

The EU Nickel Directive revisited – future steps towards better protection against nickel allergy

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Summary

In July 2001, the EU Nickel Directive came into full force to protect European citizens against nickel allergy and dermatitis. Prior to this intervention, Northern European governments had already begun to regulate consumer nickel exposure. According to part 2 of the EU Nickel Directive and the Danish nickel regulation, consumer items intended to be in direct and prolonged contact with the skin were not allowed to release more than 0.5 µg nickel/cm²/week. It was considered unlikely that nickel allergy would disappear altogether as a proportion of individuals reacted below the level defined by the EU Nickel Directive. Despite this, the EU Nickel Directive part 2 was expected to work as an operational limit that would sufficiently protect European consumers against nickel allergy and dermatitis. This review presents the accumulation of epidemiological studies that evaluated the possible effect of this major public health intervention. Also, it evaluates recent exposure assessment studies that have been performed using the dimethyl glyoxime test. It is concluded that the EU Nickel Directive has started to change the epidemiology of nickel allergy in Europe but it should be revisited to better protect consumers and workers since nickel allergy and dermatitis remain very frequent.

Key words: allergy prevention; EU Nickel Directive; nickel allergy; nickel dermatitis; nickel exposure; public health.

In July 2001, the EU Nickel Directive came into full force to protect European citizens against nickel allergy and dermatitis. This Directive was included in REACH, the EU chemicals regulation, during 2009. Prior to this intervention, northern European governments had already begun to regulate consumer nickel exposure; in Denmark, a statutory order was implemented to reduce nickel release from certain items in 1990 (1); in Sweden, ear-piercing

with nickel-containing piercers or rings was banned in 1991, if the alloy contained more than 0.05% nickel (2); and in Germany, certain nickel-containing consumer items were required to be labelled 'contains nickel and may cause an allergic reaction' after 1991 (2). The Danish and Swedish nickel regulations and the EU Nickel Directive can be regarded as pioneering consensus approaches aimed at reducing the nickel allergy problem, but not attempts to totally abolish nickel allergy (3, 4); a total ban on the use of nickel in consumer products would evidently reduce the nickel allergy problem more efficiently than a restriction. Nevertheless, this approach was never considered, as nickel has many useful applications, being inexpensive and corrosion-resistant. It is also important to recall that many nickel-containing alloys do not release

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nickel ions at levels causing dermatitis, and a demand for nickel-free consumer items would thus be irrelevant.

The limit proposed by Menné et al. (4) (i.e. nickel release should not exceed 0.5 µg nickel/cm²/week from consumer items intended to be in direct and prolonged contact with the skin), and upon which the Danish nickel regulation and Part 2 of the EU Nickel Directive are based, is considered to protect most nickel-allergic individuals. Nevertheless, a minority of nickel-allergic individuals may react below this limit value (5). It is known that the elicitation threshold varies between individuals and over time, depending on factors such as degree of sensitization, genetic predisposition, presence of skin irritants, occlusion, duration and frequency of exposure, area size, and anatomical site. These observations evidently make a 'one-goes-for-all limit' (except, of course, total prohibition of the use of nickel) an impossible way in which to protect consumers from developing nickel allergy and dermatitis. In line with this, Gawkrödger predicted in 1996 that it was unlikely that nickel allergy would disappear altogether, as a proportion of individuals reacted below the level defined by the EU Nickel Directive (3, 4). Despite this, the EU Nickel Directive Part 2 was expected to work as an operational limit that would sufficiently protect European consumers against nickel allergy and dermatitis.

Since the Danish nickel regulation was introduced in 1990, 10 years before the EU Nickel Directive came into force, possible epidemiological changes in nickel allergy and dermatitis following the regulation were expected to appear first in Denmark. So far, a decrease in nickel allergy has indeed been observed in young Danish women from the general population (6) and in young Danish female dermatitis patients seen in private dermatology practice (7) and a university clinic (8). Furthermore, women who were ear-pierced after the regulatory intervention in Denmark had a significantly lower prevalence of nickel allergy and dermatitis than women who were ear-pierced before it (9). Finally, the association between hand eczema and nickel allergy in young Danish women and the strength of positive patch test reactions (2+ and 3+) in Danish dermatitis patients have been reduced after regulation (6, 10). In line with these findings, the prevalence of nickel allergy has decreased in patients from other European countries in recent years, for example Sweden and Germany (11, 12). Only a few reports from other parts of Europe have described the development of nickel allergy after nickel regulation. In Italy, one study found a stable prevalence of nickel allergy (13), whereas another study showed a decrease in young female dermatitis patients (14). In Poland, the prevalence of nickel allergy decreased from 15.9% in 1995 to 10.0% in 2004 in female dermatitis patients aged under 20 years patch tested in

Warsaw (15). However, the prevalence of nickel allergy among adolescents (12–16 years) who were patch tested between 1970 and 1994 reached 15.3% in girls and 5.5% in boys (16), as compared with 27.8–31.8% in girls and 6.7–7.7% in boys aged 16–17 years who were patch tested in the years 2007–2009 (17, 18). It seems, therefore, that no direct or indirect effect of the EU Nickel Directive can yet be observed in Poland. This is not very surprising, given that the Nickel Directive officially came into force in Poland only in 2004, and a survey carried out 2 years later showed that it still remained at the planning stage, with no practical implementation (19).

