

Allergic Contact Dermatitis to Gold

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Gold is a relatively common allergen that appears to induce dermatitis about the face and eyelids, as well as at sites of direct cutaneous contact. In this study, 355 patients with suspected contact dermatitis were evaluated; 17 (4.8%) were found to be allergic to gold. Fifteen of these 17 patients were re-evaluated at >2 months after patch testing. When contact with gold jewelry was discontinued, 7 of 15 (46.7%) of the gold-allergic patients reported that their dermatitis cleared. In 3 of 7 patients (42.9%), discontinuing contact with gold jewelry was the only modification to their behavior; whereas in 4 of 7 (57.1%), discontinuing contact with gold jewelry and other documented allergens was necessary to affect resolution. Despite continuous contact with gold (jewelry and/or dental appliances), 7 of 15 (46.7%) of our patients had complete clearing of their symptoms by avoiding other documented allergens. None of our patients required the removal of dental gold.

Allergic contact dermatitis (ACD) to gold has become a challenging and enigmatic issue for dermatologists. As the 1990s unfolded, most medical personnel involved in the evaluation and treatment of ACD gave little thought to gold allergies, except perhaps when confronted with a patient who was occupationally exposed to gold (jewelers, electroplaters, etc.) or parenterally to medicinal gold. Allergic reactions to gold were thought to be uncommon because metallic gold was assumed to be relatively inert, resisting attack from air and water. However, within the past few years, the reported prevalence of allergic patch-test reactions to gold sodium thiosulfate among patients evaluated for presumed ACD has been significant. Studies from Asia, Europe, and North America have shown positive patch test frequencies to gold of 0.78%, 2.1%, 3.2%, 4.6%, 8.6%, 10% and 13%.¹⁻⁷ Furthermore, many of

these studies have demonstrated that ACD associated with gold may produce long-lasting allergic patch reactions. In one recent report, a gold patch reaction lasted for 3 weeks.⁸ Gold allergies have been associated with occupational and medicinal exposure, as well as with exposure to metallic gold in jewelry and in dental appliances. Many of these allergic reactions have been epidemiologically linked to dermatitic reactions overlying the face, eyelids, ears, hands, and perianal/perivulvar areas.^{4,6,7}

Oral mucosal reactions as a manifestation of gold allergy seem to be infrequent, despite the widespread use of dental gold. This has been attributed to the yet-unexplained resistance of mucosal surfaces to the manifestation of delayed type hypersensitivity.⁹ The dearth of reported intraoral reactions cannot be explained by the relatively insoluble nature of gold metal, since the interaction of oral bacteria, saliva, and salivary enzymes may result in the slow release of gold.⁸ Thus, it is not surprising that there have been some reports of gold-allergic patients presenting with stomatitis, oral ulcers, oral lichenoid reactions, and even laryngitis/pharyngitis, which resolved after the removal of the gold fillings.¹⁰⁻¹³

In many studies, women have accounted for the preponderance of gold-allergic patients.^{1,4,7} This female predilection has been attributed to ear piercing and wearing gold jewelry. In one study,¹⁴ allergic reactions to gold were a close second to reactions to nickel among patients with pierced ears patch tested to 18 metals. Thus, it is not surprising that ACD to gold has been statistically associated with earlobe dermatitis.⁶ While most of these eruptions have consisted of an eczematous dermatitis, unusual forms have been described including a lymphomatoid response¹⁵ and a sarcoidal-like granulomatous reaction.¹⁶

While intraoral complaints related to dental gold and cutaneous reactions directly associated with gold jewelry (earlobes, neck, wrists, and fingers) fit the expected reaction patterns induced by ACD to this metal, reports of gold-related dermatitic reactions in such ectopic locations as the face, eyelids, and genitalia piqued our interest in this allergen. Therefore, we measured the prevalence of positive patch-test reactions to gold among patients evaluated at the Uni-

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Table I

Demographic Data and Clinical Responses of Patients Allergic to Gold Sodium Thiosulfate: 1994-1998

