COD
Contact Dermatitis

Nickel allergy is still frequent in young German females – probably because of insufficient protection from nickel-releasing objects

Axel Schnuch[1], Jörg Wolter[2], Johannes Geier[1] and Wolfgang Uter[3]

[1] *Information Network of Departments of Dermatology (IVDK), University of Göttingen, 37075 Göttingen, Germany,* [2] *State Office for Agriculture, Food Safety and Fisheries (LALLF) Mecklenburg-Vorpommern, 18059 Rostock, Germany, and* [3] *Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen/Nürnberg, 91054 Erlangen, Germany*

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Summary

Background. Nickel contact allergy is still frequent both in patch-tested patients and in the general population.
Objectives. To explain this observation by relating clinical epidemiological data with recent chemical analyses of nickel release from costume jewellery.
Methods. (i) The trend of nickel allergy was analysed using data registered between January 1994 and December 2009 in the Information Network of Departments of Dermatology. (ii) In 2008, different parts of items of costume jewellery purchased at random on the German market ($n = 609$) were analysed for nickel release according to EN 1811:1998 + A1:2008 in five official German laboratories of food and non-food investigation.
Results. (i) Between 1994 and 2009, nickel allergy decreased in men (18–30 years) and in women (1–17 and 18–30 years); however, after 2000, there was no significant decrease in nickel allergy in the women aged 1–17 years. (ii) Of the post-assemblies, 28.0% exceeded the migration limit of $\geq 0.2\ \mu g/cm^2$ per week, and 5% released $\geq 26.8\ \mu g/cm^2$ per week. In articles with direct and prolonged contact with the skin, 12.8% of decorative parts and 17.1% of clasps exceeded the migration limit. If an adjustment factor was applied, according to the above norm, about half of the items otherwise rejected became acceptable.
Conclusion. Exposure to nickel-containing products exceeding the (unnecessarily relaxed) permitted limit may explain why nickel contact allergy remains a problem.

Key words: allergy; nickel; surveillance.

Since the EU Nickel Directive was adopted by the Council and the European Parliament in 1994 (1), we have noted a significant decrease in nickel contact allergy in female patients under the age of 31 years, from 36.1% in 1994 to 25.8% in 2001 (2). However, annual unpublished analyses of Information Network of Departments of Dermatology (IVDK) data revealed that from 2002 to 2009 there was no further decline: allergy prevalence remained clearly above 20% in this particular subgroup.

The European population is still highly exposed to nickel-containing, and potentially nickel-releasing, objects. Piercing of the earlobes is very common, particularly in women (3). According to a recent questionnaire study in 5000 patients in Germany (from dental and dermatological practices), 84% of women and 22% of men had ear piercings (4). However, piercing of other parts of the body has become increasingly popular too; 27.2% of the age group 15–30 years reported having a 'body piercing' (4). Furthermore, 52.8% had obtained

Correspondence: Dr Axel Schnuch, IVDK-Zentrale, Institut an der Universität Göttingen, Von Siebold Str. 3, 37075 Göttingen, Germany. Tel: +49 551 39 64 39; Fax: +49 551 39 60 95. E-mail: aschnuch@med.uni-goettingen.de

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their first piercing under the age of 18 years, the vast majority (about 90%) of them between the ages of 11 and 17 years (4). In addition, other exposures exist, including sources only recently covered by the Nickel Directive, for example mobile phones (5–7).

Moreover, nickel exposure may exceed the permitted threshold for items (i) inserted into pierced parts of the body (post-assemblies and 'studs') or (ii) those coming into direct and prolonged contact with the skin (e.g. necklaces and buttons). Originally, in 1994, a nickel content of less than 0.05% was set as the limit for the post-assemblies, whereas for the other items, nickel release was limited to $\leq$0.5 μg/cm^2 per week (1). (The term 'release' is preferred to 'liberation' and 'migration' throughout, unless the latter is used as 'migration limit', the term defined in the law.) Only recently, in 2004, the regulation for post-assemblies changed from a maximum allowed nickel content (0.05%) to a maximum allowed release, which was set at $<$0.2 μg/cm^2 per week (8), whereas it remained at 0.5 μg/cm^2 per week for all other items.

