

Cobalt-containing alloys and their ability to release cobalt and cause dermatitis

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Background: Cobalt, nickel, and chromium are important skin sensitizers. However, knowledge about cobalt exposure and causes of cobalt sensitization is limited.

Objectives: To study release of cobalt, nickel, and chromium from some cobalt-containing hard metal alloys and to test reactivity to the materials in cobalt-sensitized patients.

Methods: Discs suitable for patch testing were made of some hard metal alloys. Cobalt, nickel, and chromium release from the materials was determined by immersion in artificial sweat (2 min, 1 hr, 1 day, and 1 week). Patch test reactivity to the discs and to serial dilutions of cobalt and nickel was assessed in previously patch-tested dermatitis patients (19 cobalt positive and 18 cobalt-negative controls).

Results: All discs released cobalt, nickel, and chromium. Some discs released large amounts of cobalt (highest concentration: 290 µg/cm²/week). Seven discs elicited three or more positive test reactions.

Conclusions: The concentration of released cobalt was high enough to elicit allergic contact dermatitis in cobalt-sensitized patients. As the materials in the discs are used in wear parts of hard metal tools, individuals with contact allergy to cobalt may develop hand eczema when handling such materials.

Key words: acid wipe sampling; allergic contact dermatitis; chemical analysis; chromium; cobalt; nickel; occupational exposure; patch tests. © Blackwell Munksgaard, 2009.

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Cobalt, nickel, and chromium are important skin sensitizers. The metal ions, alloys, and compounds have the ability to cause allergic contact dermatitis. Knowledge about cobalt exposure to skin is limited and not well studied. It is generally assumed that it is often associated with simultaneous exposure to nickel or chromium (1). Based on results in animal experiments, it is assumed that cobalt is a potent skin sensitizer and that the frequently occurring simultaneous reactivity to cobalt and nickel in patients is due to multiple sensitizations rather than cross-reactivity (2, 3). Nickel allergy is common, and well-studied cobalt allergy, however, is less studied. Chromium allergy has historically

been considered mainly a male occupational problem within the construction industry (1).

Under the influence of human sweat, pure cobalt and nickel as well as many alloys containing cobalt, nickel, or chromium will release metal ions that may cause allergic contact dermatitis. Even when alloys have been given a coating, they may release the metal ions due to pores and cracks in the coatings that are not impermeable (4). Nickel allergy is common, especially among women, but it is also increasing among men (5). Cobalt allergy has been studied in hard metal workers in Sweden (6, 7) but not in the Swedish general population.

One exposure route of nickel for men is tools. In a study by Lidén et al. (8), 565 hand-held tools with metal parts in contact with the skin were tested with the dimethylglyoxime test. Twenty-seven per cent of the hand-held tools showed a positive test result indicating release of nickel ions. Furthermore, a selection of tools was investigated concerning release and content of a range of metals in artificial sweat. In that study, cobalt was not detected in any of the tools tested.

The aim of the present study was to test a selection of cobalt-containing hard metal alloys with different surface coatings, used in hard metal wear parts for cutting, to find out if they release cobalt, nickel, and chromium when stored in artificial sweat. Second, cobalt-allergic patients were patch tested with the materials to study if they could elicit a positive patch test reaction in the patients.

Material and Methods

The study was approved by the Ethical Committee at the Medical Faculty of Lund University. Informed consent was obtained from each patient before the start of the study. The clinical part of the study was carried out at the Department of Occupational and Environmental Dermatology at Malmö University Hospital, Sweden. The metal release part of the study was performed at the Department of Occupational and Environmental Health, Stockholm Centre for Public Health, Stockholm, Sweden. Chemical analysis was performed by Analytica AB, Luleå, Sweden.

Patients

Invitations to participate in the study were extended to patients who had been patch test positive to cobalt when patch tested with the Swedish baseline series of contact allergens (cobalt chloride, CoCl_2 , 0.5% in petrolatum, pet.). All patients had also had a simultaneous patch test reaction to nickel (nickel sulfate, NiSO_4 , 5% in pet.). A total of 19 female patients participated. Their average age was 47 years, range 28–66 years. The control group was selected among patients who had been patch test negative to cobalt and nickel when patch tested with the Swedish baseline series. A total of 18 controls were included of which nine were females. The average age of the control group was 56 years, range 36–68 years.

