

Electrochemical Screening Spot Test Method for Detection of Nickel and Cobalt Ion Release From Metal Surfaces

Morten S. Jellesen, PhD,* Christian Bang Olsen, MSc,* Samine Ruff, MD,† Radoslaw Spiewak, PhD,‡ Dathan Hamann, MD,§ Carsten R. Hamann, MD,† Ian R. White, PhD,|| Jeanne D. Johansen, MD, PhD,† and Jacob Pontoppidan Thyssen, MD, PhD†

Background: Present screening methods to rapidly detect release of nickel and cobalt ions from metallic surfaces involve colorimetric dimethylglyoxime (DMG)- and disodium-1-nitroso-2-naphthol-3,6-disulfonate-based spot tests with a cotton bud. There is a risk of false-negative test reactions because test outcomes are dependent on the pressure, area, and duration of surface wiping.

Objective: The aim of the study was to develop a miniaturized electrochemical device that uses a voltage to accelerate nickel and cobalt release from the tested item and perform an initial validation.

Methods and Results: A device was built in plastic, and its performance was investigated using 0.5 mL of test solutions of, respectively, DMG and disodium-1-nitroso-2-naphthol-3,6-disulfonate. Cotton buds that had been wetted in test solution were pressed against different metal surfaces at various voltages (0–9 V) and a range of test durations (0–120 seconds). Duplicate testing for nickel and cobalt release was also performed on a sample of 163 jewelry items.

Conclusions: This novel electrochemical device makes it possible to perform nickel and cobalt ion release testing without rubbing, thereby reducing interindividual differences in testing technique. The nickel testing with the device seemed to be superior to conventional DMG spot testing.

Metal allergy is prevalent worldwide, predominately because of prolonged and excessive skin contact with metallic items and leather products that release allergenic metal ions. In particular, nickel, cobalt, and chromium are common culprit allergens because they result in significant morbidity in both children and adults.^{1,2} For this reason, colorimetric spot tests have been developed to rapidly screen for metal ion release that exceeds the threshold levels for

elicitation of allergic contact dermatitis.^{3–5} These spot tests allow patients to avoid skin contact with metal ion-releasing items that will result in allergic contact dermatitis, and clinicians can perform rapid and inexpensive exposure analyses of metallic items brought in by their patients.

The nickel spot test, which is based on dimethylglyoxime (DMG), is used both by dermatologists and by consumers and is considered a reliable test method.⁴ The test is positive when a white cotton bud applicator becomes pink after it has been rubbed against a metal surface that releases nickel in concentrations of greater than 0.5 µg nickel/cm² per week. Although the specificity of the DMG spot test is high (98%), the sensitivity is only moderate (59%).⁴ Nickel-allergic individuals can therefore rely on positive test results, because the metal surface under investigation indeed releases nickel ions in amounts that may elicit allergic nickel dermatitis after prolonged skin contact. However, negative test results do not necessarily ensure absence of excessive nickel release and may therefore result in accidental allergic nickel dermatitis or even primary sensitization.

The recent introduction of a cobalt spot test gave dermatologists and scientists a novel tool to screen for cobalt ion release from metal surfaces.^{3,6} However, based on our experience, it is sometimes difficult to reliably detect positive test reactions in a real-life setting because the color change from yellow to orange can be difficult to determine or be masked by dirt, rust, or other particulate matter

From the *Department of Mechanical Engineering, Technical University of Denmark, Kongens Lyngby; †National Allergy Research Centre, Department of Dermatology and Allergy, Herlev-Gentofte Hospital, University of Copenhagen, Hellerup, Denmark; ‡Department of Experimental Dermatology and Cosmetology, Jagiellonian University Medical College, Krakow, Poland; §Division of Dermatology, Department of Internal Medicine, The Ohio State University, Columbus; and ||St John's Institute of Dermatology, Guy's Hospital, London.

Address reprint requests to Jacob Pontoppidan Thyssen, MD, PhD, National Allergy Research Centre, Department of Dermatology and Allergy, Herlev-Gentofte Hospital, University of Copenhagen, Kildegaardsvej 28, DK-2900 Hellerup, Denmark. E-mail: jacob.p.thyssen@regionh.dk.

