

Occupational hand eczema caused by nickel and evaluated by quantitative exposure assessment

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doi:10.1111/j.1600-0536.2010.01819.x

Summary

Background. EU legislation has reduced the epidemic of nickel contact allergy affecting the consumer, and shifted the focus towards occupational exposure. The acid wipe sampling technique was developed to quantitatively determine skin exposure to metals.

Objectives. To assess the clinical usefulness of the acid wipe sampling technique as part of the diagnostic investigation for occupational nickel allergy-associated hand dermatitis.

Patients and methods. Six patients with vesicular dermatitis on the hands were included. Acid wipe sampling of skin and patch testing with a nickel sulfate dilution series were performed.

Results. Nickel was detected in all samples from the hands. In all patients, the nickel content on the hands was higher than on the non-exposed control area.

Conclusions. Occupational exposure to nickel-releasing items raised the nickel content on exposed skin as compared with a non-exposed control site. Nickel-reducing measures led to complete symptom relief in all cases. In cases of a positive nickel patch test reaction and hand eczema, patients should perform the dimethylglyoxime (DMG) test on metallic items at home and at work. The acid wipe sampling technique is useful for the diagnosis of occupational hand eczema following screening with the inexpensive DMG test.

Key words: acid wipe sampling, allergic contact dermatitis, nickel, occupational exposure, skin exposure assessment.

In the beginning of the 20th century, allergic contact dermatitis caused by nickel was observed primarily on the hands and forearms of workers in the plating industry. In the second part of the 20th century, uncontrolled nickel exposure was caused by consumer products such as suspenders, buttons, spectacle frames, jewellery, and, most recently, earrings; occupational nickel exposure gradually attracted less attention.

The EU Nickel Directive (1) has, to some extent, reduced the nickel contact allergy epidemic affecting consumers (2–6), and, as a result of the Danish Nickel Regulation (2), the association between hand eczema and nickel allergy has weakened among young women in the general population. It is now considered probable that a large proportion of the remaining cases of nickel allergy-associated hand eczema are caused by unregulated occupational nickel exposure.

The aim of the present study was to assess the clinical usefulness of the acid wipe sampling method for quantitative assessment of metals deposited on the skin (7, 8). Consecutive nickel-allergic patients with suspected occupational nickel allergy-associated hand eczema were invited to participate. They were offered quantitative nickel hand exposure measurement following 2 hr of

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Conflicts of interest: The authors have declared no conflicts.

Accepted for publication 27 July 2010

normal work, as well as dose–response patch testing with a nickel sulfate dilution test series. This pilot study presents the findings from the first use of the acid wipe sampling technique in dermatitis patients.

Patients, Materials and Methods

Patients

The inclusion criteria were nickel allergy and ongoing dermatitis on the hands that from the history and clinical examination was suspected of being occupationally related (Table 1). Six consecutive patients (five women and one man) referred to us, who fulfilled the inclusion criteria, participated in the study, which was performed at the Department of Dermato-Allergology, Copenhagen University Hospital Gentofte, Denmark. Prior to study entry, all patients had a positive nickel patch test result and a positive dimethylglyoxime (DMG) test outcome with at least one frequently handled item from their workplace. DMG testing was performed by trained laboratory nurses at our institution. The patients' occupations were as follows: psychiatric nurse ($n = 2$), industrial worker ($n = 1$), dressmaker ($n = 1$), sandwich maker ($n = 1$), and carpenter/house painter ($n = 1$). All subjects were right-handed and did not have palmar hyperhidrosis. Two patients (A and B; Table 1) had shown reactivity to nickel when wearing inexpensive earrings.

Work exposure

A random workday was selected, and the patients were instructed to perform their normal job routines for the first 2 hr of the workday without avoiding nickel-releasing items. Information about protective measures and how to reduce occupational nickel exposure had been given by their consultant dermatologist when occupational nickel dermatitis was suspected (before the acid wipe sampling).

The patients were instructed to ignore these protective measures only during the 2-hr work session preceding acid wipe sampling. After this work session for exposure, they left work without cleaning their hands and attended our clinic at Copenhagen University Hospital Gentofte, where we performed acid wipe sampling from their hands for skin exposure assessment. We did not record whether or not the patients had cleaned their hands before the 2-hr work period, and we did not interfere with or observe the 2-hr work session.