Materials

The materials consisted of three different hard metal alloys with at least one coating per alloy. A full description of the metal discs is shown in

Table 1. Specific information on the different cobalt-containing alloys and their coatings that were made into metal discs for this study^a

Disc number	Cobalt and chromium content in base alloy	Coating	Usage
A	Co 6%	No coating	Tools ^b
B	Co 6%	TiCN + Al_2O_3	Tools ^b
C	Co 6%	TiN	Tools ^b
D	Co 7.5%	No coating	Tools ^b
E	Co 7.5%	TiCN + Al_2O_3 + TiN	Tools ^b
F	Co 15%, Cr 0.6%	No coating	Tools ^b
G	Co 15%, Cr 0.6%	TiCN + Al_2O_3 + TiN	Tools ^b
H	Al, Finn Chamber	No coating	Control disc ^c

Al, aluminium; Co, cobalt; Cr, chromium.

^aThe discs were used for patch testing and for cobalt, nickel, and chromium release in artificial sweat. Disc H was used as a control disc in the study. All discs were nickel free according to the producers. The size of the discs was 1.12 cm diameter and 0.13 cm thick for A–G.

^bProduced and supplied by Sandvik AB, Sandviken, Sweden.

^cProduced by Epitest Ltd. Oy, Tuusula, Finland.

Table 1. According to the producers, all discs were nickel free. Discs A–C, D–E, and F–G make up groups of the same base alloy with different types of coating material. As a control disc, a standard FinnTM Chamber (Epitest Ltd. Oy, Tuusula, Finland) disc was used. The alloys are used as raw material in the production of wear parts for hard metal tools. None of the discs had any sharp edges. The total surface area of the metal discs was, in average, 2.7 cm² (range 2.6–2.8 cm²). The metal discs used in the study were specially made for the present study and supplied by the producers of the alloys.

Patch testing

The patch test was performed on the upper back of the patients, as in ordinary patch testing, according to the recommendations by the International Contact Dermatitis Research Group (ICDRG) (9, 10). By request, one patient was tested on the upper parts of the arms. This was due to the fact that the patient had strong reactions in an earlier patch test and wanted to be able to remove the discs quickly if it occurred again.

Each metal disc was tested in every patient. The discs were placed at random order and fixed with Scanpor[®] tape (Norgesplaster A/S, Oslo, Norway). To establish the patch test reactivity of the patients, at the time of the study, a serial dilution of cobalt chloride (1.25, 0.5, 0.2, 0.08, and 0.032% w/v in aq. corresponding to 93, 37, 15, 3, and 1.2 µg/cm²) and nickel sulfate (12.5, 5.0, 2.0, 0.8, and 0.32% w/v in aq. corresponding to 840, 335, 134, 53.5, and 21.4 µg/cm²) was

applied simultaneously. Fifteen microlitres of each solution was applied to filter paper that was placed in Finn Chambers (8 mm; Epitest Ltd. Oy, Tuusula, Finland) on Scanpor tape. The exposure time was 2 days, and the result was recorded by readings on D4. The minimum criterion for a positive (+) reaction was erythema and infiltration (10). The discs were coded in the patch test protocol to avoid bias when reading.

Metal release in artificial sweat

In this study, the European standard 'Reference test method for release of nickel from products intended to come into direct and prolonged contact with the skin' (EN 1811) was applied (11). The release of cobalt, nickel, and total chromium in artificial sweat, from the materials, was analysed at four different time periods: 2 min, 1 hr, 1 day, and 1 week.

The artificial sweat was made from deionized and aerated water containing sodium chloride 0.5% (M/M), lactic acid 0.1% (M/M), and urea 0.1% (M/M). To adjust the pH of the solution, ammonia (1% M/M) was added until a stable pH value of 6.5 was received. The solution was used within 3 hr of preparation, which is in accordance with the procedure described in the EN 1811 standard document (11).

