

Validity of self-reported nickel allergy

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Background: To estimate the prevalence of nickel allergy, self-reports are sometimes used in epidemiological studies. Self-reports are practical and may facilitate estimation of prevalence provided that the questions are validated.

Objectives: To investigate the validity of self-reported nickel allergy.

Methods: Three hundred and sixty-nine women, aged 30–40 years, from the general population participated in the study. The participants answered a questionnaire before a clinical examination and patch testing. The two questions being validated were 'Are you sensitive/hypersensitive/allergic to nickel?' and 'Do you get a rash from metal buttons, jewellery or other metal items that come in direct contact with your skin?'

Results: Patch test showed nickel-positive reaction in 30% of the subjects. Self-reported prevalence of nickel allergy as indicated by the two respective questions was 40% and 35%. Positive predictive values for the two questions were 59% (95% CI 50–67) and 60% (95% CI 51–69). History of childhood eczema was over-represented among women with 'false-positive' self-reported nickel allergy ($P = 0.008$). Self-reported hand eczema or 'high wet exposure' did not influence the validity.

Conclusions: The validity of self-reported nickel allergy is low. The questions regarding nickel allergy overestimate the true prevalence of nickel allergy.

Key words: epidemiology; patch test; predictive value; questionnaire; sensitivity; specificity. © John Wiley & Sons A/S, 2010.

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Nickel allergy is the most common contact allergy and the prevalence of nickel allergy is higher among women than men. Eighteen population-based studies that included patch testing, published during the past 30 years, were reviewed by Thyssen et al. in 2007 (1). The median prevalence of nickel allergy was 17.1% (range 3.9–38.8%) in women of different ages. Nickel allergy is related to exposure and for the past few decades, piercing has been an important factor of sensitization (2–4). The European Nickel Directive, which came into full force in 2001, limits nickel release from items in prolonged contact with the skin, e.g. jewellery, watches, buttons, and zips (5). It is of interest to follow the prevalence of nickel allergy to evaluate the effect of the Nickel Directive (6). The prevalence of nickel

allergy is sometimes estimated through self-reports in epidemiological studies. Self-reports are practical and may facilitate estimation of prevalence, provided that the questions are validated.

In a recently published study of Swedish adolescents, 20.7% of the girls reported metal dermatitis (7). However, the question used showed low validity in predicting nickel allergy, with a sensitivity of 52%. In two other studies, questions about skin reactions after contact with metals had a positive predictive value of 54% (8, 9). Mortz et al. found that only 31% of adolescents with self-reported metal-related eczema reacted positively to a nickel patch test (3).

The aim of the present study was to investigate the validity of self-reported nickel allergy.

Subjects and Methods

Study population

In a Swedish study in 1982–1983, 958 schoolgirls were patch tested for nickel allergy (10). Twenty years later, in 2003, 908 of the same individuals (i.e. all who could be located) were invited to participate in a follow-up questionnaire study (11). In 2006, current addresses of all the women who responded ($n = 735$) were retrieved; 478 of them were still living in Örebro County, Sweden. These women were invited to a clinical examination including patch testing. After receiving a letter and a telephone call, 77% (369/478) of individuals participated. The results were published in 2009 (12).

Questionnaire

The participants answered a second questionnaire immediately before undergoing a clinical examination and patch testing. This questionnaire contained 21 questions regarding the occurrence of hand eczema, history of childhood eczema, nickel sensitivity, and wet exposure. The questions about nickel sensitivity were: (i) 'Are you sensitive/hypersensitive/allergic to nickel?' and (ii) 'Do you get a rash from metal buttons, jewellery or other metal items that come in direct contact with your skin?' The response alternatives are shown in Table 1. In the analysis, the answers to question (i) were simplified to 'yes' or 'no' and all answers that included 'yes' were added together. Regarding history of childhood eczema the question posed was 'Have you had childhood eczema (before age 15)?'. The question regarding hand eczema was 'Have you ever had hand eczema after age 15?'. 'High wet exposure' was defined as reported occupational skin exposure to water of more than 2 hr/day, and/or hand washing more than 20 times/day, and/or housework more than 2 hr/day.

Table 1. Questions used regarding nickel sensitivity

(i). Are you sensitive/hypersensitive/allergic to nickel?	☐ Yes, with severe symptoms
	☐ Yes, with mild symptoms
	☐ Yes, without symptoms when I avoid contact
	☐ No
(ii). Do you get a rash from metal buttons, jewellery, or other metal items that come in direct contact with your skin?	☐ Yes
	☐ No

Patch testing

The clinical investigation and the patch test were performed in April to May 2006 and October 2006 to March 2007. A standard patch test, MekosTest® (Vitaflor Scandinavia AB, Göteborg, Sweden) was used. The test contains 24 different substances, among which nickel sulfate was 0.16 mg/patch. The tests were left on for 2 days, after which they were removed by the women themselves. All reactions were read by the same doctor (A.J.) on D3. The present study is based on a follow-up, and to be congruous with the baseline-study the definition of a 'positive reaction' to nickel sulfate required erythema, infiltration, and papules (++) reaction (13). The reaction was said to be 'doubtful' if it was + or weaker.

