

ORIGINAL ARTICLE

Causative exposures and temporal development of cobalt allergy in Denmark between 2002 and 2017

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Abstract

Background: Cobalt contact allergy is common, but clinical relevance is often difficult to determine.

Objectives: To examine the aetiology, prevalence and clinical characteristics of cobalt-allergic patients who were patch tested between 2002 and 2017 at the Department of Dermatology and Allergy, Herlev-Gentofte Hospital.

Methods: Patch test data, along with patient characteristics and causative exposures, from all adult dermatitis patients seen and tested between 2002 and 2017 were analysed. Associations were tested with the χ^2 test and logistic regression.

Results: A total of 13 475 adults aged 18 to 99 years were patch tested. The overall prevalence of cobalt allergy and the prevalence of isolated cobalt allergy were 3.3% and 1.5%, respectively. The prevalence of isolated cobalt allergy decreased from 2.4% in 2006 to 2009 to 1.1% in 2014 to 2017 ($P_{\text{trend}} = 0.00003$). Leather exposure as a relevant cause of allergic cobalt dermatitis increased from 3.7% in 2002 to 2009 to 8.3% in 2010 to 2017 ($P = 0.04$). The current clinical relevance of positive patch test reactions, that is, a positive reaction to cobalt combined with a history of current skin exposure to a source of cobalt, was 20.1%.

Conclusions: We conclude that cobalt allergy is relatively common, but causative exposures are largely unknown, and the proportion of positive patch test reactions with clinical relevance is low. It is therefore currently unclear how we can better protect consumers and workers from cobalt exposure.

KEYWORDS

cobalt, contact allergy, exposure, leather, prevalence, relevance, trend

1 | INTRODUCTION

Cobalt is a strong skin sensitizer,¹ and an estimated 5.9% and 7.4% of patch tested dermatitis patients in Europe and North America, respectively, are cobalt-allergic.^{2,3} However, clinical relevance is often difficult to determine, and previous identification of occupational and consumer sources of cobalt seems to be insufficient. According to a Danish study, only 25% of positive patch test reactions to cobalt have clinical relevance, as exposure sources were largely unknown.⁴

Historically, occupational cobalt exposure has mainly been observed in metal workers, bricklayers, and pottery workers.⁵ The hard metal industry is believed to represent the main source of occupational cobalt exposure, particularly in the EU and North America, as almost 15% of the worldwide production of cobalt is used for hard metal production.⁶ Dental tools and alloys have also been reported to contain and release high levels of cobalt.⁷ Consumer exposure sources have also been described, including jewellery and, recently, leather items.⁸ Whereas piercing jewellery may indeed contain and release

cobalt, a large study of inexpensive earrings showed that very few contained cobalt.⁹ Also, a North American study showed that cobalt allergy was not independently associated with piercings.¹⁰ We have observed single cases of allergic cobalt dermatitis caused by leather items,^{11,12} but suspect that leather might be a more important source of cobalt exposure than hitherto realized. In this respect, a recent questionnaire case-control study from our clinic showed that leather was the most frequently reported exposure source causing dermatitis in patients with cobalt allergy without concomitant allergy to hexavalent chromium.¹³

In the present retrospective database study, we examined the development of cobalt allergy prevalence over a 16-year period, and investigated the causative exposures and clinical characteristics of cobalt-allergic dermatitis patients in our clinic.

2 | METHODS

2.1 | Study population

This study was performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.¹⁴ Data were extracted from the National Database for Contact Allergy in Denmark. All adult patients (≥ 18 years) with suspected allergic contact dermatitis (ACD) who were patch tested January 2002 to December 2017 at the Department of Dermatology and Allergy, Herlev-Gentofte Hospital were included. Through a retrospective review of patient data regarding patch testing (test year, reading day and test results, that is, presence or absence of allergy to cobalt, nickel, or chromium), the clinical relevance of cobalt allergy (current, past, or unknown), MOAHLFA index (Male, Occupational dermatitis, history of Atopic dermatitis, Hand eczema, Leg dermatitis, Facial dermatitis, and Age > 40 years),¹⁵ and sources of exposure were retrieved. Permission was obtained from The Danish Data Protection Agency.