The metal discs were placed in individual acid prewashed plastic containers, and 10 ml of artificial sweat was added to the containers. For the two shortest time periods (2 min and 1 hr), the sweat was already preheated to 30°C, before the materials were added to the solution.

The container was covered with a lid and stored in an oven at 30°C for the different time periods. At the end of the release period, the discs were taken out of the solution and rinsed with 0.1 ml deionized water. The test solution was acidified using 0.4 ml of nitric acid (25%) to inhibit deposition of released metals to the interior surface of the containers

according to EN 1811 (11), giving a total volume of 10.5 ml. The average total area of the metal discs was calculated to approximately 2.7 cm² for discs A–G. For calculation of the concentration of metal/cm², the definite total area of each disc was used, and not the average area. Disc H (aluminium, Finn Chamber; Epitest Ltd. Oy, Tuusula, Finland) was not treated with artificial sweat, and consequently, no chemical analysis is available for the disc.

Metal release from the discs was performed at our laboratory, and the chemical analysis of the test solutions was done by Analytica AB. The chemical analysis was performed on the test solutions using inductively coupled plasma/mass spectrometry detection. The reporting limits were 0.05 µg/l for cobalt, 0.3 µg/l for nickel, and 0.2 µg/l for total chromium. The release of each metal was calculated and reported as µg/cm². The corresponding reporting limits for the metal release were 0.001 µg/cm² for all three metals.

Results

Metal release from discs in artificial sweat

Cobalt, nickel, and chromium were released by all discs ($n = 7$) at varying concentrations and increasing with time in artificial sweat (Table 2). For the time periods of 2 min, 1 hr, and 1 day, the result is presented as the mean value of the concentration for three discs, whereas for 1 week, only two discs were put in artificial sweat and therefore both concentrations are reported.

Cobalt. All discs released cobalt above the chemical reporting limit (0.001 µg/cm²), at all time periods (2 min, 1 hr, 1 day, and 1 week). Even at the shortest time in artificial sweat (2 min), disc D and F released cobalt (1.4 and 1.1 µg/cm², respectively) corresponding to the lowest patch test concentration in the serial

Table 2. Metal release (µg/cm²) from hard metal alloys (discs A–G) in artificial sweat for four different time periods (2 min, 1 hr, 1 day, and 1 week) for cobalt, nickel and chromium^a

Discs	Cobalt (µg/cm ²)				Nickel (µg/cm ²)				Chromium (µg/cm ²)			
	2 min	1 hr	1 day	1 week	2 min	1 hr	1 day	1 week	2 min	1 hr	1 day	1 week
A	2.2	13	87	230; 180	0.003	0.013	0.081	0.21; 0.16	<0.001	<0.001	0.005	0.020; 0.006
B	0.21	4.0	53	140; 180	0.004	0.002	0.050	0.14; 0.17	<0.001	<0.001	0.002	0.001; 0.026
C	2.7	11	110	220; 160	<0.001	0.011	0.12	0.20; 0.16	<0.001	<0.001	0.004	0.011; 0.005
D	1.4	12	110	240; 290	<0.001	0.020	0.17	0.39; 0.48	<0.001	0.005	0.055	0.062; 0.15
E	0.15	2.1	41	140; 160	<0.001	0.006	0.067	0.23; 0.24	<0.001	0.001	0.008	0.031; 0.082
F	1.1	10	70	150; 140	0.003	0.003	0.006	0.011; 0.012	0.006	0.038	0.44	0.43; 0.55
G	0.021	0.036	1.9	9.4; 7.6	0.008	0.001	0.002	0.001; 0.001	0.002	0.001	0.028	0.14; 0.11

^aValues for time periods 2 min, 1 hr, and 1 day are presented as the mean from three discs, whereas for 1 week, two individual values are presented. The analysis was performed by inductively coupled plasma/mass spectrometry with a chemical reporting limit at 0.001 µg/cm² for all three metals. Disc H (Finn Chamber; Epitest Ltd. Oy, Tuusula, Finland) was not put in artificial sweat for analysis.

dilution test ($1.2 \mu\text{g}/\text{cm}^2$) on the patients. At 1 week in artificial sweat, cobalt from discs A–F exceeds the highest concentration in the serial dilution test ($93 \mu\text{g}/\text{cm}^2$), with a release of cobalt in the interval $140\text{--}290 \mu\text{g}/\text{cm}^2$ (Table 2).

