Gold Nuggets

Gold is an allergen surrounded by considerable controversy. Its clinical relevance has been questioned, concerns about the risk of sensitizing patients have been expressed, and how reaction patterns to gold should be interpreted has been debated. Yet, in 2001 when the American Contact Dermatitis Society (ACDS) selected gold as their Allergen of the Year, expert patch tester, Dr. Joseph Fowler, wrote that gold should perhaps not only be the allergen of the year but the allergen of the millennium! This year Chen and Lampel have revisited the ongoing debate about gold in a thoughtful review. It is clear that many mysteries remain about this fairly common sensitizer.

Elicitation of symptoms has been linked to gold in jewelry, occupational exposure to gold, dental hardware, gold-plated intracoronary stents, eyelid implants, and a homeopathic medication containing gold. In particular, contact allergy to gold strongly correlates with medical and dental applications of gold. For example, the frequency of gold allergy is high in patients with gold in the oral cavity. Contact allergic gastritis has even been attributed to dental gold. Patients with contact allergy to gold have developed localized dermatitis after receiving gold eyelid implants, and the dermatitis has resolved when the gold was removed. Patients also have developed flare ups at old sites of clinical contact dermatitis after systemic provocation with ionic gold. In an unusual case, a woman taking a homeopathic medicine that contained gold for heart disease developed systemic contact dermatitis that disappeared after she discontinued use of the drug. Finally, gold-coated coronary stents have been associated with an increased frequency of restenosis and contact allergy to gold. In vivo corrosion of bare-metal stents has been associated with the release of heavy metal ions into adjacent tissue, with ensuing vasculitis and restenosis.

The clinical relevance of gold as an allergen, however, has been questioned. The primary reason is that some patients have a positive patch test reaction to gold sodium thiosulfate (GST), the salt often preferred for patch testing in North America, but no reaction to jewelry made from gold. That, however, a contact allergic reaction to the gold salt is more common than allergic contact dermatitis to elemental gold or its alloys is not surprising. Metallic gold is mostly inert and not that easy to solubilize. Specific conditions may need to be present to encourage the formation of gold ions. For example, the sulfa-containing amino acid cysteine enhances the release of gold in artificial body fluids. Microabrasives in cosmetic powders such as titanium dioxide may abrade jewelry and help transfer gold ions to the face. And low-karat gold alloys, for instance, those with a relatively high copper content, release more gold than higher-karat alloys. The finding suggests that lower-karat gold may elicit more intense reactions than higher-karat gold. Furthermore, although many patients do not exhibit dermatitis at the site of contact with gold jewelry, their dermatitis has cleared after they stopped wearing gold jewelry. Finally, more than half a century ago, a colloidal gold stain was developed to identify Langerhans cells in the skin, clearly demonstrating that physiological binding of gold is possible.

Despite variations in test substances, test doses, and study designs, large patch testing series support the clinical relevance of gold as an allergen. In their 2001-2002 study period, the North...
Gold Nuggets…continued

American Contact Dermatitis Group (NACDG) found that 10.2% of 4,900 patients tested positive for gold sodium thiosulfate (GST), and the relevance of 10% of the reactions was deemed probable. In their 2003-2004 study period, the rate of positive reactions to GST had dropped but was still a substantial 8.7%. Thereafter, the NACDG dropped GST from their standard series in favor of aimed patch testing to sidestep concerns about delayed reactions and persistent reactions. In an NACDG patch test study stratified by age, adults between 19 and 64 years had the highest frequency (10%) of positive reactions to 0.5% GST compared to adults older than 64 (7.3%) years and to children 18 years or younger (6.1%). Of the 19- to 64-year-old group, 4.1% of the positive reactions were deemed relevant. Women are also more likely to test positive than men, a finding that has been attributed to their potentially greater exposure to gold in the form of wearing jewelry. In a patch test study of metal allergens conducted by Mayo Clinic, positive responses were seen in 23% of patients tested with 2% GST and in 18% tested with 0.5% GST. The percentage of relevant allergic responses was almost 24% and 40%, respectively. In a subsequent study from Mayo Clinic using their standard series of 71 allergens, the allergen with the highest percentage of positive allergic responses (17%) was 2% GST, almost 20% of which were deemed relevant. As recently as 2013, the ACDS opted to include GST in their Core Series.

