Dear Reader,

Exposure to metals in our daily life is unavoidable and, for most of us, unremarkable. We think nothing of the keys we stick in our pocket, the jewelry we wear, or the coins we handle. Chances are we also give little thought to the sensitizing potential of common medical implants such as knee or hip replacements or dental devices. Yet some of the metals from which these products (and many more) are manufactured can be highly sensitizing while the allergenic potential of other metals is under debate.

This issue gives you a glimpse at how expert patch testers approach metal hypersensitivity, a timely topic about which you can learn more if you join us in Barcelona in June at the Congress of the European Society of Contact Dermatitis where we will host a special symposium on metal allergies. In this issue you can also read about how to maximize the effectiveness of our cobalt spot test product, Reveal & Conceal, and about the outcome implications of the variability associated with the many different patch testing systems used around the world. All of these efforts reflect our commitment to push the envelope in the field of contact dermatitis to ensure that patients everywhere obtain the diagnosis that they deserve.

Kind Regards,

Dr. Curt Hamann
President & CEO, SmartPractice

The Bionic Man and Woman Meet Metal Hypersensitivity

Back in the 1970s when the American television program, The Bionic Man, was introduced, few could have predicted how widespread metal implants would become more than 4 decades later thanks, of course, to many remarkable technological advances dovetailing with an aging population. Even fewer might have guessed that bionic implants would become associated with metal hypersensitivity reactions. Today, however, at some point, a patch test practitioner may expect to receive a referral to evaluate a patient who needs or already has some type of metal implant, whether cardiac, dental, or orthopedic. So how should such patients be managed? What are the criteria for diagnosis? What recommendations are appropriate for the patient and referring physician?

As of yet, no clear-cut answers to these questions are available. The cause-and-effect relationships between implants and metal hypersensitivity are poorly defined and heavily debated among experts. However, a timely survey by Schalock and Thyssen helps characterize how leading patch test practitioners approach such consultations. Respondents included participants from two international conferences—the annual meeting of the American Contact Dermatitis Society (ACDS) in 2013 and the Congress of the European Society of Contact Dermatitis (ESCD) in 2012.

The rate of respondents was low (10% for the ESCD and 32% for the ACDS) and primarily reflects conference participants self-selected for their interest in metal hypersensitivity reactions. Although this pattern limits generalization of the findings to all patch testers, it does likely represent clinicians actively practicing on the front-line of this controversy: 83% patch tested more than 100 patients a year, while 43% patched tested more than 300 patients a year.

Most respondents were attending physicians (91%), and most worked in an academic or hospital setting (72% compared to 28% working in private practice). On average, orthopedic devices were involved in 33.5% of the cases that respondents evaluated, and the percentage was similar for dental devices (30%). Less frequently involved were cardiovascular devices (21.5%) and unspecified other devices (15%).

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Respondents rarely used the lymphocyte transformation test and intradermal testing, but most did use patch testing for evaluation—60% with a standard series for metal implant hypersensitivity and 33% with specific allergens based on the patient’s medical history and type of implant. The majority (82%) also tested for plastic and glues when they evaluated patients with a hip or knee device.

Respondents were also asked how a patient with moderate or severe metal dermatitis should be managed before they underwent implantation of a metal device. A slight majority (54%) recommended preoperative patch testing or in vitro testing while 38% thought that recommending that the treating surgeon implant a low-allergenic device (e.g., made from a titanium alloy) was sufficient. Only 8% held the opinion that there was no need for preoperative testing of any kind or any need to advise the treating surgeon against any specific alloy. Significantly more respondents from ESCD held the latter opinion than did respondents from the ACDS, perhaps, as the authors note, indicating differences in legal and health care systems.

These preliminary data will provide a baseline against which future changes in practice can be compared. It is unlikely, however, that a gold standard for evaluation of metal hypersensitivity reactions will be established in the near future. Too little research is available, and findings can be contradictory. To help foster communication on this topic, SmartPractice will be hosting a special symposium on metal allergies at the ESCD meeting in Barcelona this coming June. Topics by noted experts will include how to diagnose metal allergies with in vitro tests and a close look at titanium allergies. Furthermore, the international dialogue on metal allergies will be expanded by a presentation on metal allergies in Japan. Please join us for this cutting-edge experience!

Although a relatively rare sensitizer in the population at large, cobalt allergy is common in patients with dermatitis. In the Mayo Clinic's most recent 5-year retrospective review of patch test results, cobalt chloride 1% was associated with the fourth highest percentage of allergic reactions (11.6%). The percentage of reactions to cobalt was increased compared to that reported in their previous 5-year review (10.3%). Based on the results of the North American Contact Dermatitis Group's 2009-2010 patch testing results published in 2013, cobalt, which was associated with positive reactions in 6.2% of those tested, was the sixth most common allergen even though its prevalence had decreased significantly compared to the previous reporting period of 2007-2008. In Europe the reported prevalence of cobalt sensitization ranges from 6.2 to 8.8%.

The risk of exposure to cobalt is relatively high in occupations such as metal workers, bricklayers, toolmakers, printers, and pottery workers. Although recent studies indicate that cobalt is rarely detected in consumer items like jewelry and belt buckles, the metal is used to produce jewelry. Consumers also may be exposed to cobalt via nonmetallic products such as detergents; make up; pigments used in tattoos, shoes, and paints; and surgical implants used in cardiology, dentistry, gynecology, and orthopedic surgery where it can be released and associated with not only allergic sensitization but also device failure.