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Figure 1. A photograph of the electrochemical device with an ampoule inserted and another ampoule lying next to the device.

on the item of interest. One example was a baker with cobalt allergy who was recently treated in our clinic because of allergic contact dermatitis in the interdigital space.⁷ Metallic trays were suspected of releasing cobalt, but conventional cobalt spot testing with cotton sticks could not confirm cobalt release. However, a napkin soaked in cobalt spot test solution was then pressured against a tray for minutes and confirmed cobalt release.

Based on our experience, nickel and cobalt spot testing may show interindividual testing differences, and the cotton bud-based tests are not always sensitive enough. There was therefore a need to develop a new device for spot testing for nickel and cobalt with improved sensitivity and decreased risk of interindividual subjective differences (Fig. 1). To this end, we developed an electrochemical device based on anodic dissolution of nickel and cobalt found in the surface of examined products. In this article, we describe this electrochemical colorimetric spot test performance along with test results from x-ray fluorescence (XRF) analysis.

MATERIALS AND METHODS

Theoretical Considerations

A constant voltage can be applied between the tested part connected as anode and an inert metallic part as cathode through a cotton swab wetted with colorimetric test solution. Faraday law, Equation 1, gives a quantitative relationship between the flow of electricity and the amount of metal dissolution.

$$m = \frac{I \times M \times t}{n \times F} \quad 1$$

In Faraday law, Equation 1, m is the mass of metal dissolution over time (t), and I is the anodic current, n is the number of electrons, and F is Faraday constant 96485 (coulomb per mole). The anodic current will accelerate metal release and should in theory result in faster and more sensitive detection of nickel and cobalt as compared with standard colorimetric identification methods.

Metals

The following materials were used for nickel release studies: aluminum, stainless steel AISI 316, and a guitar string (nickel-plated steel 250R; Fender). In addition, nickel-plated stainless steel, electroplated nickel, electroless nickel plating (deposited by chemical means only), and electroplated samples were investigated (all samples used for teaching purposes at the Technical University of Denmark, Lyngby, Denmark). For cobalt release investigations, different custom-made cobalt-containing metal discs of the same batch as used by Julander et al⁶ were used. The authors had shown that these discs released cobalt in artificial sweat and elicited positive cobalt patch test reactions in cobalt-allergic patients.^{3,8} The alloys are used as raw material in the manufacturing of wear parts for hard metal tools (Sandvik AB, Sandviken, Sweden) and as dental alloys (Dentaurum, Ispringen, Germany).

Electrochemical Device

All experiments were carried out with a device as shown in Figure 1. In total, 2 prototypes were built from polymer materials (SPT Villecon A/S, Hillerød, Denmark) and used throughout the validation study. The cathodic part of the electrical contact was a flexible metal strip ($\text{CuNi}_{18}\text{Zn}_{20}$) designed to grip into the cotton swab inserted in the ampoule cylinder. The electrical contact for the anode was established via a flexible contact (a 2-part spring probe made of phosphor bronze supplied by RS-online, Denmark). The flexibility ensured that electrical contact was established once the cotton swab was pressed against the metal to be analyzed. With this setup, the effects of voltage and analysis time were investigated with a constant load between device and test piece of 700 g. The damage on tested metal surfaces was investigated using a light optical microscope ZEISS Axio Lab A1 (Zeiss, Oberkochen, Germany). Polymer ampoules (James Alexander Corporation, Frelinghuysen, NJ) containing 0.5 mL 0.9 wt% NaCl and 3.8 wt% DMG in a 25/75 vol% mixture of water/ethanol in an internal glass cylinder were used for the nickel experiments, and ampoules (James Alexander Corporation) containing 0.1 wt% oxalic acid, 0.02 wt% nitroso-R salt, and 5.0 wt % sodium acetate (disodium-1-nitroso-2-naphthol-3,6-disulfonate) in deionized water were used for the cobalt experiments. All chemicals used were supplied by Sigma-Aldrich Chemie GmbH, Darmstadt, Germany. The ampoules were mounted on the drawer part of the device and pushed into the housing (Fig. 2). Once the ampoule internal glass wall was pressed until breakage, the test solutions wetted the cotton swab to be pressed against the metal item of interest.

The applied voltage was supplied by 2 serial connected 1.5 V LR44 batteries (Renata batteries; Renata SA, Switzerland) inside the drawer compartment or by a power supply (EA-PS 2032-025) or a potentiostat (ACM Instrument Gill AC, Cumbria, United Kingdom) when performing leakage current investigations.