In this study we analysed:

(1) the age-stratified time trend of nickel contact allergy, with a focus on the subgroups of patients aged 1–17 years and 18–30 years, using the clinical data of the IVDK network;
(2) nickel release from costume jewellery (see below) randomly purchased on the German market to examine compliance with the EU Nickel Regulation as part of a nationwide surveillance project in Germany (Bundesweiter Überwachungsplan–2008) (9).

Methods

Nickel allergy trend in females and males

The IVDK (www.ivdk.org), a contact allergy surveillance network in Germany, Switzerland, and Austria, has been described elsewhere (10). Briefly, results of all patients patch tested in the participating departments are electronically recorded, along with important demographic and clinical data. The diagnostic procedure follows international guidelines (11), further refined by the German Contact Dermatitis Research Group (12), of which all IVDK participants are members. All data are transmitted in an anonymous format twice-yearly to the data centre in Göttingen, where they are checked and, if satisfying internal quality control criteria (13), analysed according to international guidelines (14), using SAS™ software (version 9.2; SAS Institute, Cary, NC, USA) and the statistical package R (version 2.8.1; http://www.r-project.org/).

For the present analysis, data of all patients patch tested between January 1994 and December 2009 were included. Nickel sulfate hexahydrate (5% petrolatum) was provided by Almirall-Hermal/Trolab (Reinbek, Germany). Weak (+) to strong (+++) positive patch test reactions on the third day after application of the test or, if this was not read, after the fourth day were aggregated as outcome 'positive' and contrasted with non-positive (non-allergic) reactions, comprising negative, doubtful and irritant reactions.

Chemical analyses of costume jewellery samples

From January to June 2008, different types of costume jewellery ($n = 209$) were obtained by responsible authorities for surveillance of food and non-food products, and investigated in five laboratories from six German Federal States (Table 1). Pieces were purchased at random on the German market, mainly from retailers (single fashion jewellery shops, discount markets, department stores, clothing and accessory chains, and piercing studios), but occasionally also from wholesalers/importers.

Of the 209 jewellery items, 22 were subjected to a 'total measurement' without specification; these were not further considered in our analysis. The remaining 187 pieces of jewellery were categorized according to their use (post-assembly, clasp, and decorative part), in 164 of 187 cases after dismantling the piece of jewellery for separate analyses of the different parts. These parts were separated into those items for insertion into pierced parts of the body (post-assemblies: ear studs or body-piercing articles, $n = 264$, taken from 157 different pieces of jewellery), and those with 'direct and prolonged contact with the skin' such as clasps ($n = 111$) from 78 pieces of jewellery and

Table 1. Participating surveillance laboratories with Bundesamt für Verbraucherschutz und Lebensmittelsicherheit Berlin acting as coordinator

Laboratory	No. of samples	LOD (μg/l)	LOQ (μg/l)	Analysis methods used
LLBB Berlin	79	25	50	ICP-OES
CVUA-OWL, Detmold	38	0.5	1	ICP-MS
LUA Sachsen, Dresden	68	0.9	2.8	ICP-OES
LAVES, IfB Lüneburg	180	0.8	2.5	ICP-OES
LALLF MV, Rostock	244	0.3	1	ICP-MS

ICP-OES, inductively coupled plasma optical emission spectrometry; ICP-MS, inductively coupled plasma mass spectrometry; LOD, limit of detection (in undiluted measuring solution); LOQ, limit of quantitation (in undiluted measuring solution).
Jewellery items were sent in from seven different federal states.

decorative parts ($n = 234$) from 113 pieces of jewellery. This subdivision was used because Annex XVII No. 27 of the new REACH regulation (EC 1907/2006) (15) has set the migration limits for the former products at ≥0.2 µg/cm² per week and for the latter products at >0.5 µg/cm² per week. Thus, a single piece of jewellery (one sample) could result in one sample (in 23 cases), in two subsamples (70 cases), in three subsamples (37 cases), in four subsamples (21 cases), and in five or more subsamples (36 cases). Moreover, different combinations of the above parts were encountered: most often, only post-assembly ($n = 47$) or a combination of these with decorative parts ($n = 46$), followed by jewellery in which clasps were additionally analysed separately ($n = 38$), or, less often, post-assembly and clasp ($n = 26$), decorative parts only ($n = 16$), decorative parts and clasps ($n = 13$), and clasps only ($n = 1$).