Our understanding of gold as an allergen may be further impeded, as Chen and Lampel noted, because sensitivity to gold can be overlooked. Late reactions are well known; consequently, reading a patch test to gold only on Day 3 risks missing patients with reactions that develop later. Some expert patch tester recommends a final patch test reading as long as 3 weeks after patch removal to minimize missing positive reactions.

Persistent reactions are another common feature of patch testing with GST that concerns many clinicians. Prolonged reactions to gold have been reported in 26% of patients with no known allergies. Such reactions, which can persist for weeks or months, should alarm neither patients nor clinicians. Although reactions to gold have been reported to persist as long as about 3 months, there have been no serious clinical repercussions. Patients sensitive to gold may be most likely to have a prolonged reaction. Possible explanations for persistent test reactions to GST include slow elimination of the allergen at the reaction site or a tendency to elicit chronic inflammation. Patients should be informed that they might develop a persistent or a late reaction, but neither is reason to avoid patch testing with GST. If patients develop an uncomfortable persistent reaction, an over-the-counter topical steroid may provide relief until the response dissipates.

Many patch testers, however, prefer aimed testing. The ACDS has noted that patch testing to gold may be particularly worthwhile in individuals with facial or eyelid dermatitis and in those with long-term exposure from oral gold. Fingers and earlobes also may be involved. Careful questioning of patients may yield clues, such as a potential occupational exposure, that support the presence of a gold allergy. Provocation by an intramuscular injection of gold sodium thiomalate for the treatment of rheumatoid arthritis has even been associated with a flare up of allergic contact dermatitis from a gold necklace previously worn around the neck.

As with any allergen, many complicated factors are involved in interpreting the clinical relevance of patch test reactions to gold. Currently, our ability to identify gold allergies is limited because the appropriateness of screening agents, concentrations, and time course is still largely undetermined. However, strategies for establishing clinical relevance include careful questioning of the patient to determine past and present reactions and exposures (i.e., occupational and nonoccupational) to the allergen as well as further testing as deemed necessary. For example, different dilutions of the same gold salt or different gold salts altogether may need to be tested to identify patch-test positive patients. The ACDS has stated that patients who have a positive reaction to gold but who have no dermatitis or who lack exposure to gold can be considered to have an irrelevant sensitization.

Patients who are deemed allergic to gold must avoid products that list any of the following names in the ingredients, material safety data sheet, label or package insert: gold sodium thiosulfate; gold trisodium bis(thiosulphate); thiosulfuric acid, gold(1+) sodium salt (2:1:3); and thiosulfuric acid (H,S2O3), gold(1+) sodium salt (2:1:3). Patients should avoid working with products that contain gold and wear protective or utility gloves made of natural or synthetic rubber or vinyl if occupational contact is unavoidable. Patients should inform their doctors about the test result. They can discuss with their dentist whether existing gold fillings or crowns should be removed. However, data suggest that it is unnecessary to remove crowns or fillings unless sores are present in areas of the mouth in contact with the gold. Although definitive answers to all the questions remaining about gold as a sensitizer await further research, Fowler as well as Chen and Lampel encourage continued patch testing with gold and a multidisciplinary approach to understand its clinical relevance.

References


Davis MDP, Wang MD, Yannis JA, et al: Patch testing with a large series of metal allergens: Findings from more than 1,000 patients in one decade at Mayo Clinic. Dermatitis 2011; 22(5):256-271

Fowler JF Jr: Gold remains an important allergen. Dermatitis 2015, 26(2):67-68


Schloch PC, Dunnick CA, Nedorost S: American Contact Dermatitis Society Core Allergen Series. Dermatitis 2013; 24(1):7-9

Positive Patch Test Reactions — Now What?

Although he failed to act on his father's request for a few years, Dr. Yiannis's repeated encounters with confused patients eventually spurred him to design just such a database. His efforts began by learning Microsoft's database software, Access. He built the rudiments of the database while taking a course to learn the software. Despite initial limitations such as an inability to deal with cross-reactors or synonyms, the program was constructed so that both products and ingredients could be added as could allergens that might be recognized in the future.

