Cobalt

Joseph F. Fowler, Jr, MD

Cobalt has been a recognized allergen capable of causing contact dermatitis for decades. Why, therefore, has it been named 2016 "Allergen of the Year"? Simply put, new information has come to light in the last few years regarding potential sources of exposure to this metallic substance. In addition to reviewing some background on our previous understanding of cobalt exposures, this article will highlight the recently recognized need to consider leather as a major site of cobalt and the visual cues suggesting the presence of cobalt in jewelry. In addition, a chemical spot test for cobalt now allows us to better identify its presence in suspect materials.

Metals in general are the most common causes of allergic contact dermatitis (ACD). Nickel, gold, chromium, palladium, and cobalt all rank highly in lists of positive patch test reactions from studies around the world.[1,2] Although cobalt has always been recognized as a common allergen, several new features of cobalt allergy have recently been elucidated (Table 1).

Cobalt (atomic number 27) is a shiny gray, magnetic, brittle metal, which in the earth, is often found with nickel and copper, with almost half coming from nickel ores. It is produced primarily in Australia, Zaire, Canada, China, Congo, Morocco, and Zambia.[3] It is the first element of group 9 in the periodic table, accompanied by rhodium, iridium, and meitnerium. Cobalt was discovered by Georg Brandt in the 1730s in Sweden. The name comes from the German word *kobald* meaning *goblin* or evil spirit.[4]

The metal is commonly used as an alloy in steel that requires high strength and endurance, such as for tools, vehicle engines, magnets, and orthopedic and other medical devices. It is also found in a number of other metal items; in ceramics, cement, and other construction materials; in some plastics; in leather tanning; and in a variety of other items.

EPIDEMIOLOGY OF COBALT ALLERGY

Allergic cobalt dermatitis was, in the past, thought to be more common in Europe than in the United States. This concept probably developed because, for many years, the North American Contact Dermatitis Group did not routinely test with cobalt. However, more recent data show the rates of patch test reactions in North America to be similar to those in European studies.[2,5–7]

Uter and colleagues[7] reported that 5.23% of more than 185,000 patients had a positive patch test to cobalt (cobalt chloride hexahydrate 1% pet.). Women were approximately twice as likely as men to be allergic, and there was a 20% higher rate in atopics. This exhaustive review documented many sources of cobalt exposure. The most recent North American Contact Dermatitis Group data showed that 7.3% of 4231 patients reacted to cobalt.[2]

Another fallacy was that cobalt allergy almost always occurs in concert with nickel allergy. In fact, this is not true, although some metal objects that contain cobalt may also contain nickel. North American Contact Dermatitis Group data indicated that 40% of patients positive to cobalt were negative to nickel (unpublished data). Edman[8] similarly found 23 (32%) of 73 cobalt-positive patients not allergic to nickel.

Kranke and Aberer[9] analyzed positive patch test reactions to metal in 11,516 patients. The findings were that 79% of cobalt-allergic patients reacted to nickel, 42% reacted to palladium, and 15% reacted to chromate.

Rystedt and Fischer[10] concluded that nickel sensitivity, in combination with irritant eczema, induces a higher risk of developing cobalt allergy. It is possible that a preexistent nickel allergy increases the risk of developing cobalt allergy because of the high frequency of hand eczema among nickel-sensitive individuals. All the hard-metal workers in Rystedt and Fischer's study with simultaneous nickel and cobalt sensitivity had severe dermatitis of the hands. Eight hundred fifty-three hard-metal workers were examined and patch tested. Nickel sensitivity was found in 2 men and 38 women. In 25% of the cases, nickel-sensitive individuals developed cobalt allergy, compared with 5% in the total population investigated.

The relationship of cobalt and nickel allergy, in an animal model, was studied by Lammintausta and colleagues.[11] An increase in positive patch tests to either metal was found in guinea pigs sensitized to both metals as compared with those sensitized with only one. For example, 4 of 13 sensitized only to nickel later had positive patch tests to nickel, whereas 7 of 13 that were first sensitized to cobalt and then to nickel later reacted to nickel.

SOURCES OF COBALT EXPOSURE

Cobalt in Leather

Although chromium has classically been associated with dermatitis due to leather goods, cobalt has recently been shown to be

From the University of Louisville, KY.

Address reprint requests to Joseph F. Fowler, Jr, MD, 501 S 2nd St, Louisville, KY 40202. E-mail: fowlerjoe@msn.com.