Sampling from skin surface and chemical analysis

We used the acid wipe sampling technique, which has a recovery rate of more than 90% (7, 8), to assess the amount of nickel deposited on the skin. Sampling was performed in accordance with the method described by Lidén et al. (7, 8). In each patient, the samples were taken from a 2 cm² area on the right volar index fingertip, a 7.5 cm² area on the right palm, and a 7.5 cm² non-exposed control area on the medial aspect of the right upper arm. Sampling was performed from dermatitis-free skin areas. Before wiping, areas for sampling were outlined with single-use plastic foil templates. Cellulose wipes (Paper-Pak Sweden AB, Sundbyberg, Sweden) were moistened with 0.5 ml of 1% nitric acid [nitric acid 65% p.a. (Merck KGa A, Darmstadt, Germany), diluted with deionized water to 1%], and each skin area was wiped with three consecutive wipes. Gentle pressure was applied, and the skin surface was wiped three times per wipe. The wipes from each area were then pooled together in acid-cleaned polypropylene containers (Sarstedt, Landskrona, Sweden) containing 25.0 ml of nitric acid for extraction of nickel. The containers were then placed on a vibrating table for 30 min, after which the nitric acid solutions were transferred to new acid-cleaned polypropylene containers for transport to the Karolinska Institutet (Stockholm,

Table 1. Description of nickel-allergic patients with hand eczema, their work activities during the 2 hr before sampling for assessment of nickel on skin^a, dimethylglyoxime (DMG) test-positive items handled, and exposure-reducing alternatives introduced after the skin exposure assessment

Patient	Sex	Job title	Activity; DMG test-positive item	Exposure to nickel reduced by alternatives
A	Female	Psychiatric nurse	Nursing; keys	Pushbutton locks
B	Female	Psychiatric nurse	Nursing; keys	Pushbutton locks
C	Female	Industrial worker	Assembly; electrical components	Job change, unrelated to nickel allergy
D	Female	Dressmaker	Sewing; embroidering, sewing needles	DMG test-negative needles and tools
E	Female	Sandwich maker	Cooking; bread pans, baking trays	Job change, pursuit of another career owing to nickel allergy
F	Male	Carpenter/house painter	Maintenance work, painting, carpentry; tools	Protective gloves

^aAll patients carried out their normal work routine for 2 hr prior to acid wipe sampling from the skin surface (7), without washing their hands in between.

Sweden) for analysis of nickel. For practical reasons, we allowed storage for up to 14 days at 8°C before shipment, as this does not affect the analytical result (8). The technician used metal-free plastic forceps and vinyl protective gloves during preparatory work and sampling. Gloves were changed between each surface cleaning to avoid cross-contamination.

Quantitative analysis of nickel in the acid extracts of the wipes was performed by inductively coupled plasma–mass spectrometry, which has been previously described in detail (7).

Serial dilution patch testing

Within 2 weeks of the first consultation, we performed a patch test with a nickel sulfate dilution test series ($\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$ in 10% ethanol/90% water) with 12 different concentrations, ranging between 0.00125 and 200 $\mu\text{g}/\text{cm}^2$. The selection of concentrations for the dilution patch test series was based on the results from a statistical review of nickel elicitation thresholds (9), in which Fischer et al. showed that about 10% of a nickel-sensitized population will react to 1.04 μg nickel sulfate/ cm^2 . Finn Chambers® (8 mm; Epitest Ltd, Oy, Finland) were used on Scanpor® tape (Norgesplaster A/S; Alpharma, As, Norway). The patch tests were applied to the upper back and occluded for 2 days. Readings were performed on D2, D3 and D7 according to the recommendations of the International Contact Dermatitis Research Group (10).

Ethics

The ethics committee of the Capital Region of Denmark approved the study, and written informed consent was obtained from all participants.

