

Leather Contains Cobalt and Poses a Risk of Allergic Contact Dermatitis: Cobalt Indicator Solution and X-ray Florescence Spectrometry as Screening Tests

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Background: Cobalt was recently identified in a leather couch responsible for dermatitis. Cobalt content/release in leather in the United States is unknown. We evaluated leather for cobalt content/release and investigated screening methods for identifying cobalt in leather.

Methods: One hundred thirty-one leather swatches were screened for cobalt content/release with X-ray fluorescence (XRF) spectrometry and cobalt indicator solution (CIS). Samples with positive screens and 1 negative control were analyzed using inductively-coupled plasma mass spectrometry (ICPMS).

Results: CIS showed that 5 of 131 samples contained cobalt, subsequently found to be between 1 and 190 parts per million (ppm) when evaluated with ICPMS. The XRF analysis showed that 6 samples contained >5% cobalt, subsequently found to contain greater than 300 ppm cobalt by ICPMS. 7 of 12 tested swatches contained cobalt in excess of 100 ppm. One sample contained greater than 1000 ppm cobalt. The prevalence of swatches containing cobalt at levels in excess of 190 ppm was at least 5% (n = 7; total, N = 131).

Discussion: Some leather consumer goods contain and release cobalt. Cobalt indicator solution is a poor screening test for cobalt in leather while XRF screening may be effective. Leather is a new source of cobalt exposure. Exposures to metal allergens are changing in ways that impact clinical decision making.

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Nickel, cobalt, and chromium are common metals allergens that cause allergic contact dermatitis (ACD) in individuals who are cutaneously exposed to these metals in high amounts or for a prolonged time.¹ Nickel is by far the most common allergen and recent studies using the validated colorimetric nickel spot test have identified several new sources of nickel exposure including mobile phones, laptop computers, and other electronic devices.¹ Cobalt allergy is less prevalent than nickel but is also common, with approximately 8% of dermatitis patients having a positive cobalt patch test reaction.² Cobalt allergy is also often found together with nickel allergy. Traditionally, the coexistence of nickel and cobalt allergy has been explained by concomitant exposure to the metals from, for example, inexpensive jewelry, because nickel and cobalt are found together in nature. However, until recently, few studies have specifically evaluated sources of cutaneous cobalt exposure. The development of a colorimetric cobalt spot test has rapidly resulted in a better insight into current sources of cobalt. So far, cobalt seems to be infrequently released (or not at all) from mobile phones, nonprofessional work tools, belts, and inexpensive jewelry. A recent German study highlighted that cobalt was indeed released from a significant proportion of jewelry when placed 1

week in synthetic sweat.³ Nonetheless, it is difficult for clinicians to identify relevant sources of cobalt exposure for cobalt allergic patients.⁴ As the definitive treatment for ACD is avoidance, the lack of identifiable sources of common, contemporary cobalt exposure is a frustrating clinical problem with significant consequences.

In addition to coexisting with nickel allergy, cobalt allergy also occurs together with chromium allergy.⁵ For example, cobalt and chromium allergy has historically been observed together in construction workers as both metals are found in cements. A contemporary example of occupational cobalt and chromium allergy may be seen in dental laboratory workers as both metals are found in dental tools and alloys.⁶ Although leather products constitute a well-known source of chromium exposure,^{7,8} a recent case report surprisingly showed that widespread dermatitis in a patient with cobalt allergy was caused by cobalt exposure from a leather couch.^{8,9} Because the use of cobalt in leather has not previously been investigated, we evaluated 131 leather samples for cobalt content with 2 potential screening tests, a cobalt indicator solution and x-ray fluorescence spectrometry (XRF). Furthermore, we compared the screening results in a subsample with inductively coupled plasma mass spectrometry (ICPMS) results to verify the presence of cobalt.

METHODS

Sample Selection

A convenience sample of 131 leather swatches from 14 different companies producing leather furniture for the US market was obtained from the internet and retail sources. No duplicates were collected. Swatches were characterized according to color in the following categories: black, light brown, medium brown, dark brown, red, blue, green, and gray.