The author has no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000154

TABLE 1. New Findings in Cobalt Allergy

-Exposure to cobalt from leather
-Characteristics of jewelry made from cobalt
-Cobalt as an allergen in implanted devices
-Poral irritant patch test response to cobalt

another cause. A patient with chronic ACD reported symptoms after using a leather sofa and was positive on patch testing to cobalt but not chromium. No other exposure source was found, and the leather from the sofa was found to contain cobalt.[12] This finding led to a search for more cases of leather as a cause of ACD from cobalt. Researchers identified 183 patients positive to cobalt but not chromium. Leather was the single most likely exposure causing ACD.[13] This research was performed in Scandinavia, but presumably, leather goods from other countries may be expected to also contain cobalt. Leather exposure now must be considered an important source of cobalt allergy.

Cobalt in Jewelry

Perryman and Fowler[14] tested 28 patients with known cobalt allergy to a jewelry alloy (containing platinum and cobalt). The manufacturer felt the alloy would bind the cobalt tightly and thus be "hypoallergenic." In fact, only five (18%) reacted to a patch test with a disc of the alloy applied for 7 to 8 days continuously. This novel alloy is felt likely to be tolerated by most cobalt-allergic patients.

It has been suggested that jewelry containing cobalt will tend to have a dark silver appearance, in contrast to the more shiny appearance of jewelry without cobalt.[15] By appearance alone, therefore, a jewelry buyer may be able to determine whether it is likely that a piece contains cobalt. In addition, a spot test for cobalt has been developed by Thyssen and colleagues[16] that is similar in concept to the dimethylglyoxime spot test for nickel. Cobalt may be detected (in the presence of 1000 times as much nickel) by using a 1% aqueous solution of 2-nitroso-1-naphthol-4-sulfonic acid at pH 7 to 8. Instead of the pink color given by the nickel test, the cobalt spot test gives a yellow-orange color in the presence of cobalt.

A report from Thailand, which has no legislative controls regarding nickel or cobalt content of jewelry, found 37% of 551 jewelry items positive on the cobalt spot test. More expensive items (>US $20) were less likely to release cobalt, whereas items that were gray, brass, or pink-gold in color commonly were positive.[17]

Cobalt in Children's Toys

Jensen and colleagues[18] tested 212 toys purchased in Denmark or the United States. None was positive on the cobalt spot test.

Cobalt in Orthopedic and Other Implanted Devices

Allergy to orthopedic implants, especially artificial hip and knee joints, has been proposed as a possible cause of both skin disease (mostly dermatitis) and problems with the implant (pain, loosening, delayed healing). [19] An illustrative case was reported from Australia of an 84-year-old woman who developed an intractable generalized dermatitis after a hip implant. The dermatitis began at the site of the implant. She had a positive cobalt patch test, and serum cobalt level was highly elevated (approximately 50-fold over normal). Within several months after replacement of the prosthesis with a titanium device, her dermatitis cleared.[20] In contrast is the case report of a patient with metal allergy who unintentionally received a total knee replacement with a cobalt chromium alloy in 1 knee and a titanium alloy in the other knee. The patient did not experience any adverse effects despite being allergic to cobalt and chromium.[21]

Other metallic implants such as vascular stents, pacemakers, and medication pumps are also of concern. The major potentially allergenic metals in these devices include cobalt, chromium, and nickel.[22] Jakobsen and colleagues[23] tested 52 removed hip components and found cobalt in 44% of the implants on x-ray analysis. Only 4 items gave a positive cobalt spot test, but this test may underestimate in vivo release.

Although there is no question that occasional patients with allergy to cobalt and/or other metals can develop allergy-related complications from implanted devices, it seems likely that the majority of people with metal allergy will tolerate these implants. Schalock and colleagues[24] suggest patch testing only those "reporting a history of metal sensitivity of a magnitude sufficient to cause concern to the patient or a healthcare provider."

Vitamin B_{12} and Cobalt Dermatitis

Cyanocobalamin is essential for life. Allergy to the cobalt contained in it is likely to be exceedingly rare but has been reported. Allergy to vitamin B_{12} (cyanocobalamin) was recognized in 2 patients shown to be sensitive to cobalt on patch testing by Rostenberg and Perkins[25] and Fisher.[26] One case of recurrent cheilitis was in a patient who was found to be allergic to cobalt and who ingested vitamin B_{12} tablets regularly. The patient later developed stomatitis of the hard palate when her dentist unwittingly made her a denture out of a cobalt alloy.