In all, a total of 609 subsamples (Table 3) resulted, analysed by the five laboratories (Table 1) for nickel release according to reference test method EN 1811:1998 + A1:2008 (16), with the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit acting as coordinator. Objects to be tested were stored in artificial sweat at 30°C for 1 week. The concentration of dissolved nickel in the solution was analysed with one of the methods recommended by EN 1811:1998 + A1:2008, namely inductively coupled plasma mass spectrometry (ICP-MS), inductively coupled plasma optical emission spectrometry (ICP-OES), or graphite furnace atomic absorption spectrometry (GF-AAS), depending on the local equipment (Table 1). As only those areas that come into direct and prolonged contact with the skin or the pierced parts of the body are considered, the remaining areas were covered by a suitable wax or lacquer or removed from the object. Areas were measured according to EN:1811:1998, using digital callipers. Objects with nickel-free coatings were subjected to the simulation of wear and corrosion according to EN 12472, simulating 2 years of normal use.

A second identical sample was investigated for determination of surface coatings. To ascertain whether there was a surface coating, a small area of the sample surface was carefully filed down and observed visually. To decide whether this coating was nickel-free or not, most samples were analysed by X-ray fluorescence prior to and after filing. Alternatively, the composition of the sample was determined by dissolving and measuring the metal content of the solution by ICP or AAS (see above).

Nickel release was then measured according to EN 1811:1998 + A1:2008. Items were analysed in the respective laboratories only once. Inter-laboratory comparisons on the same items were neither intended nor undertaken. The dimethylglyoxime (DMG) test was not performed in parallel.

Results

The total number of patients tested was 127 098; of these, 62% were female and 38% were male. These subgroups were further stratified for age (Table 2), with a special focus on the age intervals 1–17, 18–30 and 31–44 years. In these subgroups of women, there were 2357, 13 936, and 16 478 patients, respectively, and the corresponding numbers for men were 1295, 7830, and 11 678. Nickel contact allergy frequencies per year per subgroup are presented in Table 2, and, to better illustrate the trend, in Fig. 1 (women) and Fig. 2 (men). Considering the whole period (1994–2009), a significant decrease in nickel allergy was noted in men (18–30 years) and in women (1–17 and 18–30 years). In women aged above 30 years, allergy to nickel increased significantly (Fig. 1 and Table 1). However, during the period 2000–2009, there was no trend in men (all age groups). Nickel allergy decreased in women aged 18–30 years and increased in women aged 45–60 years. More importantly, there was no significant decrease in nickel allergy in the age group 1–17 years (Fig. 1 and Table 2).

The results of chemical analyses are presented in Table 3. In more than half of the jewellery components studied, the nickel concentration in the eluate remained below the detection level. However, 28.0% of the post-assemblies exceeded the migration limit of ≥0.2 µg/cm² per week, and 5% had released ≥26.8 µg/cm² per week, which is an excess factor of more than 100, with a maximum of 684 µg/cm² per week. According to 7.2 of EN 1811:1998, the measured values have to be multiplied by the adjustment factor of 0.1 to consider 'the inaccuracies of the analytical method'. Even if this adjustment factor of 0.1 was applied to the measured values, there were still 14.4% of objects exceeding the limit. In a pending revision of EN 1811 (prEN 1811: 2010), it has been proposed to greatly reduce the adjustment factor, namely to a limit of ≥0.35 µg/cm² per week, which would lead to the rejection of an object. Evidently, a much larger proportion of post-assemblies would be regarded as non-compliant if the proposed criterion was applied (Table 3, column 10).

In contrast, objects with direct and prolonged contact with the skin (decorative parts and clasps) complied somewhat better with the new REACH regulation (EC 1907/2006) (15), which has 'replaced' the former Directives (1, 8) (Table 3). Nevertheless, 5% of objects released ≥5.33 µg/cm² per week and ≥17.1 µg/cm² per week, respectively, with maxima of 1204 and 132 µg/cm²

Table 2. Frequencies of allergy to nickel (5%) in patients tested between 1994 and 2009 ($n = 127\,098$); men ($n = 48\,303$) and women ($n = 78\,795$) stratified for age group; trend (overall and from 2000 to 2009)