Colorimetric Test Solutions

For the conventional nickel spot test experiments, a cotton stick was wetted with 2 drops of 1 wt% DMG dissolved in ethanol and 2 drops

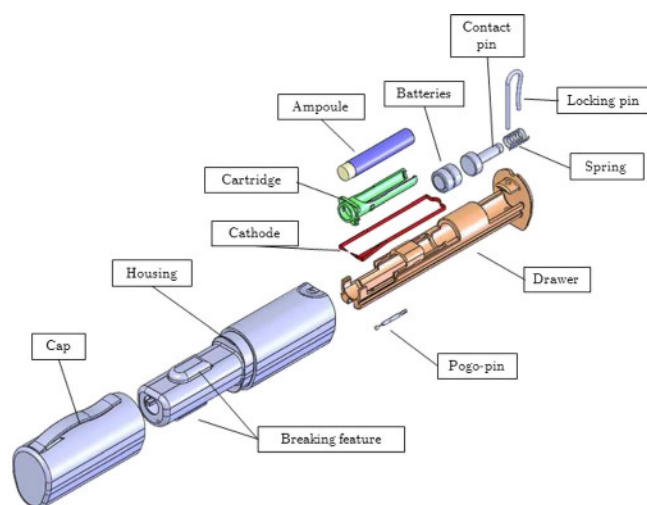


Figure 2. The miniaturized electrochemical device including batteries for voltage supply, electrical contacts, and ampoule with colorimetric solution inside a glass cylinder and cotton swab for color detection.

of 5 M of ammonia solution (Sigma-Aldrich Chemie GmbH, Darmstadt, Germany). For the conventional cobalt spot testing, 4 drops of a solution containing 0.1 wt% oxalic acid, 0.02 wt% nitroso-R salt, and 5.0 wt% sodium acetate (disodium-1-nitroso-2-naphthol-3,6-disulfonate) in deionized water were used. The wetted cotton sticks were then rubbed against the jewellery item for 20 seconds.

Jewelry for Validation

For further validation of the device performance, 163 pieces of jewellery were analyzed with the electrochemical device and compared with the outcome of conventional cobalt and nickel spot tests. All jewellery items had been XRF analyzed before this study.⁹ All tested samples contained nickel from 0.6 wt% to 75.7 wt% and were bought in United Kingdom, Poland, and Japan. For the nickel validation, 163 jewelry pieces with nickel were tested, and for the cobalt validation, 26 pieces were tested. All tests were conducted for 20 seconds with 0.5 mL of the respective spot test solutions. All tests using the conventional cotton stick method were conducted for 20 seconds as described previously.

RESULTS

Nickel

Investigation of Time and Constant Voltage Settings for Electrochemical Device

The effect of voltage and testing time on the release of nickel was investigated. Because the voltage was increased greater than 3 V, no additional effect on color formation was observed (Fig. 3).



Figure 3. Color change of the ampoule tip as a function of voltage applied after testing nickel-plated stainless steel for 120 seconds.

The effect of testing time was investigated by increasing the duration of testing from 0 to 120 seconds in steps of 10 seconds at a constant voltage of 3 V (Fig. 4). After each experiment, the color of the swab surface was photographed, and light optical microscopy was performed on the metal surface in contact with the swab. There was a clear coloration of the cotton swab with a testing time of more than 10 seconds. Light optical microscopy showed signs of degradation of the tested metal surface when testing time exceeded 45 seconds. After 60 seconds of testing, the corrosion degradation was naked eye visible.

Figure 5 shows the resulting current at a constant voltage level of 3 V for various metal samples for 120 seconds. The current measured was within 1 to 3 mA for all samples. The current levels are proportional to the total ion release and/or oxidation processes taking place. It is important to mention that for stainless steel the total current contribution is arising from oxidation of Ni, as well as Cr and Fe. Clear red coloration from DMG nickel complex formation was seen on all samples except for the reference sample (pure aluminum). On the stainless steel (AISI 316) and nickel-plated guitar string, a brownish discoloration was seen, presumably due to the high content of iron.

Cobalt

Cobalt Detection With Electrochemical Device

The coloration of cotton swab after cobalt testing various cobalt-containing items with the electrochemical device (120 seconds and a voltage of 3 V) is given in Figure 6.

All tested items, except G and H, resulted in an evident red coloration. Sample H was a control sample consisting of pure aluminum and showed no reddish coloration. Sample G had 15 wt% cobalt content in the base alloy but also a coating consisting of layers of TiCN, Al₂O₃, and TiN, which prevented the base alloy from releasing cobalt, whereas H was the negative control (0 wt% Co).

