

Contact allergy to metals in adolescents. Nickel release from metal accessories 7 years after the implementation of the EU Nickel Directive in Poland

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Summary

Background. Contact allergy among adolescents is an important issue.

Objectives. To assess the prevalence of contact allergy to metals in adolescents aged 15 years and nickel release from metal accessories that are in direct contact with the skin.

Methods. Three hundred and nine females and 219 males, all 15 years old, from randomly selected secondary schools were examined and patch tested with nickel sulfate, cobalt chloride, palladium chloride, and potassium dichromate. Three hundred and ninety-nine metal accessories were tested with the dimethylglyoxime (DMG) test.

Results. 'Metal dermatitis' was reported by 19.4% of females and 0.5% of males. Positive patch test reactions were found in 8.5% of the adolescents (12.9% in females; 2.3% in males), namely to: nickel (12.3% of females; 1.4% of males); palladium (5.2% of females; 0.5% of males); cobalt (3.2% of females; 1.4% of males); and chromium (1.3% of females; 0.9% of males). Allergic contact dermatitis caused by metals was diagnosed in 9.7% of females and in 0.5% of males. Of the metal items, 26.1% gave positive DMG test results: 10.0% of earrings, 11.4% of snaps, and 56.2% of belt buckles.

Conclusions. Despite the implementation of the Nickel Directive in Poland, nickel still remains an important causal factor for allergic contact dermatitis. Numerous metal accessories do not comply with the Directive.

Key words: adolescents; contact allergy; metals; nickel release.

It is estimated that contact allergy is present in about 20.0% of the general population of Europe (1). The epidemiological data derive mainly from adult population studies. Among the studies concerning children and adolescents, the majority included selected groups with eczematous skin lesions who were suspected of having

allergic contact dermatitis or atopic dermatitis (2, 3). However, population-based studies were also performed, and they showed that contact allergy among children is by no means less frequent than among adults. In these studies, a positive response to at least one allergen was found in 13.3–24.5% of the examined children (4–7). The findings indicated that the most prevalent sensitizers were metals, especially nickel (8). Patch testing with palladium was rarely performed, despite the fact that this metal is frequently used as a component of metal alloys applied in the process of manufacturing jewellery and dental materials (9, 10).

The aims of our study were as follows:

1. To assess the prevalence of contact allergy to the metals nickel, cobalt, chromium and palladium

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in a population of Polish adolescents aged 15 years;

2. To evaluate nickel ion release from metal accessories that are in direct contact with the skin, are currently used by adolescents, and were delivered by them during the examination.

Materials and Methods

Among 310 secondary schools in central Poland, from both urban and suburban areas, 15 were randomly chosen. Only 10 schools agreed to take part in the examination. The invitation to the test was directed to all pupils aged 15 years attending those schools (621 pupils in total). Finally, when written informed consent concerning participation in the study had been obtained from the pupils' parents or legal guardians, 528 adolescents (309 females; 219 males) were included in the study population.

The examinations were conducted in 2009 and 2010 on the schools' premises, and comprised:

- 1a) An interview (preceding the clinical examination and patch testing) regarding:
 - Body piercing (ears and/or other body parts)
 - Symptoms of cutaneous intolerance reactions to metal accessories upon direct contact with the skin, including itching, burning, and eczematous reaction ('metal dermatitis') (5)
 - *Atopy*. Participants were asked whether they had ever been diagnosed with atopic diathesis, atopic dermatitis, allergic rhinitis, allergic conjunctivitis, or atopic asthma, and whether positive prick test reactions to common aeroallergens (grass, weed, tree, dust mites, moulds, cats, and dogs) had been found in them. Only adolescents with confirmed positive prick test results for one or more aeroallergens were regarded as suffering from allergic rhinitis, allergic conjunctivitis, or atopic asthma.

The questions asked during the interview are shown in Table 1.

