Group as well; however, this rise was followed by a decrease in sensitization, probably because of greater use of vinyl and non-natural rubber latex gloves in healthcare professions (12). Assuming a similar shift in glove components takes place in Europe, similar shifts in sensitizations to thiuram mix may be seen in the future.

Sensitization to mercury can be detected by patch testing with both ammoniated mercury and thimerosal. Our baseline series contained only ammoniated mercury. We found significantly more positive reactions to ammoniated mercury in 2000–2004 (3.6%) than in 1990–1994 (<1.4%)

($P < 0.0001$). Compared to the results of the IVDK study, our sensitization rates are slightly higher (13). Especially high sensitization rates occur among females and males aged below 30 years (9.3%, 4.9%, respectively) (Table 3). This could be explained by exposure to childhood preventive vaccinations containing thimerosal (31, 32). Further testing with thimerosal would be necessary to confirm this. However, cross reactivity between these allergens should be taken into account (33). Furthermore, the higher sensitization rates in young women could be because of exposure to mercury contained in cosmetics. It is important to mention that in most cases sensitization to mercury has no clinical relevance, except in patients with oral stomatitis after exposure to dental amalgam (31, 32, 34). Therefore ammoniated mercury was excluded from the baseline series in 2006.

The rising trend of sensitization to fragrance mix I and *M. pereirae*, observed by Bangha and Elsner (3), did not persist. However, over the years 2000–2004 we noticed a decrease in sensitizations to fragrance mix (Linear-by-linear association test, $P < 0.001$). A similar observation was made by the IVDK (35) and by Danish dermatologists (36). The decrease in sensitization rates to fragrance mix I during the years 2000–2004 could partly be because of a reduced exposure owed to 1999s EU recommendations (37). As sensitization rates to *M. pereirae* remained steady over the years 2000–2004, the prevalence of sensitization to *M. pereirae* relative to fragrance mix was rising, a trend also observed by the IVDK (35). The persisting sensitization rate of *M. pereirae* in contrast to the decreased rate for fragrance mix could be explained by the increased use of other fragrance compounds cross-reacting with *M. pereirae*, but not with fragrance mix I. *M. pereirae*, in contrast to fragrance mix I, thus may assume a marker function for fragrance sensitization in a broader sense (38).

Propolis sensitization rates at 2.0% were slightly lower than sensitization rates from ESSCA (2.9%) (16). Only included into the baseline patch test series in recent years, no comparison for propolis over time was made.

In spite of a certain variation in our study populations over a decade, we feel that patch test sensitization rates may be a valuable indicator for changing trends in contact allergic dermatitis and may yield important regional information, complementing more broad-based data such as the IVDK registry.

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References

1. Wahlberg J E. Patch testing. In: *Textbook of Contact Dermatitis*, 3th edition, Rycroft R J G, Menné T, Frosch P J, Leppoittevin J-P (eds): Berlin, Heidelberg, Springer-Verlag, 2001: 435–468.
2. Aberer W, Komericki P, Uter W, Hausen B M, Lessmann H, Kränke B, Geier J, Schnuch A. Epidemiologische Überwachung von Kontaktallergenen. Der "Monitorblock" des IVDK. *Hautarzt* 2003; 54: 741–749.
3. Bangha E, Elsner P. Sensitizations to allergens of the european standard series at the department of dermatology in Zurich 1990–1994. *Dermatology* 1996; 193: 17–21.
4. Schnuch A, Aberer W, Agathos M, Brasch J, Frosch P J, Richter G. Leitlinien der Deutschen Dermatologischen Gesellschaft (DDG) zur Durchführung des Epikutantest mit Kontaktallergenen. *Hautarzt* 2001; 52: 864–866.
5. Diepgen T L, Stüben O. ALLDAT: an allergy data system for storage and analysis of test data with regard to epidemiological and occupational dermatology. *Semin Dermatol* 1989; 8: 101–102.
6. Uter W, Schnuch A, Gefeller O. Guidelines for the descriptive presentation and statistical analysis of contact allergy data. *Contact Dermatitis* 2004; 51: 47–56.
7. Schnuch A, Geier J, Uter W, Frosch P J, Lehmaner W, Aberer W, Agathos M, Arnold R, Fuchs T, Laubstein B, Lischka G, Pietrzyk P M, Rakoski J, Richter G, Ruëff F. National rates and regional differences in sensitization to allergens of the standard series. Population adjusted frequencies of sensitization (PAFS) in 40.000 patients from a multicenter study (IVDK). *Contact Dermatitis* 1997; 37: 200–209.
8. Uter W, Gefeller O, Geier J, Schnuch A. Changes of the patch test population (MOAHLFA index) in long-term participants of the Information Network of Departments of Dermatology*, 1999–2006. *Contact Dermatitis* 2008; 59: 56–57.
9. Liedén C. Legislative and preventive measures related to contact dermatitis. *Contact Dermatitis* 2001; 44: 65–69.
10. Swiss Government. Artikel 25 der Verordnung über Gebrauchsgegenstände vom 1.3. 1995.
11. Katsarou-Katsari A, Bankovska E, Lambrinopoulou K, Davou E, Bolbasis A, Papakonstantinou A. Trends in allergic contact dermatitis and preventive measures among cement workers (1985–1999). *Contact Dermatitis* 2003; 48: 174–175.
12. Nguyen S H, Dang T P, MacPherson C, Maibach H, Maibach H I. Prevalence of patch test results from 1970 to 2002 in a multi-centre population in North America (NACDG). *Contact Dermatitis* 2008; 58: 101–106.
13. Worm M, Brasch J, Geier J, Uter W, Schnuch A. Epikutantestung mit der DGK-Standardreihe 2001–2004, Ergebnisse des IVDK. *Hautarzt* 2005; 56: 1114–1124.
14. Geier J, Brasch J, Schnuch A. Contact allergy to dichromate in women. *Dermatosen* 2002; 48: 4–10.
15. Thyssen J P, Jensen P, Carlsen B C, Engkilde K, Menné T, Johansen J D. The prevalence of chromium allergy in Denmark is currently increasing as a result of leather exposure. *Br J Dermatol* 2009; 161: 1288–1293. (Online early view ahead of print).
16. Uter W, Hegewald J, Aberer W et al. The european standard series in 9 European countries, 2002/2003 – first results of the European Surveillance System on Contact Allergies. *Contact Dermatitis* 2005; 53: 136–145.
17. Wakelin S H, Smith H, White I R, Rycroft R J G, Mcfadden J P. A retrospective analysis of contact allergy to lanolin. *Br J Dermatol* 2001; 145: 28–31.
18. Andersen K E, Burrows D, White I R. Allergens from the standard series. In: *Textbook of contact dermatitis*, 2nd edition,