In case of doubtful reaction to nickel sulfate, an additional test was performed with a dilution series. The dilution procedure has been presented previously (12). Individuals with doubtful test reactions to nickel, who did not participate in the dilution test ($n = 14$), were excluded from further analysis. Thus 355 women were eligible for analysis.

Statistics

The data were analysed using SPSS® version 15 (SPSS Inc., Chicago, IL, USA). Sensitivity, specificity, and negative/positive predictive values were calculated using the patch test results as gold standard. These proportions were supplemented with 95% confidence intervals using binomial distribution and calculated with STATA® version 10 software (College Station, TX, USA). Chi-square test was used for comparison of proportions. The study was approved by the Ethics Committee of Uppsala, Sweden.

Results

Patch tests gave 30% (111/355) nickel-positive individuals, including the results from the dilution test for nickel. Self-reported nickel allergy according to question (i) and question (ii) in relation to patch testing are shown in Table 2. The self-reported prevalence of nickel allergy was higher than the occurrence of positive patch test to nickel. In the questionnaire, 40% (140/348) answered 'yes' to question (i) and 35% (126/354) answered 'yes' to question (ii). The answers to the two different questions regarding self-reported nickel allergy are compared in Table 3.

The calculated sensitivity, specificity, and positive and negative predictive values for the two different questions are shown in Table 4. The positive predictive value for question (i) is 59%, which means that nickel allergy was verified in 59% of

Table 2. Self-reported nickel allergy in relation to patch test results

Self-reported nickel allergy		Patch test result		Total
		Positive	Negative	
Question (i) (Are you sensitive/hypersensitive/allergic to nickel?)	Yes	82	58	140
	No	26	182	208
	Total	108	240	348
Question (ii) (Do you get a rash from metal buttons, jewellery, or other metal items that come in direct contact with your skin?)	Yes	76	50	126
	No	35	193	228
	Total	111	243	354

Question (i) was answered by 348/355 women and question (ii) was answered by 354/355 women.

Table 3. Comparison of the answers from the two questions regarding self-reported nickel allergy

		Question (ii) (Do you get a rash from metal buttons, jewellery, or other metal items that come in direct contact with your skin?)		Total
		Yes	No	
Question (i) (Are you sensitive/hypersensitive/allergic to nickel?)	Yes	112	27	139
	No	11	197	208
Total		123	224	347

Question (i) was answered by 348/355 women and question (ii) was answered by 354/355 women.

the women who had reported nickel allergy. Thus, the questions used to overestimate the prevalence of nickel allergy.

The different response alternatives for question (i) make it possible to form a conception of the symptoms associated with nickel allergy (Fig. 1). Of the 348 women who answered question (i), 108 had a positive patch test to nickel. Thirty-four of these reported that they had no symptoms if they avoided contact. Another 26 patch test positive women answered 'no' to question (i). Thus, 60/108 (56%) reported no symptoms in spite of positive patch test to nickel. Of those who reported severe symptoms of nickel allergy, 4/4 patch tested positive to nickel.

Factors that might contribute to false-positive answers to the question about nickel allergy were studied. A comparison between nickel-negative women who answered 'yes' versus 'no' to the question about nickel sensitivity is shown in Table 5. Childhood eczema was over-represented among the

Are you sensitive/hypersensitive/allergic to nickel?

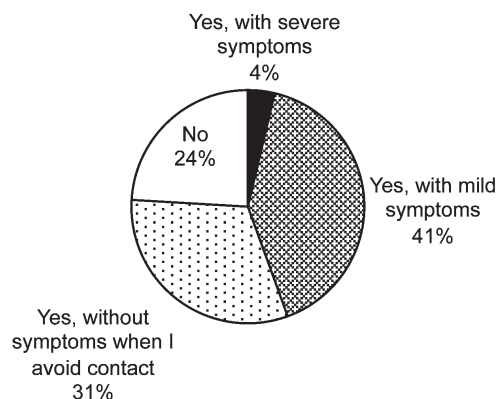


Fig. 1. Proportions of answers to the four response alternatives of question (i) in women patch tested positive to nickel ($n = 108$).

false positives: 50% with versus 31% without ($P = 0.008$).

Doubtful patch test reactions to nickel were found in 14 individuals who were not able to participate in a dilution test and were therefore excluded from further analysis. If all of them were regarded as positive, the positive predictive value for question (i) would be 61%. If all of them were regarded as negative, the positive predictive value would be 56% for the same question.