Figure 1. Cobalt spot-test mixture as developed by Dr Jacob Thyssen (photograph provided by Jacob P. Thyssen).

Figure 2. Color is more intense with increasing cobalt level (photograph provided by Jacob P. Thyssen).

Fisher[26] reported 1 cobalt-allergic patient that correlated with an allergic reaction to an injectable vitamin B_{12}. (One mL of the injection contained more than 43 mg of cobalt.) This patient had a positive patch test to both 2% aqueous solution of cobalt chloride and the vitamin B_{12} in the strengths of 100 and 1000 mg/mL. In addition, there were positive delayed scratch and intradermal reactions to the vitamin B_{12}. The patient noted that, after each injection of vitamin B_{12}, the injected area became red, tender, and pruritic but not eczematous. Oral ingestion of vitamin B_{12} produced similar flares. The patient also had an intractable hand eczema. In another case, there was a delayed allergic reaction to intradermal injection, but not to subcutaneous and intramuscular injections, of vitamin B_{12}.[27]

Anaphylaxis and urticaria have been reported in 2 patients from intramuscular B_{12} injections with positive intradermal testing to the preparations.[28]

Kalenský and Schwank[29] described hypersensitivity to cobalt in a cream used for hyperhidrosis. Patch tests were positive to cobalt, and in 1 patient, vitamin B_{12} produced positive epicutaneous and intradermal test reactions.

OTHER CAUSES OF COBALT DERMATITIS

Metals in Heavy Industry

As noted in Skog,[30] cobalt is used as a binding agent to make "hard" metal, which consists of metal carbides and a binding agent that are presented and sintered into plates. Wolfram carbide (a tungsten compound) and the carbides of titanium, nobilium, and tantalum are frequently used. Hard metal is characterized by a high degree of wear resistance. Consequently, it is used for rock drills, cutting tools, drawing, pressing and stamping tools, and mechanical parts exposed to heavy strain.

Fischer and Rystedt[31] reported that "hard metal" contains approximately 10% cobalt. Eight hundred fifty-three hard-metal workers were examined and patch tested with substances from their environment. Initial patch tests with 1% cobalt chloride showed 62 positive reactions. Allergic reactions to cobalt were reproduced in 9 men and 30 women by means of secondary serial dilution tests. Hand etching and hand grinding, often associated with hand trauma, involved the greatest risk of cobalt sensitization. Twenty-four women had cobalt allergy and also nickel allergy.

Alloys containing cobalt include alnico, duralumin, nobilium, permalloy, stellite, ticonium, and vitallium. Allergic dermatitis in workers making alloys of cobalt has been shown by patch tests to be due in some instances to the dust of metallic cobalt.[32] The dust also has been reported as causing asthma. It is believed that a dusty atmosphere containing metallic cobalt particles favors a sensitization to cobalt.

Figure 3. "Dark" metal jewelry is more likely to contain cobalt (photograph provided by Jacob P. Thyssen).

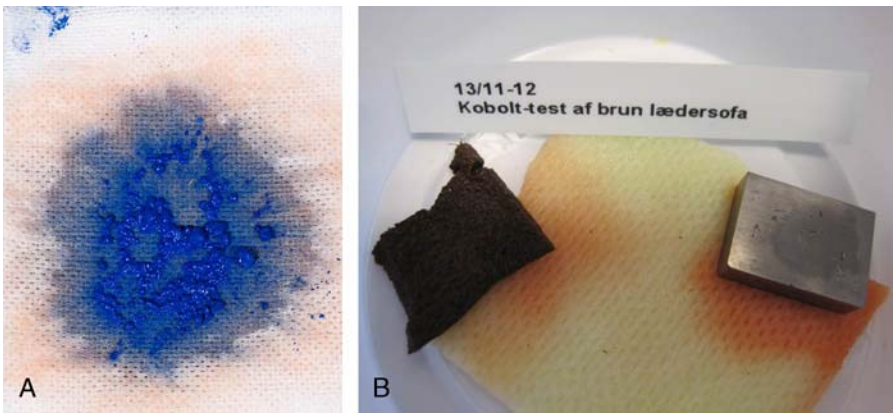

Figure 4. A, Cobalt powder (photograph provided by Jacob P. Thyssen). B, Positive cobalt spot test from sofa leather piece and from metal bar (photograph provided by Jacob P. Thyssen).