- 1b) Dermatological examination, that is, visual assessment of the participants' whole skin.
- 1c) *Patch tests containing*: 5.0% nickel sulfate, 1.0% cobalt chloride, 2.0% palladium chloride, and 0.5% potassium dichromate, dispersed in petrolatum. The tests were performed with IQ® Chambers. Allergens and chambers were supplied by Chemotechnique Diagnostics® (Vellinge, Sweden). The results were evaluated according to the recommendations of the International Contact Dermatitis Research Group. The readings were performed 2 and 4 days after

Table 1. Questions about atopy, body piercing, symptoms of 'metal dermatitis' and any symptoms of dermatitis included in interviews carried out in 15-year-old Polish schoolchildren from the general population (from randomly selected secondary schools) in 2009–2010

Questions
1. Have you ever suffered from atopic dermatitis, i.e. have you ever had itchy red or flaky skin lesions affecting flexural surfaces of knees and elbows, neck, or face?
2. Have you ever suffered from recurrent rhinitis, i.e. seasonal or year-long runny nose?
3. Have you ever suffered from recurrent seasonal conjunctivitis, i.e. redness, itch and watering of eyes?
4. Have you ever been diagnosed with atopic asthma?
5. Have you suffered from atopic diathesis in infancy or early childhood, i.e. have you had itchy red skin lesions on your cheeks or limbs related to food, for example milk?
6. Have you ever undergone prick testing with any aeroallergens (grass, weed, tree, dust mites, moulds, cats, dogs, etc.)? If yes, what were the results of the prick tests?
7. Do you have ears or other body parts pierced?
8. Have you noticed that metal items in direct contact with the skin (jewellery, clothing accessories) cause itchy red, papular or oozed skin lesions, for example of the earlobe or umbilical area?

the test application (11). Assessment of the clinical relevance of positive results of patch tests was performed. Positive reactions were regarded as clinically relevant if they were ever accompanied by symptoms of metal dermatitis or dermatitis caused by exposure to leather accessories.

2. A total of 399 metal accessories covered by the EU Nickel Directive, including belt buckles (130), snaps (219), and earrings (50), were tested. The accessories subject to examinations were those currently used by the adolescents (for < 2 years), and were worn during the examination. Nickel release from metal items was assessed with the dimethylglyoxime (DMG) test (Chemo Nickel Test; Chemotechnique Diagnostics®, containing 1.0% DMG, ethanol, and ammonium hydroxide. This is a screening test designed to detect nickel release, and it has been shown to be relevant for the assessment of nickel release exceeding 0.5 µg/cm²/week (12). After moistening of white cotton-wool-tipped sticks with two drops of the DMG test preparation, the items tested were rubbed with the sticks for up to 15 seconds. When the cotton-wool turned pink, it was considered to be a positive result, whereas no colour change was recorded as a negative reaction. A doubtful reaction, defined by a colour of the cotton stick other than pink, was retested, and, if the reaction remained still doubtful, it was registered as a doubtful reaction.

The study protocol was approved by the local Biomedical Ethics Committee.

Statistical Methods

Statistical analysis of the results was performed with the software STATA™ 11, using logistic regression and Fisher's test.

Results

The participation rate in the examination was 85.0% of the pupils from 10 schools.

- 1a) Body piercing (ears and/or other body parts) was reported by 285 females (92.2%) and 2 males (0.9%), and the symptoms of 'metal dermatitis' were found during the interview in 61 (11.6%) subjects: 60 females (19.4%) and 1 male (0.5%). A positive history of atopy was found for 24.6% of the subjects (23.0% in females and 26.9% in males). The results are shown in Table 2.
- 1b) On dermatological examination, current inflammatory skin lesions were found in 14 (2.7%) subjects: 10 females and 4 males. These included: signs of atopic dermatitis in 5 adolescents (0.9%), mild hand eczema in 4 subjects (0.8%), and erythematous papular lesions of an umbilical area in 5 subjects (0.9%).
- 1c) *Patch test results.* Contact allergy to metals (at least one positive response to the patch test) was found in 45 subjects (8.5%): 12.9% in females and 2.3% in males. Table 3 summarizes the results of patch testing and their clinical relevance. Allergy to metals was confirmed by patch testing in 50.8% of the subjects with a history of metal dermatitis (30 females and 1 male), and it was diagnosed in

2.1% of those 467 subjects who had no history of metal dermatitis (8 females and 2 males).