Results

Table 1 shows the 2-hr work sessions performed by the patients, as well as information about work items that

gave positive DMG test results. A total of 18 samples were taken from 6 patients with the acid wipe sampling technique (Table 2), and nickel was detected in all samples. All patients had more nickel on the index finger (range 0.047–0.29 $\mu\text{g}/\text{cm}^2$) than on the palm (range 0.0097–0.037 $\mu\text{g}/\text{cm}^2$). Four to 30 times more nickel was sampled from the index finger than from the palm. In all patients, the non-exposed control area on the arm had the lowest nickel level (range 0.000066–0.0045 $\mu\text{g}/\text{cm}^2$).

The largest amount of nickel (0.29 $\mu\text{g}/\text{cm}^2$) was collected from the volar index finger of the dressmaker (patient D), who used nickel-releasing sewing needles. The psychiatric nursing assistants (patients A and B) carried out similar tasks at the same place of work, and were exposed to nickel-releasing keys. Patient B reported that she carried her set of keys in her hand for almost the entire day, whereas patient A placed her keys in a pocket when not in use. The amount of nickel deposited on the hand of patient B was higher than that found for patient A.

Patch test elicitation thresholds are shown in Table 2.

All patients initially presented with vesicular dermatitis on the palms and/or fingers. They all improved significantly when occupational nickel exposure had been reduced. Nickel-reducing measures included advice from the responsible dermatologist on how to use the DMG test to identify nickel-releasing objects with which prolonged or repeated skin contact should be avoided. In addition, different measures had been taken by the patients or their work management in order to reduce skin exposure to nickel (Table 1). At 3 months of follow-up, the hand eczema in all patients remained in complete remission.

Discussion

In many highly industrialized countries, the current occupational nickel exposure is different from the pattern of nickel exposure that was observed in the plating industry during the first half of the 20th century. At present,

Table 2. Amount of nickel on the skin ($\mu\text{g}/\text{cm}^2$) assessed by acid wipe sampling and inductively coupled plasma–mass spectrometer^a and patch test elicitation threshold ($\mu\text{g}/\text{cm}^2$) in nickel-allergic patients with hand eczema

Patient	Job title	Index finger	Palm	Non-exposed control area ^b	Elicitation threshold
A	Psychiatric nurse	0.047	0.013	0.0011	200
B	Psychiatric nurse	0.10	0.028	0.000066	50
C	Industrial worker	0.19	0.037	0.0045	6.25
D	Dressmaker	0.29	0.0097	0.0017	200
E	Sandwich maker	0.072	0.014	0.00099	50
F	Carpenter/house painter	0.052	0.0099	0.00079	200 (follicular response)

^aSamples were obtained from two exposed areas (right palm and right volar index finger) after 2 hr of work. Limit of detection (LOD) of the analytical instrument, nickel 0.15 ppb; LOD of the method, nickel 2.77 ppb.

^bNon-exposed control area: medial aspect of the right upper arm; mean value 0.0016 $\mu\text{g}/\text{cm}^2$.

occupational nickel exposure is varied, and major sources are tools, keys, and coins (11–13). In addition, nickel is a problem in a wide range of occupations, which is clearly shown by the nickel release from needles used by dress-makers, hooks and scissors used by hairdressers, and tools, locks and pipes used by carpenters, locksmiths, metal workers, and workers in many other occupations (8, 13–16).

This study shows that the acid wipe sampling technique can be used in the clinical setting to identify and confirm occupational nickel exposure. The 2-hr duration of the work session was chosen on the basis of previous experience (8), to ensure that an adequate amount of nickel would be found in all study participants, even those with low nickel exposure. Further research is needed to define the optimum duration of the exposure session prior to acid wipe sampling. A normal non-monotonous work-day is characterized by different exposure scenarios, and the duration of work exposure prior to sampling must therefore be long enough to be representative. The detection limit of the analytical instrument is also an important factor to consider.

In agreement with previous experience, we have shown that deposition of nickel on different parts of the hands varies with type of work and different nickel skin contact scenarios. Often, the volar fingertips of the first three fingers of the dominant hand are more exposed than other parts (8, 12, 16). When sampling is planned and performed, it is important to consider how work is performed, so that sampling is performed on relevant areas. Ideally, the skin should be acid-cleaned before the work session for exposure (7, 8); and ideally, a non-exposed, acid-cleaned and protected control area should be included. For practical reasons, however, we were unable to do this in this pilot study. Therefore, it is impossible to determine whether nickel residues from other sources prior to the work session contributed to the total amount of nickel measured.