Polyester Resin and Plastics Manufacturing

Cobalt naphthenate is commonly used in the manufacture of polyester resin. Several instances of ACD were encountered in Great Britain that were attributed to workers handling cobalt naphthenate in polyester synthesis.[33]

Cobalt-containing catalysts may be used in plastics manufacturing. Allergy to cobalt in workers has been reported.[34,35] Cobalt naphthenate has been reported to cause ACD, with a negative patch test to cobalt chloride.[36]

Paints

Cobalt siccatives or driers, which are present in certain paints, have been reported as producing allergic contact sensitivity in paint factory workers.[37] These are organic cobalt naphthenate or cobalt resinate based on linseed oil.

Cement and Related Materials

Although the cobalt content of cements may be low (<0.01%), cement workers may become sensitized to cobalt.

Cobalt and chromate sensitivity may coexist in cement workers. Because these patients have positive patch test reactions to both chromate and cobalt, it is difficult to determine what role the cobalt hypersensitivity played in the production of the cement dermatitis. In a 5-year study of 449 construction workers, cobalt was the second most common allergen (20.5%) after chromate (42.1%).[38]

Camarasa[39] found that a high percentage of bricklayers in Barcelona showed hypersensitivity to both chromium and cobalt, but he noted that hypersensitivity to cobalt does not appear as commonly in patients allergic to chromium and working in other occupations.

Müller and Breucker[40] found that, in most of their 79 cobalt-sensitive patients, the most frequent cause of dermatitis was cement (29%) and that, when these patients showed reactions to chromium and nickel, the sensitization was due to simultaneous exposure to the 3 metals.

Dermatitis from exposure to wet clay containing cobalt may occur.[41] Cobalt dermatitis from dry clay or finished wares is rare. Cobalt may be added to clay to neutralize the yellow color produced by impurities. Cobalt is present in some pigments used for painting of pictures, china, and enameling.

Miscellaneous Exposures to Cobalt

Cobalt is used extensively in the carbide, glass, ceramic, enamel, electrical, and pigment industries. It may also be used in printing inks and in animal feeds. Cobalt in animal feeds has caused allergy in a Finnish pig farmer and an English animal feed worker.[42,43] Cobalt-2-ethylhexoate caused hand dermatitis in an offset printer.[44] Two of the ink driers he worked with contained this chemical. Inks, paints, oils, and varnishes may contain cobalt and other heavy metal catalysts, which help speed the drying process. Cobalt was reported to be present in belt buckles, much less commonly than nickel. In a survey of 701 buckles from either China or the United States, only five released cobalt, whereas approximately 55% to 60% released nickel on spot testing.[45]

Cobalt in Tattoos

In the form of cobalt blue (azure blue and cobaltous aluminate), cobalt has been reported as causing a sarcoidal allergic reaction in areas in which it was used as a light blue tattoo pigment.[46] A patch test with cobalt was positive, and cobalt was demonstrated in the pathologically altered parts of the tattoo. A tattoo test with cobalt blue elicited an inflammatory tissue reaction.

Photosensitization Dermatitis due to Cobalt

Camarasa and Alomar[47] reported a bricklayer with a chronic and severe eczema, combined with a chronic papular dermatosis in sun-exposed areas, associated with multiple sensitivities. Several other allergens were positive on patch testing, but cobalt produced a reaction only on photo patch testing. This suggests that individuals

having dermatitis in areas exposed to sunlight and having likely cobalt exposure should be considered for photo patch testing.

Romaguera and colleagues[48] found that 4 patients with chronic photocontact dermatitis were sensitive to cobalt salts. They presented as cases of contact dermatitis from cement or pig fodder with persistent lesions on exposed areas. Only two of them had standard patch test reactions to cobalt, but all showed positive photo patch tests to cobalt.

Patch Testing With Cobalt

A "reaction" peculiar to cobalt patch tests has been described by Storrs and White.[49] This consists of a "cayenne pepper" speckled appearance of the patch site without edema or uniform erythema, apparently due to a poral reaction. This is not an allergic reaction but rather an irritant reaction specific to cobalt. Testing with a lower concentration of cobalt is not recommended, as Allenby and Basketter[50] found that, of 6 cobalt-allergic patients who reacted to cobalt chloride 1% aqueous, only one reacted to 0.1% aqueous. As long as the poral reaction is kept in mind, testing at 1% would seem reasonable. Cobalt sulfate 2.5% is also commercially available for testing.

