

Detection of Nickel Sensitivity Has Increased in North American Patch-Test Patients

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Background: Nickel allergy has been studied by contact dermatitis groups around the world, and the frequency of nickel sensitivity has been reported to be decreasing in some populations.

Objective: To review the prevalence of nickel allergy as observed by the North American Contact Dermatitis Group from 1992 to 2004.

Methods: The computer database of the North American Contact Dermatitis Group was used to examine the prevalence of nickel allergy over the study period and to analyze it by time, sex, and age.

Results: From 1992 to 2004, 25,626 patients were patch-tested. The percentage of women tested was fairly constant (61.4–66.3%). A steady increase in nickel sensitivity was seen from 1992 to 2004. Subgroup analysis did not identify a population with declining nickel allergy.

Conclusions: Nickel allergy continues to increase in younger and older men and women patch-tested in North America.

THE NORTH AMERICAN CONTACT DERMATITIS Group (NACDG) has tested patients suspected of having contact dermatitis and tracked the frequency with which various allergens produce positive results.¹ Other similar groups from around the world have also reported this type of data. Prevalence data can provide cross-sectional estimates of the number of individuals affected at a given time. Data derived from patch-test patients, however, may lead to overestimation of the prevalence of allergy in the general population.

Nickel contact allergy has been widely studied.^{2–20} Several studies have evaluated nickel allergy in the general population. One such study of 2,500 females in a Danish general population found nickel sensitivity in 14.5% of that population³; an evaluation of 1,546 Danish female

twins reported a prevalence of 9.6%.⁴ In two studies of nickel allergy in the general population, 0.8%⁵ to 0.9%⁶ of men were patch test positive whereas 8.0% and 9.0% of women were patch test positive (980 and 1,159 subjects, respectively).

Prevalence rates of nickel allergy are higher in patch-test populations. The percentage of patch-tested, patients that reacted to nickel ranged from 4.5% among 2,285 Japanese patients² to 16% of 1,312 Scottish patients.⁷ When the data are analyzed by gender, nickel caused positive reactions in 1.8% of men in a European report⁸ and in 11% of 453 patients in a Nigerian analysis.⁹ For women, the reports ranged from 4.3% in Japan to 26% in Scotland. More recent reports on the rate of positive patch-test results include 17.7% of 5,557 patients from Singapore,¹⁰ 13.1% of 1,141 patients from Germany,¹¹ 13.8% of 12,058 patients from the Czech Republic,¹² and 17.3% of 10,511 patients from a group of nine European countries.¹³ A meta-analysis of 15 years of published data on the T.R.U.E. Test system of patch testing (Mekos Laboratories A/S, Hillerød, Denmark) found that 14.7% of 3,598 patch-tested patients were nickel sensitive.¹⁴

Traditionally, the female predominance in nickel allergy has been linked to ear piercing, but that difference between the sexes has been changing. Many men adopted ear piercing in the later part of the last century, and a difference in nickel allergy has been identified in men with

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and without pierced ears. Five hundred twenty Swedish men in compulsory military service were patch-tested with nickel and cobalt (which commonly co-reacts with nickel and is found in many similar environmental sources). Among those with pierced ears, 7.9% had positive reactions; in those without pierced ears, 2.7% had positive results ($p < .05$).¹⁵ A study of the relationship of nickel sensitivity to ear piercing was conducted among the general population, and 14.8% of those with pierced ears were nickel sensitive, compared to 1.8% who were not pierced. In this cohort of 567 patients, 11.1% of women and 2.2% of men were allergic to nickel.^{16,17}

Methods

All patients presenting for patch testing at NACDG patch test sites were eligible for inclusion. During this time interval (1992–2004), our method of testing was unchanged although NACDG membership varied as some members left and others were added. Patients were patch-tested as described previously.¹ Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Aksjeselskap, Vennesla, Norway) were used to apply allergens from Chemotechnique Diagnostics AB (Malmö, Sweden). The patches were applied for 2 days, removed and interpreted, and reinterpreted 1 to 5 days later. Patch tests results were scored as positive if + or greater. Macular erythema was scored as doubtful and was not included in this analysis. The concentration of nickel sulfate (2.5% in petrolatum) was consistent from 1992 to 2004.

De-identified data from participating centers were sent to a central database, manually entered, and checked for consistency. All analyses were performed with SAS (Statistical Analysis System, SAS Institute Inc., Cary, NC). Pearson chi-square tests were used to examine the association between nickel sensitivity and time period, gender, or age. A significance level of .05 was used.

Results

Demographics

From 1992 to 2004, 25,626 patients were patch-tested by the NACDG (Table 1). During this time, the ratio of women who were patch-tested to men who were patch-tested remained fairly constant, at 61.4 to 66.3% women to 33.6 to 38.6% men. The data show a steady increase in nickel sensitivity from 14.5% in 1992 to 18.8% in 2004 ($p < .0001$).

Gender Effects

While more males were allergic to nickel in the late group (2001–2004) as compared to the early group (1992–1995), this difference did not quite achieve statistical significance ($p = .067$). However, females were at 1.1 to 1.2 times more likely to be nickel allergic in the late (2001–2004) group as compared with either the early (1992–1995) group (relative risk [RR], 1.2; 95% confidence interval [CI], 1.10–1.28; $p < .0001$) or the middle (1996–2000) group (RR, 1.12; 95% CI, 1.04–1.19; $p = .0011$).