Establishing the clinical relevance of a positive patch test reaction to cobalt chloride can be greatly facilitated by testing objects to which the patient is exposed for its release. Hence, in 2011, SmartPractice was pleased to introduce patch test practitioners to the cobalt spot test, Reveal & Conceal™, which was developed by Danish expert in cutaneous allergies, Dr. Jacob P. Thyssen, to detect cobalt in metal objects. This rapid, simple, and inexpensive colorimetric test works on the same principle as the well-known nickel spot based on dimethylglyoxime (DMG). In the nickel spot test, the reagent applied to the tip of cotton-tipped swab typically turns pink when it contacts a nickel-releasing object. The pink coloration of a positive is usually easily distinguished from clear-colored negative reactions. In contrast, in the cobalt spot test, the reagent solution turns orange-red when it contacts objects releasing cobalt ions and is yellow when negative. Consequently, users familiar with our Reveal & Conceal™ nickel spot test should not always expect to see as dramatic of a color change with the newer cobalt spot test. Furthermore, in a laboratory experiment, a color gradient was observed in response to serial dilutions of cobalt. Intense color reactions were associated with high concentrations of cobalt and became weaker in response to weaker concentrations.

Users of the cobalt spot test should also be aware that copper can react with its reagent, 2-nitroso-1-naphthol, to produce a color change. In this case, however, the slight change, although different from the yellow of a negative reaction, does not mimic the orange-red of positive reaction as Dr. Thyssen and his colleagues have recently noted in a letter to the editor of the journal, Contact Dermatitis. Therefore, such a color change in response to copper objects does not necessarily equate with a false-positive reaction.

By their very nature spot tests cannot be as sensitive or as specific as other complex and expensive chemical analyses and still remain accessible and affordable. Nonetheless, doubt about how to categorize a response to the cobalt spot test may be minimized by adding a drop of reagent to an unused swab to serve as a negative control for comparison. This small additional step in the spot testing process may help patients avoid contact with objects that could exacerbate their contact dermatitis while reassuring that other items are safe to handle.


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A Chamber by Any Other Name . . .

All patch tests systems are the same . . . aren’t they? Actually, no, they aren’t. To begin with, patch test systems can incorporate chambers, which are defined as having a measurable depth, or patches, which have no measurable depth. It’s good to keep this difference in mind because, confusingly enough, the term “patch” can be used to refer to both chambers and patches. Then there’s the matter of materials. Some chambers are manufactured from aluminum (e.g., Finn) and may be coated or uncoated while others are manufactured from polyethylene (e.g., allergEAZE) or polypropylene. If liquid allergens are being tested in chambers that are not manufactured with an absorbent media, filter paper may first be placed in the bottom of the chambers. Depending on the brand, patches are made of a disk of cotton or a cotton blend and may or may not be framed by a polyester film. The configuration of chambers is either round or square, and their physical dimensions vary as well. Furthermore, the panel material, which could conceivably affect adhesion, varies across products as well.

Does this variability affect patch testing? We conducted a study to address just that question by evaluating 21 different patch test systems now or previously in use around the world. We compared the minimum volume of disperse blue in petrolatum (chosen to improve visualization) needed to cover the base of the chambers and patches. Different volumes of the allergen (15, 20, 25, 30, 35, or 40 µl) were dispensed via a precision microliter pipette into the chambers and patches, which were then covered with glass and tamped lightly as they would be when applied to a patient’s back. The volume at which 100% coverage was obtained was determined visually. The choice of 100% coverage was based on the assumption that it would correspond to homogenous coverage (and hence to the likelihood of a homogenous reaction) in a clinical situation.

Not surprisingly, given the many differences across products, 100% coverage was not provided by the same dose across all patch test systems. The patches provided 100% coverage at the smallest volume (15 µl). In contrast, the largest chamber, the now discontinued 10-mm van der Bend chamber, a European product often used in research studies in the past, required 45 µl before 100% coverage was obtained. Complete coverage of the remaining chambers varied between 25 and 35 µl.

What are the implications of these findings? First, practitioners cannot assume that the same volume of allergen dispensed in different chambers corresponds to the same dose of allergen (measured in mg/cm²). Therefore, clinicians must consider this variation to avoid administering excessive or inadequate doses of allergens depending on their pre-

ferred patch test system. The corollary is that such inadvertent variation in dose could affect a patient’s response: Too low of a dose could yield a false-negative reaction while too high of a dose could risk sensitization, especially with highly sensitizing allergens like para-phenylenediamine. Furthermore, if the volume of allergen is too small to provide uniform coverage, any resulting inhomogenous skin reaction would be interpreted as negative based on the widely accepted reading criteria of the International Contact Dermatitis Research Group. Finally, the findings suggest that the meaningfulness of comparisons across clinics, national and international clinical trials, and time must be considered carefully because, again, a standard allergen volume of 15 or 20 µl dispensed in one type of chamber will not necessarily be the same dose in another study that used another type of chamber.

Studies on the variability associated with patch testing are important because they can help improve overall standardization. In turn, reducing variability should help improve our understanding of allergic contact dermatitis, which, ultimately, will help patients obtain the diagnosis that they deserve. Still the need for standardization in patch testing must be balanced against the needs of patients. The firm adhesive panel of Finn Chambers AQUA, for example, which is a good choice for active patients, may be inappropriate for elderly or other patients with fragile skin who may be more comfortable with an allergEAZE panel. Our studies of variability and its implications for patch testing outcomes are intended to help clinicians make the most informed choices possible when choosing their patch testing products. Stay tuned for the results of future studies!


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