SUMMARY

Cobalt has been known as an allergen for many years, but recently, we have realized several previously unrecognized features of cobalt allergy and potential exposure. Although, in the past, it was often thought that ACD to cobalt was incidentally due to concomitant exposure to both cobalt and nickel, now we understand that exposure to cobalt independent from exposure to nickel is often important.

REFERENCES

1. Fowler JF. Allergic contact dermatitis to metals. *Am J Contact Dermatitis* 1990;1:212.
2. Warshaw EM, Maibach HI, Taylor JS, et al. North American contact dermatitis group patch test results: 2011–2012. *Dermatitis* 2015;26:49–59.
3. Available at: http://en.wikipedia.org/wiki/Cobalt. Accessed April 25, 2015.
4. Available at: http://www.webelements.com/cobalt/. Accessed April 29, 2015.
5. Gollhausen R, Enders F, Przybilla B, et al. Trends in allergic contact sensitization. *Contact Dermatitis* 1988;18:147–154.
6. Christophersen J, Menné T, Tanghøj P, et al. Clinical patch test data evaluated by multivariate analysis. Danish Contact Dermatitis Group. *Contact Dermatitis* 1989;21:291–299.
7. Uter W, Gefeller O, Geier J, et al. Contact sensitization to cobalt—multifactorial analysis of risk factors based on long-term data of the Information Network of Departments of Dermatology. *Contact Dermatitis* 2014;71:326–337.
8. Edman B. Sites of contact dermatitis in relationship to particular allergens. *Contact Dermatitis* 1985;13:129–135.
9. Kranke B, Aberer W. Multiple sensitivities to metals. *Contact Dermatitis* 1996;34:225.
10. Rystedt I, Fischer T. Relationship between nickel and cobalt sensitization in hard metal workers. *Contact Dermatitis* 1983;9:195–200.
11. Lammintausta K, Pitkänen OP, Kalimo K, et al. Interrelationship of nickel and cobalt contact sensitization. *Contact Dermatitis* 1985;13:148–152.
12. Thyssen JP, Johansen JD, Jellesen MS, et al. Consumer leather exposure: an unrecognized cause of cobalt sensitization. *Contact Dermatitis* 2013; 69:276–279.
13. Bregnbak D, Thyssen JP, Zachariae C, et al. Association between cobalt allergy and dermatitis caused by leather articles—a questionnaire study. *Contact Dermatitis* 2015:72;106–114.
14. Perryman JH, Fowler JF Jr. A patch test study to evaluate the allergenicity of a metallic jewelry alloy in patients allergic to cobalt. *Cutis* 2006;77:77–80.
15. Hamann C, Hamann D, Hamann KK, et al. Cobalt release from inexpensive earrings from Thailand and China. *Contact Dermatitis* 2011;64:238–240.
16. Thyssen JP, Johansen JD, Menné T, et al. A spot test for detection of cobalt release—early experience and findings. *Contact Dermatitis* 2010;63:63–69.
17. Boonchai W, Maneeprasopchoke P, Suiwongsa B, et al. Assessment of nickel and cobalt release from jewelry from a non-nickel directive country. *Dermatitis* 2015;26:44–48.
18. Jensen P, Hamann D, Hamann CR, et al. Nickel and cobalt release from children's toys purchased in Denmark and the United States. *Dermatitis* 2014;25:356–365.
19. Basko-Plluska JL, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. *Dermatitis* 2011;22:65–79.
20. Wong CC, Nixon RL. Systemic allergic dermatitis caused by cobalt and cobalt toxicity from a metal on a metal hip replacement. *Contact Dermatitis* 2014;71:113–114.
21. Thienpont E, Berger Y. No allergic reaction after TKA in a chrome-cobalt-nickel-sensitive patient: case report and review of the literature. *Knee Surg Sports Traumatol Arthrosc* 2013;21:636–640.
22. Svedman C, Möller H, Gruvberger B, et al. Implants and contact allergy: are sensitizing metals released as haptens from coronary stents? *Contact Dermatitis* 2014;71:92–97.
23. Jakobsen SS, Lidén C, Søballe K, et al. Failure of total hip implants: metals and metal release in 52 cases. *Contact Dermatitis* 2014;71:319–325.
24. Schalock PC, Menné T, Johansen JD, et al. Hypersensitivity reactions to metallic implants—diagnostic algorithm and suggested patch test series for clinical use. *Contact Dermatitis* 2012;66:4–19.
25. Rostenberg A Jr, Perkins AJ. Nickel and cobalt dermatitis. *J Allergy* 1951;22:466–474.
26. Fisher AA. Contact dermatitis at home and abroad. *Cutis* 1972;10:719.
27. Young WC, Ulrich CW, Fouts PJ. Sensitivity to vitamin B12 concentrate. *J Am Med Assoc* 1950;143:893–894.
28. Caballero MR, Lukawska J, Lee TH, et al. Allergy to vitamin B12: two cases of successful desensitization with cyanocobalamin. *Allergy* 2007;62:1341–1342.
29. Kalenský J, Schwank R. Hypersensitivity to cobalt caused by the antiperspirant cream Perilacin. *Cesk Dermatol* 1968;43:423–429.
30. Skog E. Skin affections caused by hard metal dust. *Ind Med Surg* 1963; 32:266–268.
31. Fischer T, Rystedt I. Cobalt allergy in hard metal workers. *Contact Dermatitis* 1983;9:115–121.
32. Fregert S. Occupational dermatitis in a 10-year material. *Contact Dermatitis* 1975;1:96–107.
33. Bourne LB, Milner FJ. Polyester resin hazards. *Br J Ind Med* 1963:100–109.
34. Bhushan M, Craven NM, Beck MH. Contact allergy to methyl ethyl ketone peroxide and cobalt in the manufacture of fibreglass-reinforced plastics. *Contact Dermatitis* 1998;39:203.
35. Jolanki R, Tarvainen K, Tatar T, et al. Occupational dermatoses from exposure to epoxy resin compounds in a ski factory. *Contact Dermatitis* 1996;34:390–396.
36. Schena D, Rosina P, Chieregato C, et al. Lymphomatoid-like contact dermatitis from cobalt naphthenate. *Contact Dermatitis* 1995;33:197–198.