Nickel. Several discs released nickel above the reporting limit ($0.001 \mu\text{g}/\text{cm}^2$). The highest amount of released nickel was $0.48 \mu\text{g}/\text{cm}^2$ for disc D at 1 week in artificial sweat (Table 2). This concentration was much lower than the lowest concentration in the serial dilution test for nickel ($21 \mu\text{g}/\text{cm}^2$) in this study.

Chromium. As for nickel, low amounts of chromium were released overall for all the discs (Table 2). Disc F released the highest amount at all four time periods in the study, with the top concentration at $0.55 \mu\text{g}/\text{cm}^2$ at 1 week in artificial sweat. For the time periods of 2 min and 1 hr, approximately 50% of all discs released less chromium than the reporting limit ($0.001 \mu\text{g}/\text{cm}^2$).

Patch test reactivity at serial dilution

The overall result of the patch tests to cobalt and nickel are presented in Figs 1 and 2 as five categories: extremely strong positive (+++), strong positive (++), weak positive (+), doubtful (reactions such as few papules or erythema without infiltration), and negative. Of the 19 patients who participated in this study, 18 had positive readings for the cobalt serial dilution patch test and 17 had positive readings to the serial dilution patch test with nickel.

Cobalt. Fourteen patients had positive reaction to the highest concentration of cobalt in the serial dilution test (1.25% ; $93 \mu\text{g}/\text{cm}^2$) (Fig. 1). One patient was negative to the serial dilution test, and one had a doubtful reaction to the highest concentration only. At all concentrations, several reactions were classified as doubtful, with the highest number occurring at 0.2% ($15 \mu\text{g}/\text{cm}^2$) with six patients. Four patients were positive to the lowest concentration.

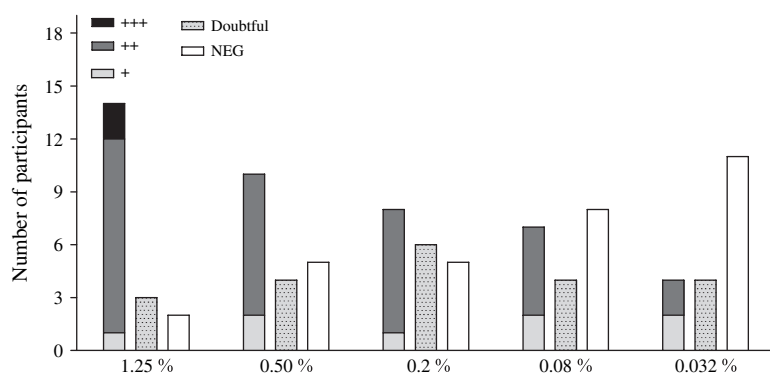


Fig. 1. Number of patch test reactions in patients to serial dilution with cobalt chloride. Positive reactions (+++, ++, and +) are presented as a cumulative bar with three segments and doubtful and negative (NEG) reactions are presented as separate bars.

Nickel. Five patients or more reacted to each concentration of the serial dilution patch test for nickel (Fig. 2). Two patients were negative to the serial dilution test, and one had a doubtful reaction to the highest concentration only (12.5% ; $840 \mu\text{g}/\text{cm}^2$). Doubtful reactions were more frequent in the lower concentrations than the two highest.

Patch test reactivity to metal discs

All the cobalt-containing discs elicited three or more positive reactions in each of the patients (Fig. 3). One patient displayed a strong positive reaction (++) to discs A, D, and F, which had no coatings. All the other patients displayed positive reactions to several discs including discs with surface coatings. The control disc (empty Finn Chamber, disc H; Epitest Ltd. Oy, Tuusula, Finland) elicited one positive reaction (+).