Validation of Device by Jewelry Testing

In total, 163 and 26 pieces of jewelry were selected based on previous XRF analysis and, in this study, examined with the conventional nickel and cobalt spot test, respectively, as well as the electrochemical device. The same surface was analyzed at different areas for conventional spot test and the electrochemical device. Of 163 nickel-containing jewellery items, 113 (69.3%) came out positive when testing was performed with the electrochemical device, whereas 88 (54.0%) of 163 came out positive when using the conventional DMG test. A similar difference was detected in jewelry from all 3 countries. Four jewelry pieces were positive when using the DMG test but negative when using the electrochemical device, whereas 25 pieces that were negative when using the DMG test were positive when using the electrochemical device. In



Figure 4. Color change of the ampoule tip as a function of time after testing of nickel-plated stainless steel at 3 V.

particular, in items with low nickel concentrations according to the XRF analysis, the miniaturized electrochemical device test showed more positive test outcomes than conventional DMG spot testing (Fig. 7). A similar validation was performed for the cobalt spot test assays. For cobalt, 14 (53.8%) of 26 pieces were positive when using the conventional cobalt spot test, whereas only 9 (34.6%) of 26 were positive when testing was performed with the electrochemical device. Conventional cobalt spot testing identified 6 pieces with positive test reactions where testing with the electrochemical testing gave negative test results. However, only 1 piece was negative when tested with conventional cobalt spot test but came out positive with the electrochemical device (Fig. 8).

DISCUSSION

Main Findings

We have developed and validated an electrochemical device, which allowed anodic dissolution of the metal under investigation, and showed that it represented a more reliable and sensitive test method for detection of nickel release compared with the traditional DMG test method. Although the test also accelerated cobalt release and led to positive test results, testing of a sample of jewelry that contained cobalt showed that the electrochemical test was inferior to the traditional cobalt spot test. Although the test per se is destructive, metal degradation after testing for 20 seconds at 3 V could be seen only by microscopic analysis and was not visible to the naked eye. Moreover, the device minimizes possibly hazardous skin contact with the colorimetric chemicals and is odorless when testing

for nickel release because ammonia is not used. Typically, ammonia is added to DMG to ensure alkaline pH for improved color change; however, when using the electrochemical device, we found that ammonia is not needed for a distinct color change to happen. By using the electrochemical device, it is possible to test without the vigorous rubbing needed for conventional spot tests, potentially making test results less prone to interindividual and intraindividual testing differences.

Interpretations

The described electrochemical device represents a well-examined starting point for future improvement and validation. The higher proportion of positive test reactions when using the electrochemical device compared with the conventional DMG test is explained by the increased dissolution of nickel ions present on the surface due to the voltage and current applied as described in Faraday law. Moreover, the electrochemical device showed enhanced cobalt release from dental alloys as compared with conventional cobalt spot testing. This could be explained by dissolution of a passivating chromium oxide layer caused by the electrochemical potential that in turn will allow cobalt release from the bulk CoCr alloy. This shows how the electrochemical device is able to detect ion release from a bulk metal alloy through porosities in a coating, which can be relevant for skin contact when handling corroded metal samples. Surprisingly, the device was inferior to the conventional cobalt spot test when a random sample of cobalt-containing jewellery was examined. The conductivity of the cobalt spot test solution is higher than the DMG test solution used for nickel spot testing with the electrochemical device. However, the color difference from negative to positive was not as