Cobalt Indicator Solution Screening

A circular 1-cm diameter circle was punched from each swatch, placed in a small petri dish containing a piece of gauze, and covered with 5 mL of disodium-1-nitroso-2-naphthol-3,6-disulfonate cobalt indicator solution (LabChem, Inc., Zelienople, PA) as this appeared to be a useful method in a recent patient.⁹ Circles were submerged for 20 minutes, and the solution was assessed for color change by comparison to negative and positive controls against a white background. The negative control was a petri dish with gauze and cobalt indicator solution. The positive control was a petri dish with gauze, cobalt indicator solutions and a small metal rod known to contain and release cobalt. A positive test reaction was indicated by a color change from yellow to red-orange comparable to that of the positive control indicating greater than 8 parts per million (ppm) cobalt in a solution.¹⁰ Negative test reactions were recorded for swatches without any change in color of cobalt indicator solution or with any color change not red, orange, or brown.

XRF Screening

A Bruker S-1 Sorter handheld XRF unit (Bruker Bioscience Corporation, Billerica, MA) was set to fundamental parameters mode

for elemental analysis. The XRF unit was placed against the leather swatch on a plastic table and XRF analysis was undertaken for 10 seconds per sample. Percentages of elemental metal content were recorded for each element above 0.5% for each sample.

ICPMS Analysis

A subsample of leather that had positive cobalt screens defined as either positive cobalt indicator solution test ($n = 5$) or cobalt total metal content greater than 5% by XRF ($n = 6$) and 1 random negative sample ($n = 1$) were sent for confirmation ICPMS analysis for cobalt with standardized acid extraction methodology at Chemical Solutions Ltd. (Mechanicsburg, PA). Results were reported in ppm.

RESULTS

Cobalt Indicator Solution Screening

Of 131 swatches analyzed with the cobalt indicator solution, 5 leather swatches had positive test reactions. These 5 leather swatches with positive test reactions were sent for ICPMS analysis and contained cobalt between, respectively, 1, 1.1, 2.7, 9.9, and 190 ppm cobalt (Table 1).

XRF Screening

A total of 15% of swatches contained cobalt with a percentage of total metal content of 1% or greater as assessed by XRF ($n = 20$), and 5% ($n = 7$) contained cobalt greater than 5%. All 6 XRF-positive screening swatches (>5% cobalt) contained greater than 300 ppm cobalt as assessed by ICPMS (Table 1). X-ray fluorescence spectrometry-positive screening swatches were medium brown ($n = 4$), light brown ($n = 1$), dark brown ($n = 1$), and green ($n = 1$). The 6 swatches identified by XRF and with cobalt in concentrations up to 1100 ppm had negative reactions to cobalt indicator solution (Table 1).

ICPMS Analysis

As described, a total of 11 items appeared to contain cobalt based on XRF and indicator solution screening. These underwent ICPMS analysis for cobalt content together with 1 random negative swatch. All tested samples contained cobalt in 1 ppm or above and ranged from 1 to 1100 ppm (Table 1). Notably, in higher concentrations, the XRF results were linear when plotted against ICPMS results ($R^2 = 0.98$) (Fig. 2).

Sensitivity and Specificity Calculations

Sensitivity and specificity of the screening tests were calculated based on binary outcomes. When a binary positive threshold for ICPMS was set greater than 100 ppm and a threshold for XRF was set at greater than 2%, the sensitivity and specificity were 100% and 100%, respectively. If binary positive thresholds for ICPMS and XRF were set at greater than 100 ppm and greater than 5%, the sensitivity and specificity were 83% and 86%,

TABLE 1. Combined Results of XRF and Cobalt Indicator Solution Screening With ICPMS Results in Prescreened Subsample of Consumer Leather Swatches, Ordered by ICPMS Results

Our Item No.	Color	ICPMS Cobalt, ppm	XRF Co, %	Cobalt Indicator Solution (+, -, Possible)
31	Medium brown	1100	15.6	—
32	Dark brown	480	7.91	—
49	Medium brown	480	7.58	—
85	Green	470	6.45	—
80	Medium brown	440	5.77	—
93	Medium brown	320	5.05	—
51	Dark brown	190	3.36	+
91	Light brown	31	<1	—
50	Dark brown	9.9	<1	+
77	Red	2.7	1.25	+
55	Light brown	1.1	<1	+
60	Light brown	1	<1	+

respectively. If a binary positive threshold for ICPMS was set at 100 ppm, cobalt indicator sensitivity and specificity was 20% and 14%, respectively.