2.2 | Definitions

The clinical relevance of positive patch test reactions to cobalt was assessed by the consulting physician: "current clinical relevance" was registered when a patient presented with a dermatitis reaction in combination with a history of current skin exposure to a source of cobalt; "past clinical relevance" was registered when a patient had a positive patch test reaction to cobalt in combination with a history of a past dermatitis reaction caused by skin exposure to a source of cobalt; and "unknown clinical relevance" or "missing" was registered in patients with dermatitis and cobalt allergy when no relationship with current or past cobalt exposure could be assessed, or when no registrations had been performed by the physician. Relevant causative exposures were based on the physician's notes in medical charts, on the use of spot tests, and, in selected cases, on chemical analysis. Isolated cobalt allergy was defined as a positive reaction to cobalt but negative patch test results with chromium and nickel. Cobalt allergy referred to a positive patch test reaction to cobalt independently from

concomitant positive reactions to chromium, nickel or other metals, and allergens.

2.3 | Patch testing

Patch testing was performed with the European baseline series by the use of Trolab allergens (Hermal, Reinbek, Germany) and Allergeaze allergens after April 2016, with Finn Chambers (8 mm; Epitest, Tuusula, Finland) on Scanpor tape (Norgesplaster, Vennesla, Norway). Dosing of the chamber was performed with 20 mg of the test preparation. Cobalt chloride 1.0% pet. was used for testing during the entire period. Patch test readings were performed according to the recommendations of the European Society of Contact Dermatitis,¹⁶ with an exposure time of 2 days and readings being performed on day (D) 2, D3 or D4, and D7. Patch test reactions designated as +, ++ or +++ were interpreted as positive reactions. Irritant responses and doubtful (?+) or negative readings were interpreted as negative responses.

2.4 | Statistical analysis

Data analysis was performed with SPSS for Windows (release 22.0). The χ^2 test of independence was used to test for associations between categorical variables. For small sample sizes (<5), Fisher's exact test was applied. Linear-to-linear association tests were used for trend analysis across test years. Two logistic regression models were applied with either "cobalt allergy" or "isolated cobalt allergy" as the dependent variable, and with sex, patch test year, age group, atopic dermatitis (AD), occupational dermatitis, foot dermatitis, hand eczema and facial dermatitis as explanatory variables. All results were expressed as adjusted odds ratios (aORs). A significance level of 5% was applied, and 95% confidence intervals (CIs) were determined.

3 | RESULTS

Baseline characteristics are shown in Table 1. In total, 13 475 (9085 women) adults with suspected ACD were included. The prevalence of cobalt allergy and the prevalence of isolated cobalt allergy were 3.3% and 1.5%, respectively. In crude data analyses, patients with cobalt allergy tended to be aged <40 years (62.4% vs 68.1%, $P = 0.0004$), and were more often affected by foot eczema (12.5% vs 5.5%, $P < 0.00001$), hand eczema (57.5% vs 37.8%, $P < 0.00001$) and occupational contact dermatitis (26.8% vs 18.4%, $P < 0.00001$) than those without cobalt allergy. Furthermore, patients with isolated cobalt allergy were more often affected by hand eczema (61.2% vs 37.8%, $P < 0.00001$), AD (23.3% vs 17.6%, $P = 0.03$) and occupational contact dermatitis (25.7% vs 18.4%, $P = 0.007$) than those without cobalt allergy.