Despite the decrease in nickel allergy shown in some European countries, it is important to emphasize that nickel allergy remains very prevalent; for instance, at least 11% of Danish adult women aged 18–35 years are allergic to nickel (6), and the proportion of positive nickel patch test reactions has remained stable at 10–20% among young female German dermatitis patients (<18 years) since the beginning of the new millennium (20). The 2005–2006 clinical patch test data registered in 10 European countries and reported to the European Surveillance System on Contact Allergies revealed high prevalences of nickel allergy in both western, southern, central and north-eastern Europe, being, respectively, 20.8%, 24.5%, 19.7%, and 22.4% (21). Dermatologists and regulators should therefore look for causative explanations and seek to rapidly optimize the EU Nickel Directive to better protect consumers, workers and dermatitis patients in Europe (Table 1). Recent studies have provided important information about the patterns of consumer nickel exposure:

- (1) The proportion of dimethylglyoxime (DMG)-positive items, among the broad range of consumer items covered by the EU Nickel Directive, decreased significantly in Stockholm, Sweden from 25% of 725 tested items in 1999, to 8% of 786 in 2002–2003, and 9% of 659 in 2010 (22–24). Since the EU Nickel Directive came into full force in 2001, the decrease in Sweden is probably an effect of the regulation. A recent study showed that approximately 22% of 354 jewellery and hair clasps (both inexpensive and moderately expensive) purchased in Copenhagen, Denmark gave positive DMG test reactions (25). A study from Warsaw and London showed that, respectively, 18.4% of 206 and 15.1% of 201 inexpensive earrings randomly purchased from different categories of stores gave positive DMG test reactions (26). Thus, the decrease observed in Sweden may, to a certain degree, be attributable to the effect of a nationwide campaign launched in 1999 by responsible national authorities, to inform

Table 1. Possible explanations for the persistence of nickel allergy and dermatitis following regulatory intervention regarding nickel exposure

| Causes | Estimated contribution to persistence of nickel allergy and dermatitis (strong/moderate/weak) |
|---|---|
| Consumer | |
| Sensitization before nickel regulation | Strong/moderate/weak* |
| Violation of the EU Nickel Directive | Moderate |
| Lack of control by and information from responsible authorities | Moderate |
| Exposure to items not covered by the regulation | Moderate/weak |
| Exposure to items personally imported from countries outside the EU | Weak |
| Exposure resulting from defect coatings on consumer items after 2 years of use | Weak |
| Occupational | |
| Exposure resulting from contact with tools, keys, locks, handles, coins, other equipment, materials, metal-working fluids, etc. | Strong/moderate/weak† |
| Other | |
| 'Adjustment' factor of 0.1 in EN 1811:1998, the reference test method for control of compliance with the EU Nickel Directive | Strong |
| Insufficiency of the contents of the EU Nickel Directive | Weak |
| Genetic vulnerability | Moderate |
| Toys | Weak |
| Medical devices with skin contact | Weak |

*Depending on age group.

†Depending on occupation.

consumers, manufacturers, importers, retailers, and local authorities responsible for control, as DMG-positive items remain common in stores in other capitals. Such campaigns are warranted elsewhere.

- (2) The accumulation of DMG test studies performed within the recent past have shown that DMG-positive jewellery (a significant proportion of which probably violates the EU Nickel Directive) is sold mainly in street markets and in stores that seem to have independent ownership and are not members of national or international chains; this was also seen in Sweden in 2010 (22, 25, 27). Authorities should prioritize information campaigns for, and random inspections of, retailers from these categories. It has been suggested that socio-economic factors such as low income and unemployment are related to nickel allergy (28).

A recent Danish questionnaire and patch test study, however, found no association between nickel allergy and educational level (29). Future research should ideally focus on the social profile of subjects with nickel allergy, with the objective of better protecting vulnerable groups. Finally, a Danish patient-based study showed that nickel-allergic patients with nickel dermatitis of current relevance very rarely reported causative exposure to DMG-positive items purchased outside of Denmark and the EU (30).