- Rycroft R J G, Menné T, Frosch P J (eds): Berlin, Heidelberg, Springer-Verlag, 1995: 435.
19. Nielson N H, Menné T. Allergic contact sensitization in an unselected Danish population. *Acta Derm venereol* 1992; 72: 456–464.
 20. Sulzberger M B, Lazar M P. A study of the allergenic constituents of lanolin (wood fat). *J Invest Derm* 1950; 15: 453–460.
 21. Schnuch A, Uter W, Lehmacher W et al. Epikutantestungen mit der Standardserie – erste Ergebnisse des Projektes, “Informationsverbund Dermatologischer Kliniken” (IVDK). *Dermatosen* 1993; 41: 60–70.
 22. Hasan T, Rantanen T, Alanko K et al. Patch test reactions to cosmetic allergens in 1995–1997 and 2000–2002 in Finland – a multicentre study. *Contact Dermatitis* 2005; 53: 40–45.
 23. Kohl L, Blondeel A, Song M. Allergic contact dermatitis from cosmetics. *Dermatology* 2002; 204: 334–337.
 24. Frosch P J, Lahti A, Hannuksela M, Andersen K E, Wilkinson J D, Shaw S, Lachapelle J M. Chloromethylisothiazolone/methylisothiazolone (CMI/MI) use test with a shampoo on patch-test-positive subjects. *Contact Dermatitis* 1995; 32: 210–217.
 25. Sasseville D. Hypersensitivity to preservatives. *Dermatol Ther* 2004; 17: 251–263.
 26. Gruvberger B, Bruze M, Tammela M. Preservatives in moisturizers on the Swedish market. *Acta Derm Venerol* 1998; 78: 52–56.
 27. Flyvholm M.-A. Preservatives in registered chemical products. *Contact Dermatitis* 2005; 53: 27–32.
 28. 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.
 29. Schwabe U, Paffrath D. Arzneiverordnungsreport. In: *Arzneiverordnungsreport*. Berlin, Heidelberg, Springer-Verlag, 2004.
 30. Nettis E, Colanardi M C, Soccio A L, Ferrannini A, Tursi A. Occupational irritant and allergic contact dermatitis among healthcare workers. *Contact Dermatitis* 2002; 46: 101–107.
 31. Heine G, Schnuch A, Uter W, Worm M. Frequency of contact allergy in German children and adolescents patch tested between 1995 and 2002: results from the Information Network of Departments of Dermatology and the German Contact Dermatitis Research Group. *Contact Dermatitis* 2004; 51: 111–117.
 32. Militello G, Jacob S E, Crawford G H. Allergic contact dermatitis in children. *Curr Opin Pediatr* 2006; 18: 385–390.
 33. Audicana M T, Munoz D, del Pozo M D, Fernandez E, Gastaminza G, Fernandez de Corres L. Allergic contact dermatitis from mercury antiseptics and derivatives: study protocol of tolerance to intramuscular injections of thiomersal. *Am J Contact Dermat* 2002; 13: 3–9.
 34. Garner L A. Contact dermatitis to metals. *Dermatol Therapy* 2004; 17: 321–327.
 35. 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.
 36. 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.
 37. The Scientific Committee on Cosmetic and Non-Food-Products intended for consumers (SCCNFP). Opinion on the issue of fragrance allergy in consumers, 1999. Available at: http://ec.europa.eu/health/ph_risk/committees/sccp/documents/out98_en.pdf, accessed on 9 March 2010.
 38. Hausen B M. Contact allergy to balsam of Peru. II. Patch test results in 102 patients with selected balsam of Peru constituents. *Am J Contact Dermat* 2001; 12: 93–102.

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