Discussion

The questions 'Are you sensitive/hypersensitive/allergic to nickel?' and 'Do you get a rash from metal buttons, jewellery or other metal items that come in contact with your skin?' do not seem to be useful for estimating the prevalence of nickel allergy. The validity of these questions is low. Nickel allergy was verified in only 59–60% of those who reported nickel allergy.

Our results are in accordance with other studies in which a low positive predictive value for self-reports by questionnaire was found (3, 8, 9). In those studies, questions about metal-related dermatitis, similar to question (ii) in the present study, were validated. To the best of our knowledge, the question 'Are you sensitive/hypersensitive/allergic to nickel?' has not previously been validated. In the present study both questions had a low positive predictive value, 59% and 60%, respectively. The overlap was not complete: 27 women considered themselves allergic to nickel but did not get a rash from metal items. Conversely, 11 women reported developing a rash after contact with metal items but denied

Table 4. Calculated validity of questions (i) and (ii)

	Question (i)		Question (ii)	
	Percentage (95% CI)	<i>n</i>	Percentage (95% CI)	<i>n</i>
Sensitivity	76 (67–84)	82/108	68 (59–77)	76/111
Specificity	76 (70–81)	182/240	79 (74–84)	193/243
Positive predictive value	59 (50–67)	82/140	60 (51–69)	76/126
Negative predictive value	88 (82–92)	182/208	85 (79–89)	193/228

Table 5. Self-reported nickel allergy [question (i)] in women patch tested negative to nickel (*n* = 240) in relation to childhood eczema, hand eczema, and 'high wet exposure'

	Childhood eczema (%)	Hand eczema after age 15 (%)	High wet exposure (%)
Self-reported nickel allergy (<i>n</i> = 58)	50	28	34
No self-reported nickel allergy (<i>n</i> = 182)	31	20	43
	<i>P</i> = 0.008	<i>P</i> = 0.246	<i>P</i> = 0.264

nickel allergy. Four of those 11 women had a positive patch test for nickel and 5 of them had a history of childhood eczema. As a consequence of the European Nickel Directive, questions about skin contact with metal buttons, jewellery, and watches will no longer be useful for assessment of symptoms related to nickel allergy, as nickel release is limited from such items (14). Sensitivity, specificity, and negative/positive predictive values were calculated for both questions and are shown in Table 4. Positive predictive value is satisfactory for understanding the validity of a question. However, sensitivity and specificity are more adequate when comparing different studies.

One possible reason that self-reported nickel allergy might be overestimated is that skin irritation from other causes confuses the symptoms of nickel allergy. However, hand eczema and 'high wet exposure', which can give skin irritation, did not influence the validity in the present study (Table 5). Women with a history of childhood eczema had a higher proportion of 'false-positive' answers on nickel allergy than those without childhood eczema. When comparing these two groups separately, the positive predictive value among women *with* a history of childhood eczema was 50% compared with 64% in women *without* childhood eczema. A plausible explanation is that individuals with atopic skin type more easily react with irritant dermatitis when exposed to metal items (15).

The present study is restricted to women from the general population between 30 and 40 years of age. The prevalence of nickel allergy in women of this age is high, and as a consequence, they are rather well informed about nickel allergy and its symptoms. The validity of self-reported nickel allergy

might not be the same in other age groups or in men. The proportion of attendance was high in the present study: 77% (369/478) agreed to participate. A missing value analysis was performed and has been previously published (12). The dropouts did not seem to have an effect on the outcome in terms of prevalence of hand eczema. However, among participants, reported childhood eczema was significantly more common – 36% versus 23% among the non-participants (*P* = 0.012). The high proportion of atopics in this study might to some extent contribute to the overestimation of nickel allergy.

For practical reasons and to imitate the patch test reading in 1982, a single reading was carried out for this follow-up. Normally nowadays, patch test readings are carried out both on D3 or D4 and on D7. If only one reading is performed, nearly 10% of the positive patch test reactions to nickel may be missed because of delayed reactions (16). If we assume that another 10% of our subjects would be positive in the patch test, and in the most extreme situation, all of them would report nickel allergy, then the positive predictive value would be 66% (92/140), which means that still the validity is low. Generally, there is a risk of false-positive nickel patch tests in atopics. In the present study this risk was limited by the definition of positive reaction as ++ reaction or more, the dilution test and that all reactions were read by the same doctor. The wording of question (ii) might be somewhat confusing. A few women may have answered 'no' if they had metal dermatitis previously but not at present. Allergy to cobalt might also cause metal dermatitis and would be a possible bias. In this study three of the women showed isolated cobalt allergy when patch tested, and one of them answered 'yes' to the question about nickel allergy.