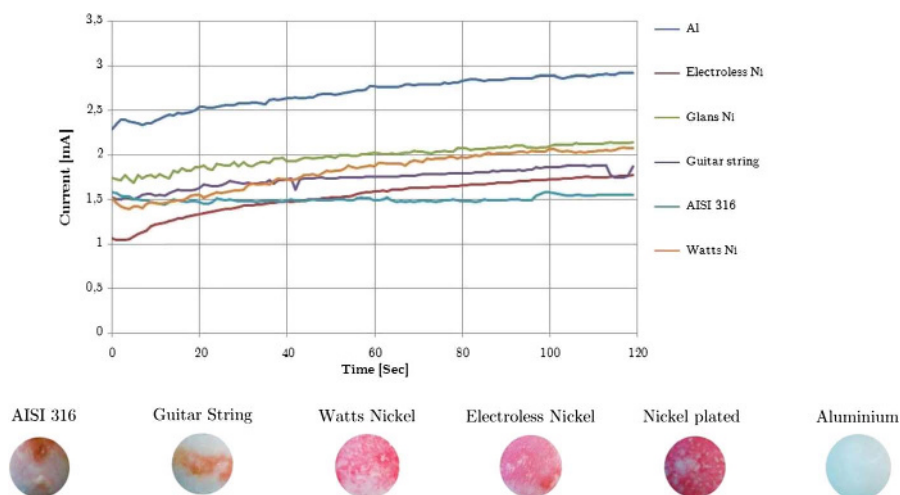


Figure 5. Current responses for various items shown as a function of time with 3 V applied and resulting color formation photographed after 120 seconds.

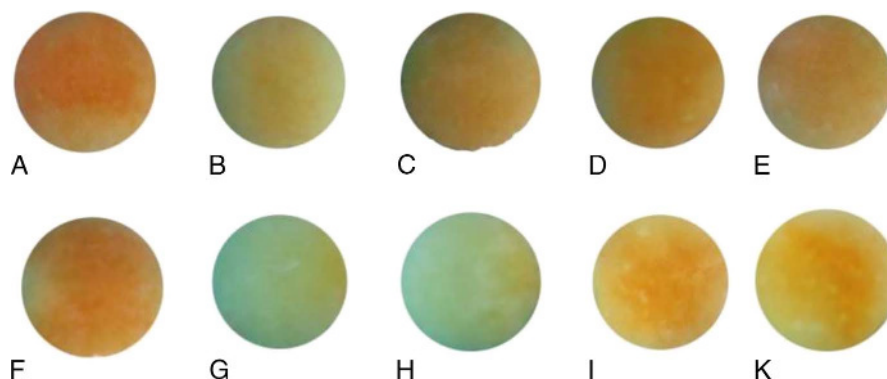


Figure 6. Cotton swab of the ampoule tip on electrochemical device after testing cobalt at 3 V for 20 seconds. The metal samples tested were as follows: A, 6.0 wt% Co; B, 6.0 wt% Co; TiCN+ Al₂O₃; C, 6.0 wt% Co TiN; D, 7.5 wt% Co; E, 7.5 wt% Co; TiCN+ Al₂O₃+ TiN; F, 15.0 wt% Co; G, 15.0 wt% Co TiCN+ Al₂O₃+ TiN; H, 0 wt% Co (aluminum control disc); I, 64.6 wt% Co dental alloy; K, 33.0 wt% Co dental alloy.

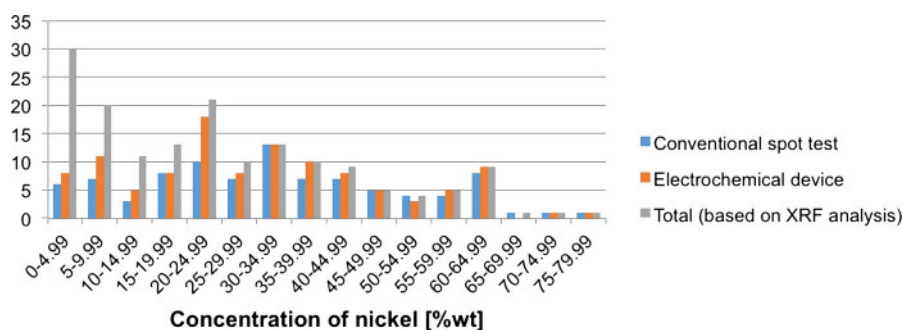


Figure 7. The XRF analysis and positive tests of a conventional DMG-based nickel spot test and the new electrochemical device test against 163 pieces of jewelry with known nickel content. The column named “total” indicates the number of items tested within the given nickel concentration limits based on previous XRF testing.

apparent for the cobalt test when compared with the nickel test. We suspect that the less evident color difference is the main reason for the reduced sensitivity of the electrochemical cobalt spot test. This was especially seen when testing earrings, where we tested millimeter-sized piercing posts. The electrochemical device only showed a thin color line, corresponding to the thin posts, which was difficult to appreciate with the naked eye (Fig. 9). Many cobalt-containing jewelry pieces were negative to both the electrochemical and the conventional

cobalt spot tests, which can be explained by the fact that some alloys contain the element without releasing the metal ion from the surface under investigation.