The prevalence of sensitization to all of the examined metals, as well as that to nickel only, among female subjects was significantly higher than among males ($p < 0.001$).

Among the subjects sensitized to metals, 55.0% of females and 3 of 5 males reacted to two or more metals. In females, allergy to nickel was most frequently accompanied by sensitization to palladium (42.1%) and cobalt (26.3%).

Among 285 females who had their ears pierced, 37 were allergic to nickel, whereas among 24 females who had no body piercing, positive patch test reactions to nickel were found in only 1 subject. However, statistical analysis did not show any significant relationship between body piercing and nickel allergy ($p = 0.33$). None of the males sensitized to nickel had body piercing.

No statistically significant difference in the rate of nickel sensitization was found between atopic and non-atopic subjects ($p = 0.35$).

At the final stage of the study, the data on the medical history, dermatological examination and patch test results made it possible to diagnose allergic contact dermatitis to metals, with past or present clinical relevance, in 31 subjects (5.9%): 30 females (9.7%) and 1 male (0.5%). Nickel was the most frequent cause of allergic contact dermatitis.

- 2) The results of the DMG test are shown in Table 4.

Discussion

The results of our study confirm that metals are still very important contact allergens. The presence of nickel, cobalt, palladium and chromium in many items of everyday use (metal and leather accessories, metal tools, pigments, building materials, dental materials, etc.) contributes to a high rate of contact allergy to metals, which can significantly worsen the quality of life and limit job selection possibilities (13–15). As in other studies (4–7), sensitization was found mainly among females (12.9% versus 2.3%), and almost 10% of females suffered from allergic contact dermatitis. Also, more than half of the sensitized pupils showed allergic responses to two or more metals. This may point to a more serious course of allergic contact dermatitis in these cases.

Nickel

Nickel has been the most common cause of contact allergy, both in patients examined with the use of the patch test

Table 2. History of atopic diseases according to interviews in 528 15-year-old Polish schoolchildren from the general population (from randomly chosen secondary schools) tested between 2009 and 2010

	Girls (n = 309) n (%), 95% CI	Boys (n = 219) n (%), 95% CI	Total (n = 528) n(%), 95% CI
Atopic dermatitis	26 (8.4), 5.7–11.9	11 (5.0), 2.6–8.4	37 (7.0), 5.0–9.4
Allergic rhinitis	27 (8.7), 5.9–12.2	29 (13.2), 9.2–18.1	56 (10.6), 8.2–13.4
Allergic conjunctivitis	6 (1.9), 0.8–3.9	8 (3.7), 1.7–6.7	14 (2.7), 1.5–4.3
Atopic asthma	15 (4.9), 2.8–7.6	14 (6.4), 3.7–10.1	29 (5.5), 3.8–7.7
Atopic diathesis	11 (3.6), 1.9–6.0	7 (3.2), 1.4–6.1	18 (3.4), 2.1–5.2
Positive prick test results with common aeroallergens	7 (2.3), 1.0–4.3	5 (2.3), 0.8–4.8	12 (2.3), 1.2–3.8

CI, confidence interval.