DISCUSSION

Using a cobalt indicator solution and an XRF device, we screened 131 swatches of leather from companies that produce leather furniture for the presence of cobalt. In a subsample of 12 leather swatches selected for ICPMS analysis, 7 samples contained cobalt at 190 ppm or above, with the highest being 1100 ppm. Thus, the prevalence of swatches containing cobalt at levels in excess of 190 ppm was at least 5% ($n = 7$, total $n = 131$) in our study. This finding is surprisingly high and shows that leather products may indeed be a hitherto unrevealed source of cobalt sensitization. The observation is important for clinicians who see patients with allergic cobalt dermatitis.⁹ Recent clinical and epidemiological data from Italy showed that workers engaged in textile and leather manufacturing had significantly higher rates of cobalt allergy than controls.¹¹ In a follow-up study, the same group showed that cobalt mono-sensitization was significantly associated with having textile and leather work.¹² In further support of cobalt in leather being a clinical issue, the prevalence of cobalt allergy has consistently been higher in patients with foot dermatitis.^{13,14} Moreover, cobalt was found in 21 shoes randomly analyzed for their metal content in Sweden (range, <0.3–16 ppm).¹⁵ Allegedly, the use of pre-metallized acid dyes, in which for example cobalt is used to form coordination complexes with dye molecules, has increased in recent years.¹⁶ Collectively, these data show that cobalt is found in leather and results in elicit allergy and dermatitis. This is particularly evident as the elicitation threshold to cobalt is low, and cobalt is a potent allergen.¹⁷

The cobalt indicator solution appeared to be a poor screening test for cobalt in leather products. Hence, only 1 of the 5 swatches that tested positive in the cobalt spot test solution contained greater than 100 ppm cobalt. The 6 swatches with a positive screen by XRF

all tested negative to cobalt solution, including a swatch with greater than 1000 ppm cobalt. Cobalt indicator solution has been used effectively to screen for cobalt release in metallic items^{10,18,19}; however, the solution often begins to assume the color of the leather swatch which may render positive test results unreliable in leathers of red, orange, or brown (Fig. 1). This cobalt indicator solution was however

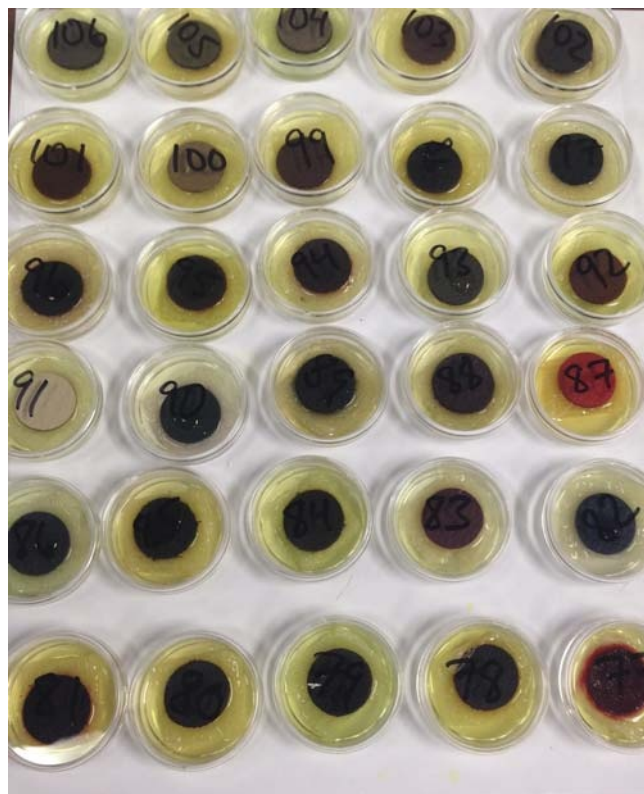


Figure 1. Leather samples undergoing cobalt screening with a cobalt indicator solution. Note evident discoloration of the yellow cobalt indicator solution by many samples including sample 104 which appears green, sample 90 which appears colorless, and sample 77 which appears dark red.

used successfully to screen for cobalt in a leather product in 1 patient⁹; nonetheless, our results provide good evidence that cobalt indicator solution is an unreliable screening test for cobalt in consumer leather products. This echoes our clinical experience because we have generally been unable to use the cobalt indicator solution to find cobalt releasing leather items from dermatitis patients with cobalt patch test reactivity thought to be clinically relevant.