To identify sources of nickel exposure, we found it advantageous to use the DMG test on work items prior to acid wipe sampling, to identify nickel-releasing sources. The amount of nickel collected on the palms or index fingers was at least five times (range 5–1682) higher on occupationally exposed skin sites than on the non-exposed skin control site on the arm. These results are in accordance with the results from the pioneering acid wipe sampling studies, which described a clear difference between the amounts of nickel on the hands in a range of occupations with and without obvious nickel exposure (7, 8). The amount of nickel sampled from the index fingers of the patients in the present study was in the same range as in carpenters and cashiers (8), lower than in

locksmiths and metal workers (8, 16), and higher than in secretaries (8), according to dose per hour. Also, our measurements are in accordance with the results obtained with the water immersion method for assessing dermal nickel exposure (17).

The clinical presentation of hand eczema in the present patient series is typical of the vesicular dermatitis seen on palms and fingertips in nickel-sensitive individuals. All patients had symptom relief after diagnostic workup, routine hand eczema counselling, and attempts to reduce nickel exposure at the workplace. This is in agreement with our experience that nickel eczema on the hands has a favourable prognosis if factors such as atopy and wet work are not involved. In two instances (patients A and B, psychiatric nursing staff), the detection of occupational nickel eczema led to a major work-related intervention, with the replacement of all conventional locks on medicine cabinets with pushbutton locks.

Experimental nickel dose–response studies performed on the hands and fingers in nickel-sensitive individuals have shown a reactivity that is probably of the same magnitude as reactions on other skin sites (18, 19). An experiment in which nickel-releasing coins were handled by nickel-sensitive individuals without hand eczema had a negative outcome (20). However, this does not exclude the possibility that nickel-sensitive individuals will react when they are repeatedly exposed to nickel at levels measured by the acid wipe method (21). An occluded nickel patch test on the palm skin or on the side of the fingers will give an oedematous and vesicular response. The palm skin might react more easily to nickel than other skin sites, because of the higher number of sweat ducts, which are known to facilitate the absorption of nickel (22).

A recent study has confirmed the moderate sensitivity and the high specificity of the DMG test (23), and, has also shown that the DMG test is able to identify the threshold for clinical reactivity for nickel in nickel-sensitized individuals. In the present pilot study of a series of clinical cases, we have shown that occupational handling of DMG test-positive tools, keys and other nickel-releasing items raised the nickel content on exposed skin significantly as compared with a non-exposed control skin site. These 6 clinical cases with symptom relief following occupational nickel exposure reduction underscore the significance of this finding.

The present study reminds us that, in the case of a positive nickel patch test result and hand eczema, the patients should be instructed to perform the DMG test on metallic items both at home and at work. Furthermore, they should be advised to bring items to the clinic for control DMG testing if feasible. Occupational health services and

employers should also be engaged to ensure that efficient measures to reduce nickel skin exposure are taken in each particular case. This may also reduce the risk of additional cases of nickel dermatitis in the same workplace.

We conclude that the acid wipe sampling method is a valuable tool in the diagnostic workup of occupational nickel hand eczema. Larger studies may confirm our present strategy of using the inexpensive DMG test for initial screening of the environment, supplemented with acid wipe sampling for quantitative skin exposure assessment in some cases, as a confirmatory test. In turn, this may help dermatologists to establish a much-needed method that will enable policy-makers to regulate occupational nickel exposure in accordance with the successful EU Nickel Directive on consumer products. Such knowledge

is important both for medical reports and for decisions that need to be made in cases of occupational disease and claims for compensation.

Acknowledgements

This work was supported by grants from the Michaelsen Foundation and the Aage Bangs Foundation in Denmark, and from the Swedish Council for Working Life and Social Research. The authors wish to thank the laboratory staff at the Department of Dermato-Allergology, Copenhagen University Hospital Gentofte, Denmark, and in the Institute of Environmental Medicine, Karolinska Institutet, Sweden for their invaluable assistance.

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