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total no.	Trend overall	*p*-value	Trend 2000	*p*-value
MALES																					
1–17 years																					
Positive (%)	7.50	4.05	2.90	3.88	6.41	5.26	2.11	4.48	6.15	7.32	8.64	5.63	5.95	2.41	1.28	6.67	—	→	0.91	→	0.998
No. tested	80	74	69	103	78	95	95	67	65	82	81	71	84	83	78	90	1295	—	—	—	—
18–30 years																					
Positive (%)	6.58	8.95	8.04	5.94	6.30	7.14	5.26	5.74	5.59	6.86	7.80	2.93	5.97	4.61	4.57	4.90	—	↓	<0.0001	→	0.24
No. tested	653	581	547	556	587	560	513	523	358	437	449	341	402	434	460	429	7830	—	—	—	—
31–44 years																					
Positive (%)	5.48	5.01	5.52	5.09	7.24	6.98	7.57	5.29	9.16	8.29	5.74	4.97	7.13	6.03	6.82	5.31	—	→	0.65	→	0.081
No. tested	766	719	706	688	774	774	766	699	655	736	766	684	729	763	718	735	11 678	—	—	—	—
45–60 years																					
Positive (%)	4.53	4.42	3.93	4.86	5.14	5.67	5.10	5.06	5.09	4.20	5.35	5.83	4.40	4.82	4.87	5.17	—	→	0.36	→	0.92
No. tested	994	815	815	884	954	988	922	830	727	809	897	875	978	1078	1068	1045	14 679	—	—	—	—
61–99 years																					
Positive (%)	3.86	5.50	3.15	2.96	2.70	5.18	2.99	4.97	4.81	6.01	5.18	3.00	4.61	4.89	4.68	3.09	—	→	0.056	→	0.44
No. tested	621	527	571	574	704	772	769	664	707	865	1043	899	997	1002	1005	1101	12 821	—	—	—	—
FEMALES																					
1–17 years																					
Positive (%)	29.19	28.85	15.18	23.95	23.03	19.46	12.00	19.21	10.20	17.24	16.00	17.65	16.90	19.20	10.53	14.29	—	↓	<0.0001	→	0.96
No. tested	161	156	191	167	178	185	150	151	98	145	125	136	142	125	114	133	2357	—	—	—	—
18–30 years																					
Positive (%)	36.60	35.68	34.94	34.83	33.43	31.79	26.72	27.50	26.97	27.76	25.53	26.64	26.19	25.45	22.51	20.19	—	↓	<0.0001	↓	0.0002
No. tested	1396	1219	1099	1002	990	887	771	709	597	753	748	672	714	774	773	832	13 936	—	—	—	—
31–44 years																					
Positive (%)	30.65	30.38	28.68	30.50	32.52	34.25	32.58	32.42	34.15	34.88	33.30	37.92	34.55	34.78	34.83	29.70	—	↑	<0.0001	→	0.93
No. tested	1279	1172	1168	1095	1153	1127	1065	944	814	949	976	886	958	943	959	990	16 478	—	—	—	—
45–60 years																					
Positive (%)	12.32	13.46	12.89	14.10	14.53	16.59	14.49	15.70	18.40	19.61	20.17	19.20	21.63	21.76	21.45	19.91	—	↑	<0.0001	↑	<0.0001
No. tested	1607	1426	1311	1404	1480	1392	1346	1191	1103	1331	1487	1318	1475	1558	1571	1818	22 818	—	—	—	—
61–99 years																					
Positive (%)	7.61	7.19	6.00	5.65	6.51	8.36	6.95	7.88	9.77	10.39	9.30	9.92	9.07	8.54	8.94	7.72	—	↑	<0.0001	→	0.97
No. tested	1090	1085	1066	1133	1352	1376	1382	1256	1280	1636	1742	1572	1665	1791	1812	1968	23 206	—	—	—	—

Cochran–Armitage trend test, two-sided; downward arrows indicate a significant decrease and upward arrows a significant increase in allergy prevalence; →, no significant trend.