X-ray fluorescence technology bombards a sample with high energy x-rays and analyzes spectra secondarily emitted from the sample. Each element has characteristic emission spectra. Some XRF devices are handheld and generally retail around US \$30,000, though refurbished devices may be purchased for less. In our tested subset, XRF screening in fundamental parameter mode with results greater than 5% cobalt appeared to be a nondestructive, rapid, and sensitive and specific methodology for detecting high concentrations of cobalt in leather. Of 6 swatches with an XRF result greater than 5% cobalt, all contained greater than 300 ppm of cobalt as assessed by ICPMS. In higher concentrations, the XRF results were linear when plotted against ICPMS results (Fig. 2). X-ray fluorescence screening detected cobalt at 3.36% in a swatch containing 190 ppm by ICPMS but did not detect cobalt at 31 ppm in the random negative swatch. These findings suggest that although XRF may be viable for screening high concentrations, it may not detect cobalt in products that may however contain sufficient cobalt to elicit ACD. Furthermore, it may not be

predictive of cobalt release in use. Further investigation of XRF cobalt screening is warranted, including using XRF to screen patients' products implicated in cobalt ACD. The authors caution that random leather samples were analyzed, not leather known to elicit dermatitis. Leather content does not inevitably entail cobalt release. As with many metal-containing consumer products, high allergen content does not necessarily predict clinically significant allergen release and more investigation into cobalt content is warranted. X-ray fluorescence, cobalt indicator solution, and other methods should be used to test samples known to elicit dermatitis.

Patients with allergic metal dermatitis frequently react to several metal allergens at the same time. Understanding the significance and relevance of multiple positive patch tests to metals has long been difficult but is pertinent to those who interpret patch test readings. Previously, it had been hypothesized that cross-sensitivity or cross-reactivity may explain multiple positive patch test reactions to metals. However, clinical and laboratory investigations do not support cross-reactivity between nickel, cobalt, and chromium.^{20,21} For example, tests in guinea pigs failed to elicit cross-reactivity between nickel and cobalt.²⁰ In another study, oral nickel challenge in recently patch tested patients elicited flare ups at the sites of nickel and palladium patch testing, but did not significantly elicit a flare at the site of cobalt patch testing.²¹ Based on the above, the best explanation for multiple metal allergies in patients has been metal allergen coexposure. Thus, concomitant metal exposures have historically been associated with occupational exposures to, for example, cobalt and chromium in cement workers⁵ and cobalt and nickel in hard metal workers.^{5,22} However, we here will discuss recent developments which may question these previously relevant co-exposures.

First, widespread coexposure to chromium and cobalt in cements must have decreased due to the Chromium (VI) Directive (2003/53/EC) limiting the level of soluble chromium to 2 ppm in cements in the European Union. This major historical source of occupational coexposure to chromium and cobalt in Europe is therefore much less significant than in previous decades. Second, the rising market price of cobalt has led to cobalt extraction from cobalt-containing nickel ores, and concomitant exposure due to cobalt contamination is likely much lower than previously.² Notably, although cobalt may still be found with nickel in jewelry, large studies of earrings, fashion accessories, and belts in the United States, Europe, Korea, China, and Thailand found very frequent nickel release (29–56%) and very infrequent cobalt release (0.007–2%).^{18,19,23–26} Third, although reliable contemporary information concerning leather tanning agents and dyes is not present in the medical literature, it is well known that chromium has long been used extensively in the tanning/preserving of leather. However, there are significant social and environmental sequelae of irresponsible leather chromium tanning and manufacturing in developing countries, notably in India²⁷ and Uganda.²⁸ Also, a regulation of chromium in leather was recently introduced in the European Union.²⁹ We suspect that chromium, but not cobalt is affected by

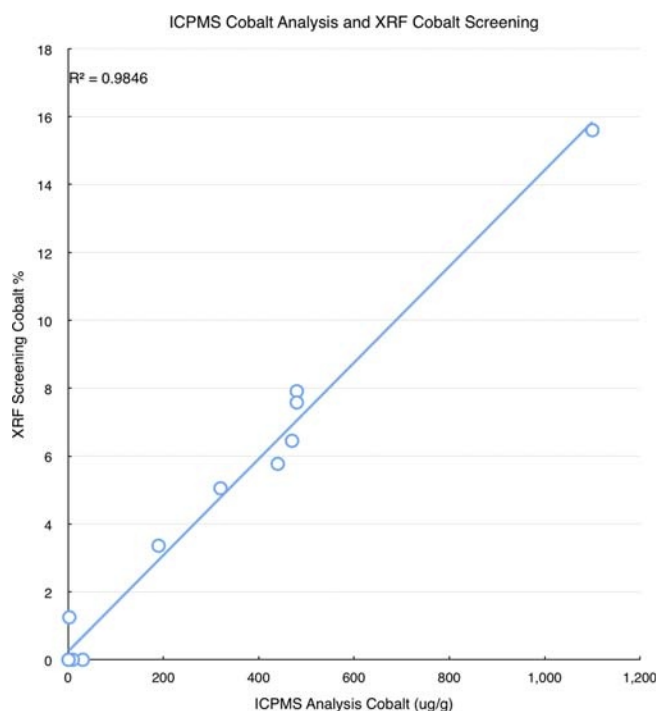


Figure 2. Cobalt percentage assessed by XRF spectrometry in fundamental parameters mode plotted against gold-standard ICPMS cobalt analysis.