Age Effects

The younger patients in our patch-test clinics were more frequently found to be nickel sensitive than were patients who were 19 years of age or older (Tables 2 and 3); 11 to 15% of younger males and 19 to 37% of younger females were nickel allergic whereas only 4 to 7% of males and 18 to 24% of females older than 18 years were nickel sensitive. Younger men were 2.33 times more likely to be nickel allergic than were older men (95% CI, 1.80–3.01; $p < .0001$), and younger women were 1.51 times more likely to be nickel allergic than were older women (95% CI, 1.34–1.72; $p < .0001$). Evaluating only those individuals who

Table 1. Prevalence of Nickel Allergy in North America

Period		Men	Women	Overall
Early	1992–1993	66/1,305 (5.06%)	434/2,152 (20.17%)	500/3,457 (14.46%)
	1994–1995	80/1,185 (6.75%)	364/1,885 (19.31%)	444/3,070 (14.46%)
Middle	1996–1997	81/1,273 (6.36%)	405/2,096 (19.32%)	486/3,369 (14.43%)
	1998–2000	123/2,051 (6.00%)	823/3,732 (22.05%)	946/5,783 (16.36%)
Late	2001–2002	106/1,632 (6.50%)	712/3,217 (22.13%)	818/4,849 (16.87%)
	2003–2004	135/1,782 (7.58%)	824/3,316 (24.85%)	959/5,098 (18.81%)
	Total	591/9,228 (6.40%)	3,562/16,398 (21.72%)	4,153/25,626 (16.21%)

Table 2. Comparison of Younger to Older Males Patch Test Positive to Nickel, by Study Period

Period	Age	
	≤ 18 Years	> 18 Years
1992–1993	15.8% (9/57)	4.6% (57/1,248)
1994–1995	11.1% (4/36)	6.6% (76/1,149)
1996–1997	12.5% (6/48)	6.1% (75/1,225)
1998–2000	13.4% (15/112)	5.6% (108/1,939)
2001–2002	15.3% (11/72)	6.1% (95/1,560)
2003–2004	15.6% (10/64)	7.3% (125/1,718)
Total	14.1% (55/389)	6.1% (536/8,839)

Table 3. Comparison of Younger to Older Females Patch Test Positive to Nickel, by Study Period

Period	Age	
	≤ 18 Years	> 18 Years
1992–1993	25.0% (33/132)	19.8% (401/2,020)
1994–1995	18.9% (7/37)	19.3% (357/1,848)
1996–1997	37.8% (17/45)	18.9% (388/2,051)
1998–2000	26.3% (31/87)	21.9% (792/3,614)
2001–2002	36.8% (45/122)	21.5% (667/3,095)
2003–2004	35.8% (44/123)	24.4% (780/3,193)
Total	32.4% (177/546)	21.4% (3,385/15,821)

were allergic to nickel, we found no statistically significant associations between time period for age (≤ 18 years vs > 18 years) for men ($p = .5361$) or for women ($p = .6506$)

Discussion

To our knowledge, this study is the first study to evaluate trends for nickel sensitivity in a large cohort of patch-tested patients in North America. We found that nickel sensitivity has increased over the last 12 years and that most of this increase is due to the prevalence in women. Our results are similar to those of other studies evaluating trends in allergy to nickel. A Danish study of 2,166 patients during 12 years found a small but statistically significant increase in nickel allergy when data from 1985 to 1986 were compared to data from 1997 to 1998.¹⁸ In the earlier period, 4.2% of men were nickel sensitive, as compared to 4.9% in the later period. For women, the numbers were 18.3% in the earlier period and 20.0% in the later period. The Danish study found that nickel allergy had actually decreased among children 0 to 18 years of age, dropping from 24.8% in 1985 to 1986 to 9.2% in 1997 to 1998. A similar report, on 7,988 patients from Poland, examined

nickel allergy from 1995 to 2004 and found that 13.96% of all patients were nickel sensitive in 1995 as compared to 19.89% in 2004.¹⁹ In 1995, 2.2% of patients 0 to 20 years of age were nickel allergic as compared to 1.7% in 2004; for those older than 20 years, nickel sensitivity increased from 11.7% to 15.2%. Both the Danish and Polish reports suggest that reduced environmental exposures in Europe secondary to nickel exposure regulation might account for the lower numbers in younger patients and that greater awareness of the problem of nickel allergy might be an additional factor. In contrast, however, an Italian study of 42,839 cases of contact dermatitis compared nickel allergy in 1984 to 1988 to that in 1989 to 1993 and found no significant difference in the sensitization rate (28.7% in the former period and 28.9% in the latter) although the study did not report sensitization groups by age.²⁰

Conclusion

Our data do not show a decrease in nickel allergy among patients of either sex who were 18 years of age or younger; instead, a slight increase in nickel sensitivity is seen. It is unclear if the increase that we are reporting is due to the popularity of body piercing or to a change in the popularity of one alloy over another. The North American Contact Dermatitis Group has recently changed our data collection instrument to include a question about the number of piercings an individual has. We hope this will allow us to determine if this is the basis for our observation. At present, we can only speculate as to the reason for the increase. The trend confirms the ongoing importance of this allergen in North America.

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