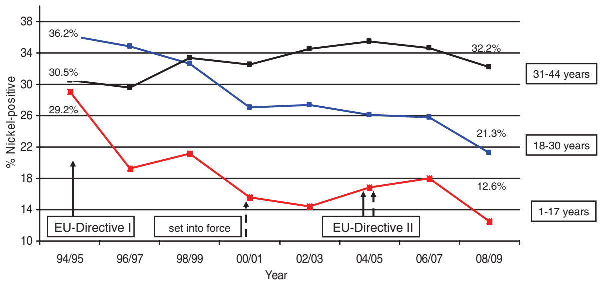

Fig. 1. Nickel allergy in women (1–17, 18–30 and 31–44 years; data from the Information Network of Departments of Dermatology 1994–2009; numbers of patients tested were 2357, 13 936, and 16 478, respectively). Decreasing and increasing trends were significant (Cochrane–Armitage trend tests: <0.0001). Nickel Directive I (1994) was put into force on 23 June 2000; Nickel Directive II (2004) was put into force on 13 July 2005 (1, 7). Most remarkably, nickel allergy in the age group 1–17 years did not decrease significantly between 2000 and 2009, indicating a failure of the Nickel Directive (1), as the vast majority of this age group came into contact with nickel after the nickel regulation.

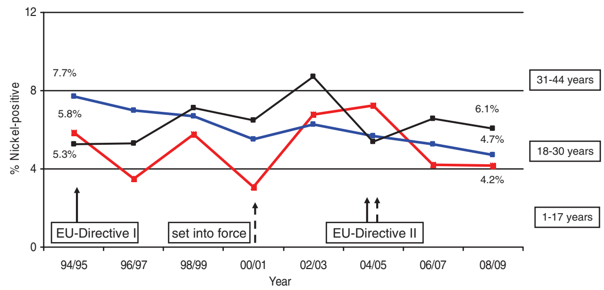

Fig. 2. Nickel allergy in men (1–17, 18–30 and 31–44 years; data from the Information Network of Departments of Dermatology 1994–2009; number of patients tested were 1295, 7830, and 11 678, respectively). The decreasing trend in the 18–30-year age group was significant (Cochrane–Armitage trend test: <0.0001). Nickel Directive I (1994) was put into force on 23 June 2000; Nickel Directive II (2004) was put into force on 13 July 2005 (1, 7).

per week, respectively. In total, 12.8% and 17.1% exceeded the migration limit. Even if the adjustment of 0.1 was applied to the measured values, there were still 5.6% and 9.0%, respectively, of objects exceeding the threshold. As above, the application of the revised limits increased the proportion of items that would be rejected, liberating $\geq$0.88 μg/cm^2 per week (Table 3, column 10).

In general, the frequency of values exceeding the limit was reduced by half through the adjustment procedure, thus disguising the real problem: 26 of 49 (49%) metal parts exceeding the limit of >0.5 μg/cm^2 per week and 36 of 74 (53%)%) metal parts exceeding the limit of $\geq$0.2 μg/cm^2 per week were found to be 'compliant' only by applying the adjustment factor of 0.1 (Table 3).

Discussion

For decades, allergy to nickel has remained the most frequent contact allergy. According to recent studies, the prevalence in clinical patch test populations was above 15% [Germany, 17.3% (17); Denmark, 16.8% (18), UK, 18.6% (19); Italy, 25.6% (20)]. In the general population, nickel is the most frequent allergen [Denmark, 5.9% (21); Germany, 5.5% (22)], with higher frequencies in adolescents [Sweden, 9.9% (23); Denmark, 8.6% (24)]. In patch test populations, significant differences were found between frequencies in different parts of Europe, with 19.7% in central Europe and 24.4% in southern Europe (25). In all studies mentioned, females were much more often nickel-allergic than men. However, a significant decrease in allergy frequency has also been noted, on comparison of the periods before and after the EU Nickel Directive in 1994 (1), in younger patients (2, 18) and in the younger general population (21, 26). This development was interpreted as a success of the EU Directive, limiting the exposure to nickel through nickel-containing objects (27). Nevertheless, nickel allergy is still frequent today.

In our study, we found a significant decrease in nickel allergy in men (18–30 years) and in women (1–17 and 18–30 years) between 1994 and 2001. In contrast, women aged above 30 years were found to be sensitized to nickel significantly more often in recent years (Fig. 1 and Table 2). This phenomenon is probably attributable to a cohort effect (which means that these patients were probably exposed to 'unregulated' nickel at younger ages and sensitized before 1994), as observed previously (2, 18, 21).