Control group

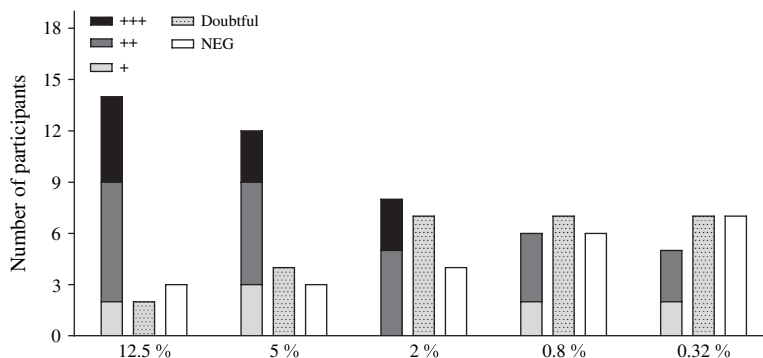
Of 18 patients acting as the control group, all, but one, were negative to the cobalt and nickel serial dilution tests. One control patient reacted with a weak positive reaction to disc A and was also positive to the nickel serial dilution test. Another control patient had doubtful reactions to all discs.

Discussion

All cobalt-containing alloys did release cobalt at concentrations that can elicit an allergic response in the skin of cobalt-sensitized patients. Several of the discs even released amounts of cobalt that were 2–3 times higher than the highest concentration in the serial dilution test ($93 \mu\text{g}/\text{cm}^2$) in this study.

It is important to understand that metal ion release from an alloy is not directly correlated to the level of metal content in the alloy. It is a well-known fact among metallurgists that alloys can have properties very different from those of the metals they contain (12). This is why the amount

Fig. 2. Number of patch test reactions in patients to serial dilution with nickel sulfate. Positive reactions (+++, ++, and +) are presented as a cumulative bar with three segments and doubtful and negative (NEG) reactions are presented as separate bars.



of metal ion release from alloys and the patch test reactivity to the alloys are not directly related to the concentration of sensitizing metals in the alloy. Examples are 18/8 stainless steel (18% chromium and 8% nickel) with very low release of the metals in artificial sweat, the copper–nickel coin alloy (25% nickel) and nickel–silver (11–13% nickel) with very high nickel release, and pure nickel (100%) with much lower nickel release than copper–nickel and nickel–silver (4, 13). The amount of metals released into artificial sweat is dependent on inherent properties of the alloy and also on factors such as acidity, composition, temperature of the medium, and surface finish and coating of the item.

The highest amount of cobalt released was for disc D ($290 \mu\text{g}/\text{cm}^2$) at 1 week in artificial sweat. The disc was made of an alloy that had a content of 7.5% cobalt. The released concentration was three times as high as the highest concentration in the serial dilution test for cobalt. When the disc was tested in 19 cobalt-allergic patients, it gave rise to two extremely strong positive (+++) reactions and 16 strong positive (++) reactions at an exposure time of 2 days. The same material coated with a layer of TiCN + Al_2O_3 + TiN (disc E) elicited eight strong positive (++) reactions, two weak positive (+), seven doubtful, and two negative reactions at patch testing. In artificial sweat, disc E released

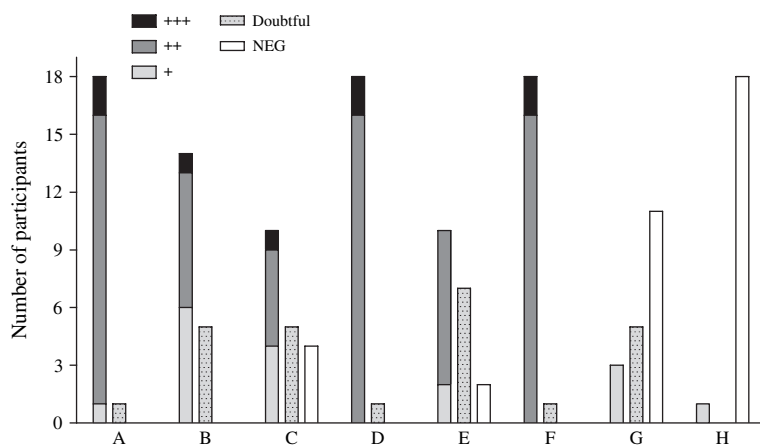
$160 \mu\text{g}/\text{cm}^2$, which was still almost two times higher than the highest concentration in the serial dilution test.