Table 2 shows patients with isolated cobalt allergy stratified by sex, age group, and patch test year. Isolated cobalt allergy more frequently affected women than men in the age group 18 to 40 years (1.8% vs 1.1%, $P = 0.007$) and in the test years 2006 to 2009 (2.8% vs 1.4%, $P = 0.02$). Fully adjusted logistic regression showed that cobalt

TABLE 1 Baseline characteristics of included dermatitis patients (N = 13 475) in 2002 to 2017 at Gentofte, Denmark

Characteristics	Total	Patients with cobalt allergy	Patients with isolated cobalt allergy	Patients without cobalt allergy
All patients, % (n)	100 (13 475)	3.3 (447)	1.5 (206)	96.7 (13 028)
Age (y) ± SD	48.8 ± 16.8	46.2 ± 15.6	48.0 ± 16.1	48.9 ± 16.8
Male, % (n)	32.6 (4390)	20.8* (93)	23.8** (49)	33.0 (4297)
Female, % (n)	67.4 (9085)	79.2* (354)	76.2** (157)	67.0 (8731)
Age > 40 y, % (n)	67.9 (9156)	62.4* (279)	67.0 (138)	68.1 (8877)
Foot eczema, % (n)	5.7 (770)	12.5* (56)	8.3 (17)	5.5 (714)
Hand eczema, % (n)	38.4 (5177)	57.5* (257)	61.2** (126)	37.8 (4920)
Atopic dermatitis, % (n)	17.7 (2381)	19.5 (87)	23.3** (48)	17.6 (2294)
Facial dermatitis, % (n)	23.8 (3207)	23.5 (105)	29.1 (60)	23.8 (3102)
Occupational dermatitis, % (n)	18.6 (2511)	26.8* (120)	25.7** (53)	18.4 (2391)
Chromium allergy, % (n)	2.2 (296)	21.0* (94)	-	1.6 (202)
Nickel allergy, % (n)	10.9 (1467)	38.0* (170)	-	10.0 (1297)

* $P < 0.05$: χ^2 test comparing patients with and without cobalt allergy. ** $P < 0.05$: χ^2 test comparing patients with isolated cobalt allergy and patients without cobalt allergy.

TABLE 2 The prevalence of isolated cobalt allergy among 13 475 adult dermatitis patients stratified by age group and patch test year

Characteristics	Total (N = 13 475), % (n)	Men (N = 4390), % (n)	Women (N = 9085), % (n)
Isolated cobalt allergy	1.5 (206)	1.1 (49)	1.7 (157)
Age group (y)			
18-40	1.6 (72/4469)	1.1 (14/1325)	1.8* (58/3144)
41-60	1.4 (79/5490)	1.2 (21/1815)	1.6 (58/3675)
>60	1.6 (55/3516)	1.1 (14/1250)	1.8 (41/2266)
Test year			
2002-2005	1.4 (45/3159)	1.3 (15/1116)	1.5 (30/2043)
2006-2009	2.4 (64/2698)	1.4 (13/907)	2.8* (51/1791)
2010-2013	1.5 (55/3691)	0.9 (10/1114)	1.7 (45/2577)
2014-2017	1.1 (42/3927)	0.9 (11/1253)	1.2 (31/2674)

* $P < 0.05$: χ^2 test comparing men and women.

allergy was significantly associated with female sex (aOR 2.1, 95%CI: 1.6-2.6), hand eczema (aOR 2.1, 95%CI: 1.6-2.6), foot eczema (aOR 2.1, 95%CI: 1.6-2.9), being aged 18 to 40 years (aOR 1.4, 95%CI: 1.0-1.9), and being tested in 2006 to 2009 (aOR 1.6, 95%CI: 1.2-2.0). When "isolated cobalt allergy" was inserted as the dependent variable, significant associations were found with female sex (aOR 1.6, 95%CI: 1.2-2.3), hand eczema (aOR 2.9, 95%CI: 2.1-4.0), facial eczema (aOR 1.6, 95%CI: 1.1-2.2), and being tested in 2006 to 2009 (aOR 2.2, 95%CI: 1.5-3.3).