Of the nickel-positive women, 24% were not aware of the allergy and 31% reported no symptoms when they avoided contact, which means that more than half of the women with nickel allergy did not have symptoms (Fig. 1). It is likely that many individuals with nickel allergy never seek medical advice. Some individuals with nickel allergy have severe dermatitis, but most nickel-positive individuals have mild symptoms or none at all. In the present study, only 4/108 nickel-positive women reported severe symptoms.

For epidemiological surveillance of common skin diseases in the general population, questionnaires are useful, provided that the questions are validated. A question on self-reported hand eczema has previously been validated, as has the question 'Have you had childhood eczema?' (17, 18). It was found that self-reported 1-year prevalence of hand eczema underestimates the true prevalence, whereas the question about childhood eczema overestimates the prevalence. The knowledge of validity concerning self-reported nickel allergy is of importance in epidemiological studies and has significant clinical relevance as well. Apparently, it is difficult to know whether there is a contact allergy or not through history.

In conclusion, the validity of self-reported nickel allergy is low. The questions studied overestimate the true prevalence of nickel allergy. Thus, to investigate the prevalence of nickel allergy, patch tests seem to be necessary.

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References

- Thyssen JP, Linneberg A, Menné T, Johansen JD. The epidemiology of contact allergy in the general population – prevalence and main findings. *Contact Dermatitis* 2007; 57(5): 287–99.
- McDonagh AJ, Wright AL, Cork MJ, Gawkrödger DJ. Nickel sensitivity: the influence of ear piercing and atopy. *Br J Dermatol* 1992; 126(1): 16–8.
- Mortz CG, Lauritsen JM, Bindslev-Jensen C, Andersen KE. Nickel sensitization in adolescents and association with ear piercing, use of dental braces and hand eczema. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis (TOACS). *Acta Derm Venereol* 2002; 82(5): 359–64.
- Nakada T, Iijima M, Nakayama H, Maibach HI. Role of ear piercing in metal allergic contact dermatitis. *Contact Dermatitis* 1997; 36(5): 233–6.
- Lidén C. Legislative and preventive measures related to contact dermatitis. *Contact Dermatitis* 2001; 44(2): 65–9.
- Thyssen JP, Johansen JD, Menné T, Nielsen NH, Linneberg A. Nickel allergy in Danish women before and after nickel regulation. *N Engl J Med* 2009; 360(21): 2259–60.
- Fors R, Persson M, Bergström E, Stenlund H, Stymne B, Stenberg B. Nickel allergy – prevalence in a population of Swedish youths from patch test and questionnaire data. *Contact Dermatitis* 2008; 58(2): 80–7.
- Fleming CJ, Burden AD, Forsyth A. Accuracy of questions related to allergic contact dermatitis. *Am J Contact Dermat* 2000; 11(4): 218–21.
- Kieffer M. Nickel sensitivity: Relationship between history and patch test reaction. *Contact Dermatitis* 1979; 5: 398–401.
- Larsson-Stymne B, Widström L. Ear piercing – a cause of nickel allergy in schoolgirls? *Contact Dermatitis* 1985; 13(5): 289–93.
- Josefson A, Färm G, Stymne B, Meding B. Nickel allergy and hand eczema – a 20-year follow up. *Contact Dermatitis* 2006; 55(5): 286–90.
- Josefson A, Färm G, Magnuson A, Meding B. Nickel allergy as risk factor for hand eczema: a population-based study. *Br J Dermatol* 2009; 160(4): 828–34.
- Wahlberg JE, Lindberg M. Patch testing. In: *Contact Dermatitis*. 4th edition, Frosch PJ, Menné T, Leppoittevin J-P, (eds): Berlin, Germany, Springer-Verlag, 2006: 365–90.
- Lidén C, Norberg K. Nickel on the Swedish market. Follow-up after implementation of the Nickel Directive. *Contact Dermatitis* 2005; 52(1): 29–35.
- Brasch J, Schnuch A, Uter W. Patch-test reaction patterns in patients with a predisposition to atopic dermatitis. *Contact Dermatitis* 2003; 49(4): 197–201.
- Lindberg M, Edman B, Fischer T, Stenberg B. Time trends in Swedish patch test data from 1992 to 2000. A multi-centre study based on age- and sex-adjusted results of the Swedish standard series. *Contact Dermatitis* 2007; 56(4): 205–10.
- Meding B, Barregård L. Validity of self-reports of hand eczema. *Contact Dermatitis* 2001; 45(2): 99–103.
- Stenberg B, Lindberg M, Meding B, Svensson Å. Is the question 'Have you had childhood eczema?' useful for assessing childhood atopic eczema in adult population surveys? *Contact Dermatitis* 2006; 54(6): 334–7.

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