It is considered likely that also the majority of doubtful reactions may represent a weak allergic response, a conclusion supported by the negative response to the metal discs and dilution series in 17 of the 18 controls. It is also well known that patch test reactivity in the same subject varies over time (14). If the doubtful reactions in this study are considered positive ones, four of the seven cobalt-containing discs only elicited positive reactions when patch tested. Generally, nickel release from an alloy corresponds well to the patch test reactivity to the alloy (4). This was true also for cobalt with most of the alloys in the present study.

It is not known to what extent the release of nickel from some of the discs may have contributed to the test reactivity. The highest amount of nickel released was $0.48 \mu\text{g}/\text{cm}^2$ from disc D after 1 week in artificial sweat. Although lower than the lowest level of the serial dilution test for nickel ($21 \mu\text{g}/\text{cm}^2$), such levels of nickel may elicit positive reactions in nickel-allergic individuals (1, 4, 15).

Approximately 75% of the discs released chromium above the chemical reporting limit ($0.001 \mu\text{g}/\text{cm}^2$). Low concentrations were observed for the shortest time periods in the artificial sweat

Fig. 3. All reactions to the eight metal discs (A–H) patch tested in patients. Disc H is a control disc made with aluminium (Finn Chamber; Epitest Ltd. Oy, Tuusula, Finland); however, one participant was positive to this disc. Positive reactions (+++, ++, and +) are presented as a cumulative bar with three segments and doubtful and negative (NEG) reactions are presented as separate bars.



(2 min and 1 hr), whereas somewhat higher concentrations were observed at 1 day and 1 week in artificial sweat. The highest amount released ($0.5 \mu\text{g}/\text{cm}^2$) was from disc F at 1 week in artificial sweat. If and how this might have influenced the result of the patch test with the discs is not known. One of the patients in the study had also shown a positive reaction to chromium at the initial clinical patch testing in 1999. It is not known if any of the other patients had developed an allergy to chromium at the time of this study.

We have recently shown that cobalt is deposited on the skin in workers handling and sharpening wear parts of hard metal tools. Acid wipe sampling (16) was used to assess the amount of cobalt, nickel, and chromium deposited onto the skin. The highest amount of cobalt on the skin was $4.5 \mu\text{g}/\text{cm}^2/\text{hr}$ for (corresponding to $9.4 \mu\text{g}/\text{cm}^2$) workers sharpening those tools (Julander A et al. submitted). This amount is higher than the lowest concentration used for patch testing in the cobalt dilution series (0.032% corresponding to $1.2 \mu\text{g}/\text{cm}^2$), which elicited allergic response in cobalt-sensitized patients in the present study.

Because humans are normally exposed to nickel, cobalt, and chromium, it is difficult to tell if concomitant patch test reactivity is due to multiple sensitization or cross-reactivity. Cross-reactivity was studied in guinea-pigs induced with chromate or cobalt and challenged with chromate, cobalt, and nickel. No cross-reactivity was shown (2). This supports the view that the concomitant reactivity often seen in humans to either of these metals is explained by multiple exposure and sensitization, and not cross-reactivity.

In conclusion, all discs in this study released cobalt, nickel, and chromium. The concentration of released cobalt was high enough to elicit allergic contact dermatitis in cobalt-sensitized patients. It is likely that these results can be extended to a cobalt-sensitized male population. As the materials in the discs are used for wear parts of hard metal tools, persons with contact allergy to cobalt may develop hand eczema when handling such tools.

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