- (3) A recent study showed that the sensitivity and specificity of the DMG test were, respectively, 59% and 98% when the DMG test was validated against the EN 1811:1998 reference test method (31). Thus, the proportion of earrings and other consumer items that release $>0.5 \mu\text{g nickel/cm}^2/\text{week}$ and, therefore, pose a risk to consumers following prolonged skin contact may even have been underestimated in past studies.
- (4) The reference test method for control of compliance with the Nickel Directive, the European standard EN 1811:1998, has an important weak point. EN 1811:1998 allows multiplication of the measured nickel release value by 0.1 ('adjustment factor') before the interpretation of compliance. Thus, items with nickel release up to $5 \mu\text{g/cm}^2/\text{week}$ are considered to comply. The 'adjustment' factor was introduced in the first version of the standard to compensate for difficulties in calculating complicated area sizes and the limited experience with the method. It may be used as a loophole for industries not willing to follow the scientific recommendations (32). We strongly recommend removing the 0.1 factor, or at least replacing it with a smaller adjustment factor, as proposed in the EC mandate of 25 June 2007 to CEN for revision of EN 1811:1998, or replacing it with a measurement uncertainty interval, as in Draft prEN 1811 of July 2009, currently in the acceptance process of CEN/TC 347. We consider the proposed uncertainty interval to be reasonable, as items with nickel release $\geq 0.88 \mu\text{g/cm}^2/\text{week}$ and $\geq 0.35 \mu\text{g/cm}^2/\text{week}$ would be deemed to be non-compliant with the limits of 0.5 and 0.2, respectively. Protection of consumers and human health by the Nickel Directive would then be much strengthened.

A recent study from Germany revealed that about 10% of several hundred parts taken from 187 jewellery items, comprising posts, clasps and ornamental parts, released

nickel in a range between 0.2 and 2 µg nickel/cm²/week for posts and between 0.5 and 5 µg nickel/cm²/week for other parts (20). Despite this, these items were 'acceptable' for the market, because the 'adjustment' factor of 0.1 according to the current version of the reference test method (EN 1811:1998) was applied.

Occupational nickel exposure may contribute modestly to the very high prevalence of nickel allergy in the general population, as nickel allergy is less frequent in men than in women, but in certain occupations it is of greater importance. Occupational nickel dermatitis typically occurs on the hands, resulting in chronic eczema, sick leave, and changes in job routines. Today, occupational nickel allergy and dermatitis may be seen following prolonged or repeated skin contact with metallic items, for example tools, scissors, crochet hooks, coins, handles, and keys, and in metal workers, owing to high levels of nickel release and deposition on skin (33–36). There is also an urgent need for nickel regulation regarding items that come into repeated or prolonged contact with the skin at work. The EU Nickel Directive should be expanded to cover such items.

We consider it necessary and urgent that all medical devices intended for more than transient contact with the skin should conform to the limit values of the EU Nickel Directive (37), as is the case with spectacle frames. Examples of such medical devices are skin closure devices, clamps, drains, infusion devices, catheters, and tubes. It is considered irrelevant to print warnings about nickel allergy on such devices, as is sometimes done. Instead, the existing regulation for protection against nickel allergy should be applied. Nickel-containing medical devices that are inserted into the body may result in cutaneous as well as extracutaneous complications (38, 39). Management of this area is difficult, and should be addressed separately.

Nickel is sometimes used in toys, and may result in nickel dermatitis, as recently shown and debated (40, 41). According to the the Danish Ministry of the Environment's Centre for Information, nickel exposure in toys is

covered by REACH and the Toy Safety Directive. Toys are defined as any products or materials designed or clearly intended for use in play by children less than 14 years of age. The current Toy Safety Directive (88/368/EEC) has recently been updated, and on 20 July 2011, the new Toy Safety Directive (2009/48/EC) comes into force (replacing 88/368/EEC), except for one section, which will be replaced on 20 July 2013. In its current form, the Toy Safety Directive does not specifically mention nickel, but it does mention many other metals (e.g. chromium, lead, and cadmium). In the new Directive (2009/48/EC), all compounds that are carcinogenic, mutagenic or reprotoxic (CMR) are forbidden in toys. Nickel is considered to be CMR class 2, but is allowed in stainless steel, as nickel is only released from such alloys in low concentrations.

Prior to regulatory intervention regarding nickel exposure, it was debated whether nickel could be replaced by cobalt in consumer products and increase cobalt exposure (2). So far, there are no indications that regulatory interventions regarding consumer nickel exposure have resulted in increased cobalt exposure or cobalt allergy (8, 42). Cobalt allergy should, however, be continuously monitored. Also, palladium released from jewellery has caused allergic contact dermatitis and allergic contact granuloma (43). The association between palladium allergy and jewellery exposure should be closely monitored in the future.

In conclusion, the EU Nickel Directive has started to change the epidemiology of nickel allergy in Europe, but it should be revisited to better protect consumers and workers, as nickel allergy and dermatitis remain very frequent. Furthermore, the 0.1 adjustment factor should be removed from EN 1811. Regulation is a toothless tiger if compliance is not appropriately checked and enforced. Moreover, the availability of exposure assessments and contact allergy surveillance data could have alerted regulatory institutions across Europe even earlier, than it hopefully does now, about a persisting problem, and the need to take action.

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