Dear Reader,

Each year the first issue of All Things Contact Dermatitis includes an article on the Allergen of the Year. This year is no different. We invite you to read about an allergen that is an oldie but a goodie—one with a colorful history that extends back to the Bronze Age, an allergen that sensitized individuals can encounter in paint and pigments but also in a standard bottle of dietary supplements that might be found on anyone’s kitchen counter. Read on to learn more about which allergen earned this dubious distinction from the American Contact Dermatitis Society for 2016.

It’s probably no surprise to most patch testers that the number of allergenic substances keeps increasing. In fact, the catalogued list now tops 4,500 known allergens. That number points to the complexity of diagnosing the cause of allergic contact dermatitis and to the importance of having a partner who can help you in the diagnostic quest. We here at SmartPractice are always happy to help you with any diagnostic conundrums that come your way.

Kind Regards,

Dr. Curt Hamann
President & CEO, SmartPractice

Another Year, Another Allergen: Cobalt

The term cobalt is derived from a sprite-like creature in Germanic folkloric traditions known as kobold. Medieval miners blamed these creatures for causing problems, especially those associated with ores such as silver, which released toxic arsenical fumes during smelting. Although the kobold may be mythical, the problems cobalt can cause in terms of allergic contact dermatitis are quite real as underscored by its selection as the 2016 Allergen of the Year by the American Contact Dermatitis Society.

This hard, ductile metal is an allergen with a colorful history. The oxides and salts of cobalt, which are usually blue, have been used as pigments in paints, glass, and ceramic glazes since ancient times. The most common cobalt pigment, cobalt blue, is composed of a double oxide of cobalt and aluminum. The earliest known uses of cobalt in objects date to the Near East Bronze Age cultures of Mesopotamia, Persia, and Egypt (ca 2000-1500 years BC), where it has been found in glass, jewelry, and ceramic glazes, respectively. It has also been found in the ruins of Pompeii, which was destroyed in 79 AD. In China cobalt first appears to have been used to color pottery in the Tang Dynasty (618-907). As trade developed along the Silk Road in the Ming Dynasty (1368–1644), Chinese porcelain decorated with a blue cobalt glaze (blue-on-white ware) became highly coveted by Europeans. Smalt, the earliest cobalt-containing pigment, is glass colored with cobalt oxide and reduced to a powder. Besides being present in ceramic glazes and underglazes, cobalt also may be present in the wet clay used by pottery workers.

Despite the widespread use of cobalt in the decorative arts for thousands of year, its identity remained unknown until the 18th century. Finally in 1735 the Swedish chemist George Brandt isolated the substance responsible for the highly desirable blue by reducing arsenic ores, and in 1780 cobalt was recognized as a single element. Its commercial potential was established in 1802 when the Frenchman L. J. Thenard discovered how to make cobalt blue (also known as Thenard blue) by heating cobalt phosphate with alumina. Because cobalt blue is a highly stable pigment, it became a popular substitute for ultramarine. Cobalt blue was used by such notable artists as Turner, Monet, Renoir, and van Gogh. Not surprisingly, painters, ceramicists, and glass workers are at risk of becoming sensitized to...

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Cobalt as are individuals who work in manufacturing capacities related to the production of paints, pigments, and glazes.

The major industrial use of cobalt is in the manufacture of alloys (e.g., steel) or as a binder of tungsten in hard, durable metals used to create drills, cutting tools, and mechanical parts. It is a common binding agent in the carbide industry. Cobalt is present in magnets, welding rods (and the resultant smoke), and welding stainless steel. Industrial exposure to cobalt can include glass, lubricating oils, and animal feeds. In the rubber tire industry, cobalt is used as an oxidizing agent in automobile exhaust control, and as a catalyst or accelerator for the production of terephthalate, polyester, and acrylate plastics. Because cobalt chloride readily hydrates and dehydrates, changing color in the process, it can be used as an indicator for water in desiccants. Other occupational sources of exposure to cobalt include bricks and cements; materials used for etching, grinding, welding, and metal working; metal carbide manufacturing; cobalt-based additives and drying agents in paints or varnishes; an oxidizing agent in electroplating; catalysts and promoters in resins and plastics; and printing and tattoo inks.