Table 3. Prevalence of positive patch test reactions to metals and their clinical relevance in 528 15-year-old Polish schoolchildren from the general population (from randomly chosen secondary schools) tested between 2009 and 2010

Allergen	Girls (n = 309)		Boys (n = 219)		Total (n = 528)		Clinical relevance (total)
	n/%	95% CI	n/%	95% CI	n/%	95% CI	n
Nickel sulfate 5.0% pet.	38/12.3	9–16.3	3/1.4	0.34–3.5	41/7.8	5.7–10.3	31
Palladium chloride 2% pet.	16/5.2	3–8.0	1/0.5	0.026–1.99	17/3.2	1.9–5.0	17 (all coexist with nickel)
Cobalt chloride 1% pet.	10/3.2	1.6–5.6	3/1.4	0.34–3.5	13/2.5	1.4–4.0	13 (all coexist with other metals; 12 with nickel; 1 with chromium)
Potassium dichromate 0.5% pet.	4/1.3	0.4–3.0	2/0.9	0.15–2.7	6/1.1	0.5–2.3	Unknown

CI, confidence interval.

Table 4. Results from testing metal accessories, which were currently used by 15-year-old Polish schoolchildren and worn during the examinations, with the dimethylglyoxime (DMG) test (Chemo Nickel Test; Chemotechnique Diagnostics®, Vellinge, Sweden), tested between 2009 and 2010

Metal accessories, n	DMG test-positive, n/%	DMG test doubtful reaction, n/%
Snaps, 219	25/11.4	8/3.6
Belt buckles, 130	74/56.2	4/3.1
Earrings, 50	5/10.0	1/2
Total, 399	104/26.1	13/3.3

because of suspected allergic contact dermatitis, and at the level of the general population (16). Data from the studies conducted among unselected groups of children and adolescents showed the prevalence of nickel sensitization to range from 5.7% to 14.9% (4, 5, 7). According to Lidén et al. (17), 30–40% of nickel-sensitive people develop hand eczema, which may become recurrent or chronic, affecting their ability to work and causing large expenses to be incurred by society.

In our study, 12.3% of females and 1.4% of males were found to be allergic to nickel. This outcome is consistent with the observations of Uter et al. (18), who showed that female sex is the main risk factor for nickel allergy.

Many authors have emphasized the relationship between body piercing and nickel allergy (5, 19, 20), and have stated that the number of body piercing points has a positive impact on the incidence of metal allergy (21). The statistical analysis in our study did not confirm an association between body piercing and nickel sensitization ($p = 0.33$). Nevertheless, considering the low number of individuals without any body piercing who were found to be sensitized to nickel, the value of this observation is limited, and the association between body piercing and nickel sensitization requires further study. If we compare the present findings on nickel allergy with the results of earlier studies carried out among adolescents of the same age in Poland in 1990s (22), we can note a slightly

decreasing trend in the prevalence of this allergy, especially among females. This decrease in the rate of nickel allergy occurrence may be associated with the fact that the EU Nickel Directive (23) was implemented into national law in Poland in 2004. The first reports from Denmark, where the Nickel Directive had been adopted earlier, and the data from Germany, where labelling of nickel content in metal items was obligatory, clearly indicate a beneficial effect of the limitation of nickel exposure (24–26). However, Schnuch et al. (27) did not find, in the period 2000–2009, a further decrease in nickel allergy in Germany, particularly in the youngest age group (1–17 years). Also in Spain, the prevalence of nickel sensitization remains stable and high (approximately 25% in recent years) (28). Some authors (27) suggest that a few factors could be responsible for this situation, for example: too many nickel-containing objects still do not comply with the EU regulations, and other sources of cutaneous nickel exposure are not covered by the EU regulations. Nevertheless, the review of the data regarding the effects of the Nickel Directive (29) showed that the epidemiology of nickel allergy is beginning to change in Europe.