However, regarding the period 2000–2009, we could not find a further decrease, particularly in the youngest age group (1–17 years). Some of these patients were born after nickel regulation, and an even larger proportion will have received the first piercing after nickel regulation. Thus, a declining prevalence would be expected in this age group, reflecting the effectiveness of nickel regulation in terms of reduced or even eliminated exposure. Instead, a 'persisting nickel allergy problem' has been identified. Four explanations could be considered for this:

(1) A significant number of nickel-containing objects do not comply with former or current EU regulations (1, 8, 15).
(2) The different limits for nickel content (0.05%, in force until 2004) and for nickel release (>0.5 and $\geq$0.2 μg/cm^2 per week respectively) were or are still too high.

Table 3. Six hundred and nine samples (different parts of costume jewellery items) analysed according to EN 1811:1998; distribution of actually measured values, and proportion of non-compliant items with and without application of the adjustment factors annotated below

		Nickel release (μg/cm² per week)						Items exceeding the respective limit		
Part of jewellery	Number of specimens	Migration limit	First quartile	Median	Third quartile	95% percentile	Maximum	Actual measurement (column 9): % (*n*)	After suggested adjustment (column 10): % (*n*)	After current adjustment (column 11): % (*n*)
Post-assemblies*	264	≥0.2	0	0	0.30	26.8	684	28.0 (74)	24.6 (65)	14.4 (38)
Decorative parts†	234	>0.5	0	0	0	5.33	1204	12.8 (30)	10.3 (24)	5.6 (13)
Clasps	111	>0.5	0	0	0.08	17.1	132	17.1 (19)	12.6 (14)	9.0 (10)

The differences between values in columns 9 and 11 indicate that $74 - 38 = 36$ of 74 post-assemblies exceeding the limit of 0.2 μg/cm² per week (53%), and similarly 26 of 49 (49%) decorative parts and clasps exceeding the limit of 0.5 μg/cm² per week, were found to be 'compliant' only by applying the adjustment factor of 0.1. Values of '0' denote measurements below the detection level (Table 1).
Column 9: Would exceed the limit without the adjustment factor of 0.1, i.e. using measurement values directly.
Column 10: Would exceed the limit after application of measurement uncertainty, i.e. against the migration limit of ≥0.88 and ≥0.35 μg/cm² per week, respectively (according to revised draft prEN1811:2010).
Column 11: Proportion exceeding the acceptability limit after application of the adjustment factor of 0.1, according to the current version of EN 1811:1998 + A1:2008.
*Ear studs and body-piercing articles.
†(Ear) jewellery in direct and prolonged contact with the skin.

(3) The application of the adjustment factor 0.1 according to the currently valid version of EN 1811 (EN 1811:1998) results in an adjusted value of 1/10th of the original measured value, leading to a higher number of 'compliant' samples, although the levels are unacceptable in reality.
(4) Other sources of cutaneous nickel exposure not covered by the EU regulation (15) are (partly) responsible.

All explanations are plausible, and all may contribute to the problem to some extent. At any rate, epidemiological data on the high persisting frequency of nickel allergy show that exposure to nickel is definitely too high. This view is supported by our chemical analyses: in total, 28.0% of the post-assemblies exceeded the migration limit of ≥0.2 μg/cm² per week. Even when the adjustment factor of 0.1 was applied to the measured values, there were still 14.4% of objects exceeding the limit. In other components of jewellery, the quality problem was not as marked, but it was still non-negligible (Table 3).

In other studies, nickel release from various objects (not only from jewellery, but also from metallic accessories of shoes and clothes, spectacle frames, and watches) was also determined by using the DMG test. A study from Sweden performed in 2001, before the Nickel Directive was put into force, reported that 25% of 725 items intended for direct and prolonged contact with the skin released nickel, as shown by a positive DMG test result. Of 15 posts intended for use during epithelialization after piercing, 60% contained more than 0.05% nickel (28). A subsequent study from Sweden, after the Nickel Directive was put into force, reported that 8% of 786 items in direct and prolonged contact with the skin still released nickel, and that three of 18 piercing posts released too much nickel (according to chemical analyses) (29). In a recent study from Denmark, DMG testing showed that 78 (22.0%) of 354 metallic pieces of jewellery and accessories randomly purchased from 36 stores in Copenhagen released an excessive amount of nickel (30).

This seems to be a worldwide problem, as many nickel-releasing earrings were also detected on the market in the United States and in East Asia (31, 32). Jewellery might be imported to the EU, particularly from East Asia. In a study of Chinese and Thai earrings using the DMG test, 31.5% of Chinese earrings and 29.2% of Thai earrings were DMG test-positive (32). These figures may even underestimate the exposure to nickel through jewellery, as the DMG test was shown to have a rather limited sensitivity of 59% (33).