Metallic cobalt is added to alloys to increase hardness at high temperatures, and it has been widely used in orthopedic and dental implants and prostheses. The classic alloy used for dental fillings is amalgam—50% pure elemental mercury, 35% silver, 13% tin, 2% copper, and a trace of zinc. Cobalt can be added to this base formula to increase resistance to enzymatic breakdown. Cobalt has also been associated with intractable generalized dermatitis in a patient who received a hip implant; the condition resolved when the implant was removed and replaced by a titanium device.

Consumer leather goods such as a sofa have recently been confirmed as the cause of contact dermatitis. Chromium hypersensitivity, which might be expected in such a case, was ruled out by patch testing. This relatively new and perhaps surprising source of exposure to cobalt was one of the reasons cited as underlying cobalt’s selection as the Allergen of the Year.

Diet is an easily overlooked source of exposure to cobalt. Nonetheless, cobalt in the form of vitamin B12 (i.e., cyanocobalamin) is essential for human health as a coenzyme in a variety of cellular processes. Some examples of foods that contain cobalt include breads, rice, cereals, dairy products, eggs, meats, poultry, fish, fruits, nuts, coffee, tea, chocolate, and beer. Patients who are highly sensitive to cobalt may need to modify their diet to minimize intake of foods with high levels of cobalt. The World Health Organization recommends a daily intake of 2.4 µg of vitamin B12 for adults. The equivalent dose of cobalt from this amount of vitamin B12 is 0.1 µg/day.

Not only are there many opportunities for individuals to be exposed to cobalt, but it is a highly sensitizing allergen. Based on data collected by the North American Contact Dermatitis Group since 2001-2002, the frequency of positive reactions to cobalt dichloride has ranged from 6.2 to 8.4%, and its ranking has increased from the 10th to the 6th most common allergen. Based on data from the Mayo Clinic, the prevalence of contact allergy to cobalt is even higher, exceeding 10% and ranking as the 4th most common allergen in their most recent patch test series. Reports from Europe are similar. Recent reports from German research groups indicate that cobalt is one of the top five allergens while in European-wide series, the rate of positive reactions ranged from 6.74% at a Danish site to 17.6% at an Italian site.

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Another Year, Another Allergen: Cobalt…continued

Patients who are allergic to cobalt need to avoid not only cobalt but cobalt dust and fumes, metal, and metal powder. Synonyms for cobalt include cobalt blue, cobaltous chloride, cobalt dichloride hexahydrate, cobalt chloride, cobaltous chloride hexahydrate, and cobalt (II) chloride hexahydrate. Only products that do not list cobalt or related chemicals on the label, list of ingredients, or Material Safety Data Sheet should be used. If no information is available, the manufacturer should be contacted. Alternative products that contain no cobalt include stainless steel, plastic, gold (18k) or silver jewelry and decorative items. Sensitized patients may use stainless steel tools and utensils or those with plastic-coated handles. Titanium or stainless steel orthodontic materials and ceramic brackets can be used for sensitized patients instead of those with cobalt. However, reactions to the metal instruments used by dental practitioners are considered unlikely because skin contact is so brief, and reactions to metal dental appliances are relatively rare. Organic nonmetallic pigments for paints, enamels, inks, and glazed can be substituted for those with cobalt.

Many metal objects contain nickel and other potentially allergenic metals; consequently, cobalt may not be the sole cause of sensitization. For example, inexpensive jewelry is a common source of exposure to both nickel and cobalt. Wearing jewelry made of sterling silver or other precious metals such as platinum rather than costume jewelry can help prevent co-sensitization. Only earrings with stainless steel posts and watches with a stainless steel back should be worn. Allergic individuals should also wear clothing with nonmetallic zippers and fasteners. Metallic items that are difficult to avoid such as keys can be coated with several layers of clear nail polish or polyurethane lacquer. Jewelry can also be coated. Larger objects such as the tools used by hairdressers and textile workers can be covered with plastic. Allergic individuals should be urged to use scissors and other tools that have plastic, wood, or high-quality stainless steel handles. When contact is unavoidable, protective gloves should be worn.