Initials	Age/Gender	Dental Gold	Site	Final Reading	Rash Cleared with Discontinuation of	
					Gold	Other Allergens
B.P.	79/F	Unknown	Face/neck	2	Unknown	Unknown
L.M.	71/F	Yes	Eyelids/arms	3	No	Yes
J.D.	22/F	No	Face	3	No	No
D.I.	44/F	No	Eyelid	3	No	Yes
B.D.	44/F	Yes	Eyelid	2	No	Yes
M.W.	44/F	No	Face	3	Yes	No
S.C.	43/F	No	Eyelid	3	Yes	Yes
S.H.	69/M	Yes	Leg/hand	2	No	Yes
M.C.	71/F	Unknown	Hand	2	Unknown	Unknown
D.M.	61/F	Yes	Generalized	3	Yes	Yes
S.J.	53/F	Yes	Face/eyelid	2	Yes	No
B.L.	56/F	Yes	Eyelid	2	Yes	No
C.C.	41/F	Yes	Face/eyelid	2	No	Yes
J.T.	28/F	No	Generalized	2	Yes	Yes
W.M.	56/F	Yes	Lip	4	No	Yes
G.R.	70/F	Yes	Face/scalp	3	Yes	Yes
T.B.	54/F	No	Generalized	3	No	Yes

versity of Kansas Medical Center for cutaneous allergies between 1994 and 1998. Furthermore, we delineated the distribution of the rash and whether these patients wore gold jewelry and/or had dental appliances containing gold. Finally, we evaluated the clinical relevance of the allergy to the patient's symptoms by assessing their response to discontinuing the use of gold jewelry.

Materials and Methods

From July 1, 1994 through June 30, 1998, 355 consecutive patients at the University of Kansas Medical Center (Kansas City, Kansas) underwent patch testing for medically indicated reasons to the North American Contact Dermatitis Group's (NACDG) standard screening tray. Demographic data regarding age, gen-

der, occupation, and chemical exposure patterns (including to gold) were collected before patch testing. During this time period, the NACDG standard screening series included gold sodium thiosulfate (GST), 0.5% (w/w) in petrolatum (Chemotechnique Diagnostics, AB, Malmö, Sweden). The allergens were placed over the upper back using Finn Chambers® (Epitest Ltd., Öy, Tuusula, Finland) and adhered with Scanpor® tape (Norgesplaster Aksjeselskap, Vennesia, Norway). The patch-test allergens were removed after 48 hours, and reaction sites were read at this time and again at 96 hours after initial placement. Positive patch-test reactions were interpreted as follows: erythema, infiltration, and possible papules (1+); erythematous papules and/or vesicles (2+); spreading blisters and/or crust with ulceration (3+); macular erythema only (?); and irritant

reaction. Exclusion criteria for patch testing included the recent use of topical steroids on the back, the use of oral steroids during the 2 weeks before testing, and any medical condition that could alter skin reactivity.

Results

Seventeen patients (4.8%) had a positive patch test to 0.5% GST. Among the 50 allergens on the standard screening series, GST was the 20th most frequent. Sixteen of the 17 patients were female (94%). The mean age of those patch tested was 53.3 years. None of our patients had any occupational contact with gold. Seven of these 17 patients (43.8%) presented with eyelid dermatitis; 6 of the 17 (35.3%) had a facial dermatitis; and only 1 of the 17 (5.1%) had a rash underlying her gold jewelry. Unfortunately, this latter patient with presumed jewelry-induced dermatitis was lost to subsequent follow-up.