The problem of measurement uncertainty deserves particular attention: in order to adjust for 'inaccuracies of the analytical method', particularly inaccuracy of measurement, difficulties in measuring the surfaces, and 'general deficiency in experience with the analysis of products from the market', an adjustment factor was introduced in EN 1811:1998 (16). However, several objections against this rule can be put forwards:

- New and more accurate ways of measuring the surface are available (33). Moreover, the surface of an ear stud is usually cylindrical and thus easy to determine.
- The laboratories have gained much experience in measuring the nickel release of samples from the market over the last 10–15 years.
- The currently used adjustment factor of 0.1 corrects the value in only one direction, and does not meet the requirements of a modern concept of scientifically and statistically justified measurement uncertainty.
- The adjustment factor jeopardizes the intention of the legislator to ensure a high level of protection of human health, as pointed out in recitals of REACH (15), and to protect the consumer by nickel migration limits: as measured values of up to 5 and 2 $\mu g/cm^2$ per week, respectively, are multiplied by the adjustment factor of 0.1, these values, which are undoubtedly too high, will nevertheless meet the limits of >0.5 and 0.2 $\mu g/cm^2$ per week, respectively (34). In fact, 26 of 49 (49%) metal parts exceeding the limit of 0.5 $\mu g/cm^2$ per week and 36 of 74 (53%) metal parts exceeding the limit of $\geq$0.2 $\mu g/cm^2$ per week were found to be ‘compliant’ only by applying the adjustment factor of 0.1 (Table 2).

Today, the current adjustment is no longer adequate and acceptable from the analytical point of view, and the issue of measurement uncertainty (expressed quantitatively as a range around the actually measured value) has still to be addressed. Clear guidance on the relationship between analytical results, measurement uncertainty and limit values have been developed for contaminants in food. They are summarized in the EU document SANCO/0064/2003-rev.4 (35). Although developed for food control purposes, this principle could generally be applied to all quantitative analytical tasks, for verifying compliance with a limit.

In the amendment to the Commission Directive 76/769/EEC in September 2004, namely in Directive 2004/96/EC, paragraph 3 states ‘The new rate of nickel release (migration limit) should be adjusted with the multiplication factor specified in EN 1811 to compensate inter-laboratory variations and measuring inaccuracies. The European Committee of Standardization (CEN) is invited to review EN 1811 in particular regarding the adjustment factor and to prepare a revised standard without adjustment factor, or with a smaller adjustment factor, if appropriate’. This request is repeated in the standardization mandate M/414 EN by the European Commission to the European Committee of Standardization (CEN). CEN TC 347 WG1 worked on this topic in recent years, and decided to implement a modern and internationally accepted concept of measurement uncertainty in the revision of EN 1811. An inter-laboratory comparison undertaken in 2008 according to ISO 5725 gave as an estimate for the combined measurement uncertainty a value of 46% (against limits of $\geq$0.88 and $\geq$0.35 $\mu g/cm^2$ per week, respectively). The revised draft (prEN 1811:2010), including an improved analytical procedure, was adopted by the working group and presented to the CEN Management Centre for the ‘Formal Vote’. The draft is expected to be in force as the new EN 1811 in 2013.

Conclusion

Relating the current clinical epidemiology of nickel allergy to the results of chemical–analytical surveillance of nickel-releasing objects, it can be concluded that persistent exposure to nickel at a level sufficiently high to sensitize has probably contributed to nickel allergy remaining a problem. In addition to an unacceptable proportion of products clearly exceeding the permitted limit, a further reason for this is most likely the ‘adjustment factor’ of 0.1, which should be abandoned, as already indicated in Directive 2004/96/EC and proposed by the working group CEN TC 347 WG1.

This study also shows the impact of continuous epidemiological surveillance. Those authorities implementing regulatory rules (EU and national) were not aware of a persisting nickel problem, as they have neglected to include epidemiological outcome control regarding morbidity as an integral part of the regulation. After having proven the first successes of nickel regulation, epidemiological surveillance has now proven the failure of regulation.

There are more general lesson to be drawn from the ‘nickel case’: future surveillance will be indispensable for monitoring the effectiveness, ineffectiveness or even unwanted (side) effects of regulatory measures of national and supranational authorities.

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