No trend was found for the prevalence of cobalt allergy in 2002 to 2017 ($P_{\text{trend}} = 0.1$) (Figure 1A). Likewise, no change in the trend of cobalt allergy was found for either men ($P_{\text{trend}} = 0.1$) or women ($P_{\text{trend}} = 0.3$) across the entire study period. Regarding isolated cobalt

allergy, we found a significantly decreasing trend from 2002 to 2017 ($P_{\text{trend}} = 0.03$) (Figure 1B). Hence, the prevalence decreased from 2.4% in 2006 to 2009 to 1.1% in 2014 to 2017 ($P_{\text{trend}} = 0.00003$); similarly, the prevalence decreased from 2.4% in 2006 to 2009 to 1.5% in 2010 to 2013 ($P_{\text{trend}} = 0.01$). No significantly decreasing or increasing trends were found for men ($P_{\text{trend}} = 0.2$) or women ($P_{\text{trend}} = 0.08$).

Table 3 shows the characteristics of dermatitis patients with isolated cobalt allergy stratified by test year. An overall increasing trend was found for facial dermatitis ($P_{\text{trend}} = 0.01$). Hence, the proportion of patients with facial dermatitis increased from 13.3% in 2002 to 2005 to 40.0% in 2010 to 2013. However, no trends were found for the other clinical variables. Table 4 shows the clinical characteristics, including exposure status, in cobalt-allergic dermatitis patients stratified by sex. Hand eczema (68.8% vs 54.5%, $P = 0.02$) and leg ulcers (6.5% vs 2.0%, $P = 0.02$) were more common in men, whereas AD was more frequently registered in women (10.8% vs 21.8%, $P = 0.02$). Furthermore, male patients were more often aged >40 years than females (76.3% vs 58.8%, $P = 0.002$). Current clinical relevance of any cobalt allergy was found in 20.1% of the patients, with no difference by sex (18.4% in women and 26.9% in men, $P = 0.08$). Past clinical relevance was registered in 25.8% of women and 10.8% of men ($P = 0.002$), yielding an overall estimate of past clinical relevance of 22.4%. Regarding causative exposures, jewellery (6.3%) and leather items (6.0%), that is, leather shoes (3.4%), leather gloves (1.3%), and "other leather items" (1.8%), were most commonly registered. Exposure to leather gloves was more frequently registered in men than in women (4.3% vs 0.6%, $P = 0.02$). Moreover, exposure to tools/metals and exposure to "other sources of cobalt" were registered in 2.2% and 2.0% of the patients, with a tendency for there



FIGURE 1 (A), Prevalence of cobalt allergy in 2002 to 2017. (B), Prevalence of isolated cobalt allergy in 2002 to 2017

Characteristics	2002-2005, % (n)	2006-2009, % (n)	2010-2013, % (n)	2014-2017, % (n)
Age group (y)				
18-40	28.9 (13/45)	34.4 (22/64)	40.0 (22/55)	35.7 (15/42)
41-60	44.4 (20/45)	40.6 (26/64)	32.7 (18/55)	35.7 (15/42)
>60	26.7 (12/45)	25.0 (16/64)	27.3 (15/55)	28.6 (12/42)
Men	33.3 (15/45)	20.3 (13/64)	18.2 (10/55)	26.2 (11/42)
Women	66.7 (30/45)	79.7 (51/64)	81.8 (45/55)	73.8 (31/42)
Hand eczema	64.4 (29/45)	68.8 (44/64)	47.3 (26/55)	64.3 (27/42)
Foot dermatitis ^a	-	10.9 (7/64)	7.3 (4/55)	9.5 (4/42)
Facial dermatitis	13.3 (6/45)	28.1 (18/64)	40.0 (22/55)	33.3* (14/42)
Atopic dermatitis	24.4 (11/45)	21.9 (14/64)	21.8 (12/55)	26.2 (11/42)
Occupational dermatitis	15.6 (7/45)	31.3 (20/64)	25.5 (14/55)	28.6 (12/42)
Clinical relevance ^b	13.3 (6/45)	42.2 (27/64)	40.0 (22/55)	33.3 (14/42)

* $P_{\text{trend}} = 0.01$.