Fifteen of the 17 patients were contacted following patch testing to assess their response to allergen avoidance, including avoidance of contact with gold jewelry. Nine (60%) of these 15 had gold fillings that were at least 5 years old and one patient reported having had a gold filling placed recently (Table I). However, none of our patients who had dental gold was advised to have the allergen removed. Seven patients reported completely discontinuing contact with their gold jewelry. Three of the seven patients allergic only to gold noted complete clearing of their eruptions despite the continued presence of oral gold in two of them. Four of the seven patients allergic to gold and other allergens removed their gold jewelry, avoided their other known allergens, and experienced resolution of their eruptions despite the continued presence of dental gold in two patients. These latter four patients have not been rechallenged with gold jewelry. Seven patients did not remove their gold jewelry or dental appliances; nonetheless their eruptions cleared with the avoidance of other allergens. One patient removed her gold jewelry, had no dental gold, had no other known allergies, and continued to experience her eruption. This patient was later classified as having seborrheic dermatitis.

Discussion

Allergic reactions to GST have recently captured the interest of dermatologists. Furthermore, the reported incidence rate of reactions to gold has risen dramatically. Björkner *et al.*⁵ reported that, among their patients, gold was the second most common allergen following nickel. There are several factors that may have a role in this recent trend. According to Fowler,¹⁷ gold sodium thiosulfate or gold sodium thiomalate should be used for patch testing instead of such previously used materials as gold chloride and/or gold leaf, which com-

monly induce false-positive (irritant) reactions and false-negative reactions. In addition, the prevalence of gold exposure in a given population may contribute to the incidence of gold allergy. It has been suggested that nickel allergies may signify a propensity to develop allergies to other metals.¹⁸ Since the prevalence of nickel allergy is relatively high and continues to increase in the United States,¹⁹ and considering the causal relationship between nickel allergy and jewelry usage,¹⁴ the increased rate of allergic responses to gold should not be surprising. Silva and colleagues¹ suggested that the degree of oral corrosion of gold fillings might also be a factor, especially if there was evidence within a population for an increased use of gold in dental materials. Finally, parenterally administered gold, especially through the oral route, has come back into favor for the treatment of rheumatoid arthritis and other rheumatologic diseases. Nonetheless, one should not overlook a more obvious reason for the sudden and dramatic increase in the reported incidence of gold allergy: established research groups such as the NACDG have only recently started to screen their patient populations for this allergy.

In our study, we used gold sodium thiosulfate (0.5%, petrolatum) for patch testing. We observed an incidence of gold allergy of 4.8%, a finding consistent with the range that other groups have recently reported.^{1,7} We found that all of our patients with gold allergies had a history of wearing gold jewelry, 60% had gold fillings (although in no cases did the placement of dental gold correlate with the onset of dermatitis), none had used dental gold "jewelry," and none had had parenteral gold treatments. As with many other investigators, we had not previously tracked incidence rates for gold allergy; therefore, whether the 4.8% incidence represents a declining, stable, or increasing prevalence of gold allergy remains elusive.

The relevance of positive patch-test reactions to GST is currently under debate. Studies have shown considerable variability in whether a positive reaction to gold has any significance. In a study conducted in Singapore, 345 patients were patch-tested to GST 0.5% and 22 (6.4%) had a positive reaction. However, only 3 (13.6%) of these 22 patients were found to have clinically relevant allergic reactions to gold.²⁰ In our study, the clinical relevance was surmised from the 15 patients with gold allergy that we re-evaluated. Three (20%) of the 15 patients had definite clinical relevance (gold was the only allergen; discontinuing gold exposure resulted in remission of their dermatitis). Four (27%) of the 15 had questionable relevance (discontinuing contact with gold and other allergens resulted in remission). It is also important to note that 14 (93%) of the 15 patients re-evaluated had clearing of their

dermatitis, and yet none of these patients had their gold fillings removed. Indeed, the only patient whose eruption persisted had no dental gold and was subsequently diagnosed as having seborrheic dermatitis. Thus, although we advise our gold-allergic patients to avoid having new dental-gold appliances placed, we do not routinely advise them to have existing dental gold removed. Nonetheless, it may be necessary to remove dental gold if there is a strong temporal correlation between the onset of a dermatitis and the placement of dental gold, or if mucosal pathology develops adjacent to dental gold in the gold-allergic patients. However, based upon our data, we strongly advise that patients allergic to gold discontinue all cutaneous contact with gold jewelry for several months to assess their response to avoidance. This is particularly true for women who present with eyelid, earlobe, facial, nuchal, and digital dermatitis. The need to avoid gold for such a prolonged time relates to the fact that allergic reactions to gold may persist for 3 weeks or more following contact with the allergen.⁸