37. Pirila V. On occupational diseases of skin among paint factory workers, painters, polishers and varnishers in Finland: clinical and experimental study. *Acta Derm Venereol (Stockh)* 1947;27(suppl 16):1.
38. Condé-Salazar L, Guimaraens D, Villegas C, et al. Occupational allergic contact dermatitis in construction workers. *Contact Dermatitis* 1995;33:226–230.
39. Giménez Camarasa JM. Cobalt contact dermatitis. *Acta Derm Venereol* 1967;47:287–292.
40. Müller R, Breucker G. Cobalt as an occupational eczematogen and as a coupling allergen with chromium and nickel. *Dermatol Wochenschr* 1968; 154:276–282.
41. Pirila V. Sensitization to cobalt in pottery workers. *Acta Derm Venereol* 1953;33:193–198.
42. Tuomi ML, Räsänen L. Contact allergy to tylosin and cobalt in a pig-farmer. *Contact Dermatitis* 1995;33:285.
43. Ratcliffe J, English JS. Allergic contact dermatitis from cobalt in animal feed. *Contact Dermatitis* 1998;39:201–202.
44. Kanerva L, Jolanki R, Estlander T. Offset printer's occupational allergic contact dermatitis caused by cobalt-2-ethylhexoate. *Contact Dermatitis* 1996;34:67–68.
45. Hamann D, Hamman C, Li L, et al. The Sino-American belt study: nickel and cobalt exposure, epidemiology, and clinical considerations. *Dermatitis* 2012;23:117–123.
46. Bjoernber A. Allergic reaction to cobalt in light blue tattoo markings. *Acta Derm Venereol (Stockh)* 1961;41:259.
47. Camarasa JG, Alomar A. Photosensitization to cobalt in a bricklayer. *Contact Dermatitis* 1981;7:154–155.
48. Romaguera C, Lecha M, Grimalt F, et al. Photocontact dermatitis to cobalt salts. *Contact Dermatitis* 1982;8:383–388.
49. Storrs FJ, White C Jr. False-positive "poral" cobalt patch test reactions reside in the eccrine acrosyringium. *Cutis* 2000;65:49–53.
50. Allenby CF, Basketter DA. Minimum eliciting patch test concentrations of cobalt. *Contact Dermatitis* 1989;20:185–190.