^aThe registration of foot dermatitis started in 2004.

^bPresent or past relevance.

TABLE 3 Profile of dermatitis patients with isolated cobalt allergy stratified by patch test year (N= 206)

to be higher estimates in men than in women, although the differences were not significant.

Table 5 shows a comparison of the exposure sources between the study periods 2002 to 2009 and 2010 to 2017 in patients with cobalt allergy. Total leather exposure increased significantly from 3.8% in 2002

to 2009 to 8.4% in 2010 to 2017 ($P = 0.04$). This was mainly driven by an increase in exposure to leather gloves from 0% to 2.6% ($P = 0.03$). Exposure to "other leather sources" increased from 0.5% in 2002 to 2009 to 3.0% in 2010 to 2017 ($P = 0.07$). Exposure to tools/metals and jewellery remained largely stable over the study period.

TABLE 4 Characteristics of 447 adults with cobalt allergy in 2002 to 2017 stratified by sex

Variable	Total, % (n)	Men, % (n)	Women, % (n)
Clinical profile			
Males	20.8 (93)	-	-
Occupational dermatitis	26.8 (120)	30.1 (28)	26.0 (92)
Atopic dermatitis	19.5 (87)	10.8 (10)	21.8 (77)*
Hand dermatitis	57.5 (257)	68.8 (64)	54.5 (193)*
Leg ulcers	2.9 (13)	6.5 (6)	2.0 (7)*
Facial dermatitis	23.5 (105)	18.3 (17)	24.9 (88)
Age > 40 years	62.4 (279)	76.3 (71)	58.8 (208)*
Foot dermatitis	12.5 (56)	17.2 (16)	11.3 (40)
Relevance of positive patch test reactions			
Current	20.1 (90)	26.9 (25)	18.4 (65)
Past	22.4 (100)	10.8 (10)	25.4 (90)*
Unknown	64.7 (289)	67.7 (63)	63.8 (226)
Exposure sources			
Jewellery	6.3 (28/447)	4.3 (4/93)	6.8 (24/354)
Leather shoes	3.4 (15/447)	5.4 (5/93)	2.8 (10/354)
Leather gloves	1.3 (6/447)	4.3 (4/93)	0.6* (2/354)
Other leather items ^a	1.8 (8/447)	2.2 (2/93)	1.7 (6/354)
Leather (total)	6.0 (27/447)	9.7 (9/93)	5.1 (18/354)
Tools/metal	2.2 (10/447)	4.3 (4/93)	1.7 (6/354)
Other sources of cobalt ^b	2.0 (9/447)	4.3 (4/93)	1.4 (5/354)

* $P < 0.05$; χ^2 test comparing men and women.

^aFurniture, clothing, and other leather items.

^bCutting oil, mobile phones, chemicals, cement, and paints.

TABLE 5 Sources of cobalt exposure in dermatitis patients with cobalt allergy in 2002 to 2009 and in 2010 to 2017 at Gentofte Hospital, Denmark

Exposure sources	2002-2009 (N = 217), % (n)	2010-2017 (n = 230), % (n)
Leather shoes	3.2 (7)	3.5 (8)
Leather gloves	0 (0)	2.6 (6)*
Other leather sources ^a	0.5 (1)	3.0 (7)
Leather (total)	3.7 (8)	8.3 (19)*
Jewellery	6.5 (14)	6.1 (14)
Tools/metals	2.3 (5)	2.2 (5)
Other sources of cobalt ^b	2.8 (6)	1.3 (3)
Unknown	84.8 (184)	83.0 (191)

* $P < 0.05$; χ^2 test comparing 2002 to 2009 with 2010 to 2017.

^aFurniture, clothing, and other leather items.