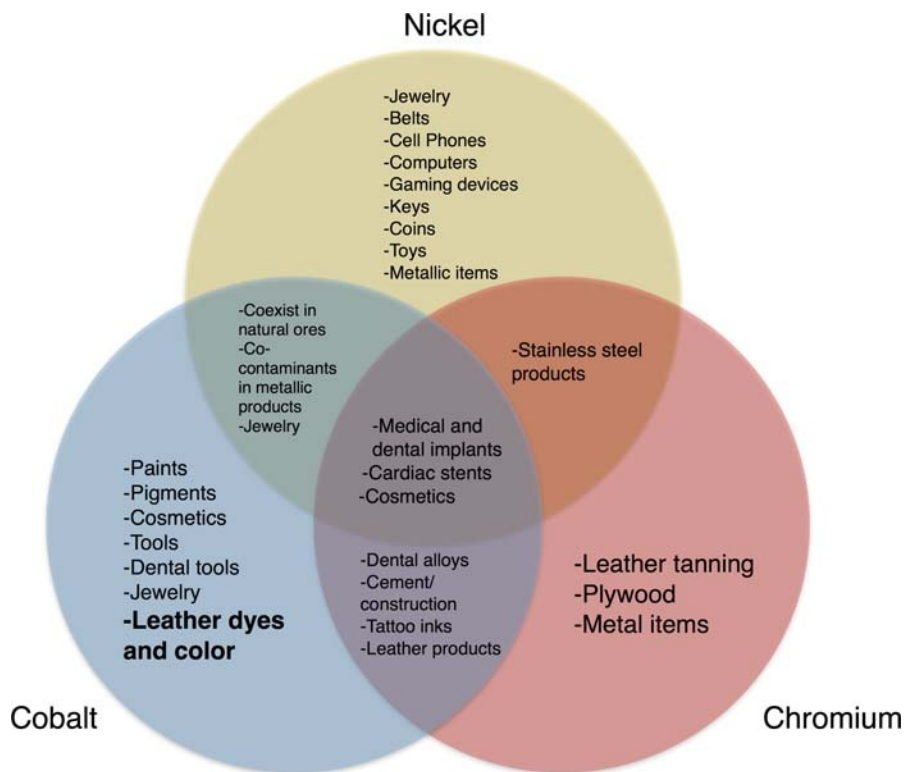


Figure 3. A set diagram illustrating common exposure sources for single and multiple metal allergens.

this pressure as cobalt is not used in the tanning process, but only for dyeing purposes in premetallized dyes.³⁰ Due to superior wash and light fastness, premetallized dyes are increasingly used instead of traditional direct dyes and acid dyes in consumer leather goods.¹⁶

CONCLUDING REMARKS

Clinicians who see patients with concomitant nickel and cobalt allergy or concomitant cobalt and chromium allergy may previously have been justified in attributing this to coexposure, but may erroneously attribute this to coexposure in a contemporary setting. We authors now propose that patients with multiple metal allergies are more likely than ever before to have different exposures explaining their allergies. In the 1960s, Fregert and Rorsman⁵ elegantly—and accurately in their context—argued that patients with contact allergy to multiple metals could be explained by coexposure and used set diagrams to illustrate the frequency of co-positivity in patch test patients. We here use a similar, but updated set diagram to illustrate sources of exposure to common metal allergens and to highlight the complexity of the contemporary landscape of exposure sources. (Fig. 3) This is not an academic distinction. Allergen avoidance is the definitive treatment for allergic contact dermatitis—correct identification of relevant allergen exposures is paramount. Positive cobalt patch tests are difficult to interpret and clinicians should not automatically attribute multiple metal patch test positive reactions to coexposure. In summary, cobalt is found in

leather in high concentrations, and relevant exposure sources of metal allergens require continued investigation.

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