REFERENCES

1. Silva R, Pereira F, Bordalo O, *et al.*: Contact allergy to gold sodium thiosulfate: a comparative study. *Contact Derm* 37: 78-81, 1997.
2. Fleming C, Forsyth A, MacKie R: Prevalence of gold contact hypersensitivity in the West of Scotland. *Contact Derm* 36: 302-304, 1997.
3. Fleming C, Lucke T, Forsyth A, *et al.*: A controlled study of gold contact hypersensitivity. *Contact Derm* 38: 137-139, 1998.
4. McKenna KE, Dolan O, Walsh MY, *et al.*: Contact allergy to gold sodium thiosulfate. *Contact Derm* 32: 143-146, 1995.
5. Björkner B, Bruze M, Moller H: High frequency of contact allergy to gold sodium thiosulfate: an indication of gold allergy? *Contact Derm* 30: 144-151, 1994.
6. Bruze M, Edman B, Bjorkner B, *et al.*: Clinical relevance of contact allergy to gold sodium thiosulfate. *J Am Acad Dermatol* 31: 579-583, 1994.
7. Sabroe RA, Sharp LA, Peachey RD: Contact allergy to gold sodium thiosulfate. *Contact Derm* 34: 345-348, 1996.
8. Aro T, Kanerva L, Hayrinen-Immonen R, *et al.*: Long-lasting allergic patch test reaction caused by gold. *Contact Derm* 28: 276-281, 1993.
9. Belsito DV: Chapter 119. "Allergic Contact Dermatitis". In, *Dermatology in General Medicine* (T.B. Fitzpatrick, A.Z. Eisen, K. Wolff, I.M. Freedberg, K.F. Austen, eds.), ed 4, pp 1531-1542. New York: McGraw-Hill Book Co., 1993.
10. Fregert S, Kollander M, Poulsen J: Allergic contact stomatitis from gold dentures. *Contact Derm* 5: 63-64, 1979.
11. Kilpikari I: Contact allergy to gold with pharyngeal and laryngeal disorders. *Contact Derm* 37: 130-131, 1997.
12. Laeijendecker R, van Joost T: Oral manifestations of gold allergy. *J Am Acad Dermatol* 30: 205-209, 1994.
13. Wiesenfeld D, Ferguson MM, Forsyth A, *et al.*: Allergy to dental gold. *Oral Surgery* 57: 158-160, 1984.
14. Nakada T, Iijima M, Nakayama H, *et al.*: Role of ear piercing in metal allergic contact dermatitis. *Contact Derm* 36: 233-236, 1997.
15. Fleming C, Burden D, Fallowfield M, *et al.*: Lymphomatoid contact reaction to gold earrings. *Contact Derm* 37: 298-299, 1997.
16. Armstrong DK, Walsh MY, Dawson JF: Granulomatous contact dermatitis due to gold earrings. *Br J Dermatol* 136: 776-778, 1997.
17. Fowler JF: Allergic contact dermatitis to metals. *J Am Contact Derm* 1: 212-223, 1990.
18. Marcusson JA: Contact allergies to nickel sulfate, gold sodium thiosulfate and palladium chloride in patients claiming side effects from dental alloy components. *Contact Derm* 34: 320-323, 1996.
19. Marks JG, Belsito DV, DeLeo VA, *et al.*: North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. *J Am Acad Dermatol* 38: 911-918, 1998.
20. Leow YH, Ng SK, Goh CL: A preliminary study of gold sensitization in Singapore. *Contact Derm* 38: 169-170, 1998.