^bCutting oil, mobile phones, chemicals, cement, and paints.

4 | DISCUSSION

4.1 | Main findings

In this cross-sectional database study, the overall prevalence of cobalt allergy and the prevalence of isolated cobalt allergy were 3.3% and

1.5%, respectively, during 2002 to 2017. Although leather and jewellery were clinically relevant causes of cobalt allergy, most cobalt-allergic cases could not be linked to a causative exposure. Current clinical relevance of positive cobalt patch test reactions was therefore identified in only one of five patients.

4.2 | Interpretation

On the basis of a clinical case of allergic cobalt dermatitis caused by prolonged contact with leather furniture, we suggested that cobalt release from leather might be responsible for hitherto unrecognized cases of ACD.¹¹ Recently, Haman et al examined 131 leather swatches from different companies producing leather furniture in the United States.¹⁷ When screened with a handheld X-ray fluorescence (XRF) device, 20 swatches were shown to contain cobalt; six swatches contained more than 5 wt.% cobalt. When subsequently assessed with inductively coupled plasma mass spectrometry, all six swatches were shown to contain >300 ppm, which is, depending on the rate of release of cobalt ions from the leather, a critically high level, given that concentrations of 30.8 to 259 ppm will elicit a positive patch test reaction in 10% of cobalt-allergic patients.¹⁸ After the tanning stage, leather might be dyed with pigments. This typically involves two classes of premetalized acid dye, that is, 1:1 and 1:2 metal complexes, in which, respectively, one or two dye molecules form strong coordination complexes with the metal ion, usually chromium or cobalt.¹⁹ In support of the latter being a relevant exposure that may cause cobalt allergy, Rui et al reported a significant association between having isolated cobalt allergy and being a textile and leather worker (odds ratio 1.9, 95%CI: 1.1-3.1) in a cross-sectional study including 12 492 patients with suspected ACD from units of dermatology or occupational medicine in 1997 to 2004.²⁰ Moreover, we found that leather shoes were the most common putative sources of leather exposure (3.4%), with a seemingly higher occurrence in men, although this was not significantly different from that in women (5.6% vs 2.9%, $P = 0.2$) (Table 4). Cobalt was also found in 21 shoes randomly analysed for metal content in Sweden (range: <0.3 to 16 ppm).²¹ In a recent study, we also identified >1 wt.% and > 5 wt.% cobalt in samples of leather gloves and leather shoes, respectively.²² Furthermore, cobalt has been reported to be the third most common shoe allergen (12.9%), preceded by hexavalent chromium (31.5%) and *p*-tert-butylphenol formaldehyde resin (17.1%).²³ The latter correlation between cobalt and shoes is supported by the significant association between foot eczema and cobalt allergy in our study (aOR 2.1, 95%CI: 1.6-2.9). Similarly, in a case-control study from Denmark including 126 cobalt-allergic patients without concomitant hexavalent chromium allergy, a significant association was shown between current foot eczema, presumably caused by leather shoes, and cobalt allergy (aOR 1.9, 95%CI: 1.1-3.3).¹³ Collectively, these data show that cobalt from leather causes allergic cobalt dermatitis, and that leather exposure should be evaluated in patients with cobalt allergy. Indeed, the increased attention in our clinic may explain the increasing relevance of leather during the study period. However, we suspect that many patients with dermatitis, for example, atotics, could become sensitized to cobalt

without knowing it. This may, to a certain degree, explain the low proportions of clinical relevance.