The cobalt spot test based on disodium-1-nitroso-2-naphthol-3,6-disulfonate was developed to identify cobalt release. The test can detect as little as 8.3 ppm of cobalt, an amount that approximates the concentration that can elicit reactions in cobalt-allergic patients. The test can help clinicians establish the clinical relevance of exposure to cobalt metal and can help sensitized patients identify the presence of the allergen in consumer products. The test is performed by rubbing a cotton-tipped stick dipped in the spot test solution against a metal piece of interest. The cotton tip is yellow when a tested item does not release cobalt and turns more reddish when an item releases cobalt. As part of its mission to help identify contact allergens and to help clinicians help their patients to avoid sensitizing agents, SmartPractice offers the cobalt spot test as part of its Reveal & Conceal™ product line (see Revealing Considerations for Use of the Cobalt Spot Test in Issue 7 of this newsletter). Patients can use this convenient test not only to identify sources of cobalt, but the product also includes a clear coat that can be added to small cobalt-containing items to minimize exposure to the allergen from items such as keys that are difficult to avoid in daily life.

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No, we’re not talking about altitude—we’re talking about the number of known allergens, and that’s excluding atopy allergens. It’s a very large number to think about when you are searching for the cause of a patient’s allergic contact dermatitis. Unfortunately, it is also a number that keeps increasing as new chemicals are introduced into our lives. In 1986 Anton de Groot first published his classic book, *Patch Testing*, which listed the test concentrations and vehicles for 2800 allergens. By the time the second edition was released in 1994—just 8 years later—that number had jumped by 900 to include 3700 chemicals. The increase averaged to more than 100 new allergens a year. In 2008 when the third edition was published, the number of allergens included in the text had increased by another 650 to 4350, or an average of about 46 new allergens per year.

In a recent publication (de Groot AC. New contact allergens: 2008 to 2015. *Dermatitis* 2015;25(5):199-215), de Groot provided an update by reviewing the number of new allergens reported in the 7 years following the last edition of his book. His criteria for identifying new allergenic compounds were limited. He included only allergens reported in the journals Contact *Dermatitis* and *Dermatitis* and those not already captured in the 2008 edition of his book. As he noted, some allergens were undoubtedly missed by this relatively narrow sampling of the literature while other allergens would not have been included had he not missed them when compiling his list for the book. Notwithstanding these caveats, de Groot identified 172 additional chemicals as allergens: 119 substances were considered to have induced allergic contact dermatitis while the remaining 53 were reported to have caused a positive reaction on patch testing but specific clinical data were unavailable.

The new data translate to an average of 17 new allergens a year. Approximately a third of the 119 news allergens were skin conditioning agents in cosmetics that functioned either as humectants and emollients or as emulsifiers and surfactants. Few of the new allergens in cosmetics fell into the more traditional category of cosmetic allergens such as fragrances, antimicrobials/preservatives, or hair dyes. About 40% of the new allergens were occupational allergens, and not quite half of those involved allergies to drugs in health care or pharmaceutical workers. However, clusters of reactions to drugs in a just a few of these patients suggest that false-positive reactions cannot be ruled out in these cases.

If de Groot’s sampling procedures have been fairly inclusive over the years, the good news to be gleaned from his data is that the rate at which new allergens are being introduced appears to have slowed. He notes that stringent premarket testing may partially account for the relatively low number of new allergens in this latest survey. However, it also can be just plain difficult to identify new allergens—ingredients may not be identified or available for testing, and when they are patients may not wish to be retested. Furthermore, not all clinicians publish their findings. Regardless of the actual number of allergens, it is clear that there are more than enough to offer the patch-testing clinician a lifetime of fascinating investigative work. That intellectual challenge, combined with the potential to improve a patient’s life dramatically by providing a correct diagnosis, are two features that make patch testing such a satisfying medical practice.