Limitations

The electrochemical device had certain limitations. To accelerate metal release by the use of an applied anodic current, the item of interest needs to be electrically conducting and hence be metallic. This

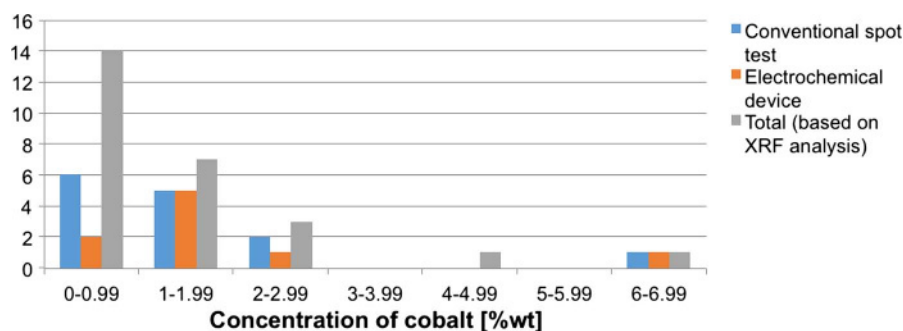


Figure 8. The XRF analysis and positive outcomes of a conventional cobalt spot test and the new electrochemical device test against 26 pieces of jewelry with known cobalt content. The column named “total” indicates the number of items tested within the given cobalt concentration limits based on previous XRF testing.



Figure 9. Comparison of an electrochemical device cotton part resulting in a positive nickel test reaction (top left) and a conventional DMG-negative test reaction (top right) when testing the same earring stick. Electrochemical device testing for cobalt showed a slight positive test reaction, which is, however, difficult to see with the naked eye (bottom left), whereas conventional cobalt spot testing clearly indicated a positive test reaction (bottom right).

means that the test method is useless on nonmetallic items, for example, leather. Moreover, the colorimetric solution used has to give an evident positive color reaction, which may be difficult if a small surface area such as a piercing post is examined. Although the increased sensitivity of nickel detection associated with the electrochemical device is expected to be clinically relevant, there is a theoretical risk that we enhance nickel release beyond clinical relevance. However, avoidance of nickel release is important in nickel-allergic individuals, and the low sensitivity of the conventional

DMG test justifies this. Future validation against the EN 1811 reference test for compliance of the European nickel regulation would be meaningful. We observed jewelry pieces that were positive with only 1 of the 2 tests, respectively, hereby indicating that neither of the tests was able to completely detect ion release.

CONCLUSIONS

This novel electrochemical device makes it possible to perform metal ion release tests without rubbing, thereby limiting interindividual differences in testing technique. In nickel testing, the device seemed to be more sensitive than conventional DMG spot testing.

REFERENCES

1. Uter W, Lares Filon F, Rui F, et al. ESSCA results with nickel, cobalt and chromium, 2009–2012. *Contact Dermatitis* 2016;75(2):117–121.
2. Zug KA, McGinley-Smith D, Warshaw EM, et al. Contact allergy in children referred for patch testing: North American Contact Dermatitis Group data, 2001–2004. *Arch Dermatol* 2008;144(10):1329–1336.
3. Thyssen JP, Menné T, Johansen JD, et al. A spot test for detection of cobalt release—early experience and findings. *Contact Dermatitis* 2010;63(2):63–69.
4. Thyssen JP, Skare L, Lundgren L, et al. Sensitivity and specificity of the nickel spot (dimethylglyoxime) test. *Contact Dermatitis* 2010;62(5):279–288.
5. Bregnbak D, Johansen JD, Jellesen MS, et al. Chromium(VI) release from leather and metals can be detected with a diphenylcarbazine spot test. *Contact Dermatitis* 2015;73(5):281–288.
6. Julander A, Hindsen M, Skare L, et al. Cobalt containing alloys and their ability to release cobalt and cause dermatitis. *Contact Dermatitis* 2009;60(3):165–170.
7. Bregnbak D, Zachariae C, Thyssen JP. Occupational exposure to metallic cobalt in a baker. *Contact Dermatitis* 2015;72(2):118–119.
8. Thyssen JP, Jellesen MS, Menné T, et al. Cobalt release from inexpensive jewellery: has the use of cobalt replaced nickel following regulatory intervention? *Contact Dermatitis* 2010;63:70–76.
9. Hamann D, Thyssen JP, Hamann CR, et al. Jewellery: alloy composition and release of nickel, cobalt and lead assessed with the EU synthetic sweat method. *Contact Dermatitis* 2015;73(4):231–238.