Jewellery was the most common single source of exposure (6.4%). In spite of this, inconsistent results have been reported regarding the content and release of cobalt from jewellery products around the world. In a recent market survey from Thailand, Boonchai et al found, using spot testing, that 206 of 551 (37.4%) costume jewellery items released cobalt.²⁴ Similarly, a study from Germany showed that 38 of 87 (43.7%) earrings and piercing jewellery items had at least one part releasing cobalt as assessed with EN1811:2011.²⁵ Nonetheless, cobalt release was detected in only four of 557 (0.7%) inexpensive earrings bought in Thailand and China.²⁶ In support of this, only four of 354 (1.1%) inexpensive consumer items from Denmark, including 170 earrings, released cobalt when examined with the cobalt spot test.²⁷ This discrepancy in results has created an ongoing debate regarding jewellery as an essential putative source of exposure to cobalt. Remarkably, in a recent study from Korea including 193 branded and 202 non-branded jewellery items, branded belts and branded hairpins more frequently released cobalt than the non-branded ones.²⁸ This finding, combined with the negligible levels of cobalt found in inexpensive jewellery by several studies, might partially be attributed to the higher price of cobalt than of nickel, and outlines a potential source of cobalt allergy in branded and more expensive jewellery items. Furthermore, previous studies have reported that dark-coloured jewellery items more frequently contain and release cobalt than lighter-coloured ones, but this needs to be confirmed in larger studies.^{24,27}

The proportion of patients in whom current clinical relevance could be established (20%) was low as compared with other allergens; for example, the corresponding estimate for chromium allergy was 60% in another study from our clinic.²⁹ The low degree of relevance for cobalt allergy has led to speculations concerning the adequacy of the patch test preparation. In a recent study by Lidén et al focusing on these technical aspects, it was shown that patch testing with cobalt chloride 1.0% caused a significantly lower proportion of doubtful and irritant reactions than patch testing with potassium dichromate 0.5%.³⁰ Moreover, the number of doubtful or irritant reactions and the number of positive reactions were of equal magnitude for cobalt 1% and 0.5%.³⁰ In the study by Uter et al in 2014, trends in the frequency of positive reactions to cobalt were statistically unaffected by excluding the weakest positive reactions (+) from the analysis.³¹ In our study, we found decreases over time in both isolated positive patch test reactions to cobalt chloride (statistically significant) and positive patch test reactions to cobalt chloride in combination with nickel and chromium. Neither of these results can be explained by non-specific reactivity during patch testing. Patch testers should carefully evaluate the clinical relevance of patch test results, which, so far, has proven especially difficult for cobalt. The cobalt spot test has considerably improved our ability to screen materials, particularly metallic surfaces, for cobalt release, owing to its high positive predictive value.³² However, the test is regarded to be poor for screening leather products for cobalt release, because of low estimates for sensitivity and specificity of 20% and 14%, respectively.¹⁷ The XRF device has

shown great feasibility and accuracy in determining the metallic compositions of various materials, including leather products. Nonetheless, the XRF device is not able to assess the profile of metal release from the surface of a product, making it insufficient for evaluating the allergic capacity of a material. The synthetic sweat immersion method, that is, EN1811, and EN ISO 17075 are gold standards for determining release of chemicals from metallic objects and leather goods, respectively. Currently, these methods are expensive, time-consuming, and might destroy the test item. Ideally, modifications of these assessment methods to create more rapid, feasible and less expensive versions, combined with the XRF device, might result in a more homogeneous and systematic approach to the cobalt problem all over the world, potentially resulting in the detection of new putative sources of exposure.

4.3 | Strengths and limitations

The relative increase in leather as a source of exposure might partially have been affected by detection bias towards leather. We were unable to estimate the prevalence of foot dermatitis in cobalt-allergic patients during 2002 to 2005, as its registration in the database began in 2004. A strength of this study comprises the standardized reading techniques for patch test reactions throughout the entire study period. Other strengths include the large number of dermatitis patients included, the fact that patch test methods were unchanged over the years, the long period covered, facilitating trend analysis, and the fact that clinical disease was diagnosed by physicians.

5 | CONCLUSION

The exposure profile of cobalt-allergic patients remains poorly understood, emphasizing the need for a continued search for important sources of exposure. A better understanding of the cobalt end-use combined with more feasible screening methods for cobalt release are strongly needed in order to detect putative sources of exposure to this metal.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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