Palladium

Palladium is a soft, silver–white metal. It is used in the telecommunication and automotive industries, in dental alloys, in jewellery, and in the production of surgical instruments (9, 10). Despite the ubiquity of this metal in the environment, knowledge about the allergic properties of palladium is insufficient. In European countries, the prevalence of sensitivity to palladium was shown to vary from 2.0% to 9.0% (30,31), and in the United States it affected 12.1% of the patch-tested population (9). In our study, positive patch test reactions to palladium were found in 3.2% of the entire tested population: 5.2% in females and 0.5% in males. Our results, like many other findings (9, 30–32), showed that allergy to palladium is usually associated with sensitivity to other metals. In the study group, all individuals who were allergic to palladium

were also allergic to nickel, and some of them were also allergic to cobalt. In such cases, it is difficult to determine the clinical relevance of palladium allergy. *In vitro* and *in vivo* studies (10, 33, 34) showed that positive patch test reactions to palladium result from cross-reactions between nickel and palladium, as they are both transition metals (35). Nevertheless, Thyssen et al. described a patient with clinically relevant monovalent sensitization to palladium (36).

Cobalt and chromium

The prevalence of cobalt allergy among children in the general population is reported to range from 0.5% to 5.7% (4, 5). In our study, allergy to this metal was found in 2.5% of the subjects: 3.2% in females and 1.4% in males. In all cases, it coexisted with allergy to nickel or chromium. It has been postulated that nickel allergy may predispose to cobalt allergy (37). Cases of monovalent sensitization to cobalt are rare. Hindsén et al. (38) described a patient with allergic contact dermatitis caused by a brown-plated necklace that released high amounts of cobalt, but not nickel. Owing to the concomitance of cobalt and nickel allergy, it is difficult to assess the clinical relevance and the source of sensitization to cobalt. Recent studies have shown that only a minority of inexpensive jewellery items release cobalt when assessed with the cobalt spot test (38). Nevertheless, dermatologists and consumers should be aware of the fact that cobalt might be released from both bright and dark jewellery, and from both inexpensive and expensive jewellery (39–41).

Allergy to chromium did not play an important role among adolescent subjects. Positive patch test reactions to chromium were found in 6 individuals (1.1%). Unfortunately, we did not manage to establish the clinical relevance of the test positivity. It is also possible that some of the reactions could be false-positive. In other studies conducted in unselected groups of children, the rate of chromium allergy ranged from 0.2% to 7.6% (4, 5). It was proven that chromium is found in various leather products, including children's shoes (42), which, in theory, may result in sensitization.

Atopy and contact allergy to metals

In this study, no statistically significant difference was found in the frequency of positive patch test results with

metals between atopic and non-atopic adolescents. These results are consistent with other authors' observations that the pattern and frequencies of contact sensitization did not differ greatly between atopic and non-atopic individuals (43).

Nickel release from metal items

The Swedish experience shows that, after implementation of the Nickel Directive, the percentage of items for which nickel release exceeded the obligatory limitations declined from 25.0% in 1999 to 9.0% in 2010 (44, 45). Despite the fact that the Nickel Directive has been binding in Poland for almost 7 years, 26.1% of the metal items subject to DMG testing, used by adolescents, were found to be DMG-positive, indicating that they do not comply with European law. It should be stressed that most of the DMG-positive items were found among belt buckles (56.2%), and far fewer among earrings (only 10.0%). On the other hand, in other studies, from 14.8% to 31.5% of the tested earrings purchased from shops and street markets released an excessive amount of nickel (27, 46–48). The lower number of DMG-positive earrings in our study than in other studies may result from a different method of selecting metal items for examination. We assessed earrings that were worn by participants during the examination. Probably, young people are aware that metal earrings may be a source of sensitization to nickel, and they seem to be more conscious about choosing 'nickel-free' earrings. On the other hand, it is surprising that they do not regard other metal accessories (belt buckles and snaps) as potential sources of sensitization.

To summarize, we presume that an effective reduction in the rate of nickel allergy may be achieved not only through limiting nickel release from certain items (which has already been regulated by the Nickel Directive), but also through educating people about the potential sources of metal allergy. In our opinion, special lectures, presenting the problem of the different sources of sensitization to nickel and the side effects of it, should be held in schools. Moreover, an increase in the awareness of the entire society concerning this subject could be obtained if an information campaign in the media (i.e. Internet, television, and radio) were to be introduced in Poland.

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