Despite its flaws, the program generated a list of products that patients with positive patch tests could safely use. After its introduction in 1998, CARD progressed to a fully Web-based user interface supported by the Mayo Clinic. In 2001 CARD became available to members of the American Contact Dermatitis Society (ACDS), and the database was awarded the Gold Triangle Award by the American Academy of Dermatology for excellence in public education. CARD was found to be as effective as traditional approaches to patient counseling, to increase patient satisfaction, and to decrease the amount of time clinicians need to spend with patients on education.

Development continued and in 2011 CARD was licensed to Preventice, an IT company in Rochester, Minnesota, to introduce a mobile phone application that consumers could use real-time while shopping. At the time of its launch in 2011, the downloadable app offered data on more than 8,000 ingredients in more than 5,500 skin products. Consumers with allergies not only can use the app to create safe shopping lists, they can create personal journals of reactions, compare products while shopping and be notified of changes in the formula of products. Patients and physicians had to pay a subscription fee to access CARD. The latest advance is a new application called SkinSAFE (see www.empowher.com), which is based on the original CARD. The intent is a more consumer-friendly product that is aimed at improving the health of the overall population without necessarily requiring a physician's input. A database that is larger than the original CARD system is planned as is expansion to include other products beyond the skin care category.

Another useful database, known as the Contact Allergen Management Program (CAMP), is supported by the ACDS. Initially developed by Matthew Zirwas, MD, CAMP is currently managed by Andrew Scherman, MD. Access to CAMP is a benefit of membership of the ACDS (see www.contactderm.org) and is intended to help guide clinicians in making recommendations to their patients. Like CARD it generates a list of products that does not include the allergens of concern and that can be used by patients with those particular allergens. The allergens or cross-reactors are selected by the physician. The list can be printed and handed to patients or can be shared with them electronically. Products can also be searched for based on the manufacturer, the product type, product name, or brand name.

The ACDS site also includes other information that can be useful in the process of patient counseling. For example, information is available on both sterile and nonsterile gloves and includes brands known to be free of specific accelerators, a common cause of hand dermatitis. The site also provides avoidance narratives in English and Spanish. Finally, patients are able to access their reports online for updates. For its members, the ACDS website provides access to Cosmetic Ingredient and Manufacturer Information, which consists of four databases developed by the Personal Care Products Council, formerly the Cosmetic, Toiletry, and Fragrance Association. Another database that members can access via the ACDS site is the Research Institute for Fragrance Materials (RIFM) Monograph Database, which provides links to fragrance raw materials.

Continued on next page
Positive Patch Test Reactions—Now What?  
...continued

Free governmental resources are also available. Depending on patients’ individual allergy, The Household Products Database of the United States Department of Health and Human Services (see householdproducts.nlm.nih.gov) may help physicians and patients determine if products are appropriate choices. This database links more than 13,000 consumer brands to health effects from Material Safety Data Sheets provided by manufacturers. The database can be searched by product category, type of product, ingredients, and manufacturers to help users identify the chemical ingredients of different brands, the potential effects of ingredients, and how to contact the appropriate manufacturer. It is worth keeping in mind that some components of products can originate overseas. In such cases it can be difficult to identify the ingredients and hence potential allergens. Nonetheless, both clinicians and patients should be aware of this vast database.

Many products simply cannot be manufactured without introducing potential allergens. Consequently, even with robust digital resources at our fingertips, allergy avoidance is likely to remain a challenge for patients and their caretakers. Just as clinicians partner with their patients, our mission is to partner with clinicians to make all aspects of patch testing—from obtaining the supplies to performing the tests to counseling and education—as easy as possible. Please feel free to explore the many patch testing resources that you will find on our website, smartpractice.com/dermatology.

References

Kist JM, El-Azhary RA, Hentz JG, Yiannias JA. The Contact Allergen Replacement Database and treatment of allergic contact dermatitis. Arch Dermatol 2006; 140(12):1448-1450

