

Determining the clinical relevance of positive patch testing to gold in evaluation of contact dermatitis

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Clinical Implications

- Gold is one of the most common positive allergens on patch testing for allergic contact dermatitis, but in many cases, a positive test result is clinically irrelevant.

TO THE EDITOR:

Contact dermatitis (CD) is an inflammatory skin condition characterized by pruritic, well-defined, eczematous plaques caused by direct contact of a substance with the cutaneous surface.¹ Most cases are due to an irritant reaction, with only a small proportion having an underlying allergic mechanism.² Patients with suspected allergic contact dermatitis (ACD) are often referred to a dermatologist for evaluation, and more recently allergists have had increased referrals for ACD.³ The criterion standard for identification of the agent responsible for CD is patch testing.¹ Patch testing attempts to recreate, in vivo, evidence of cutaneous reactivity to a nonirritating concentration of an allergen in question. More than 4350 chemicals have been identified as a potential cause of ACD, but it would be impractical to test that many substances on each patient. Therefore, the North American Contact Dermatitis Group, a domestic conglomerate of dermatologists who collect epidemiologic data on CD, has identified substances that it deems most likely to be offending agents and publishes this information every few years.⁴ Testing companies use this information to design and manufacture patch testing kits, such as the Thin-Layer Rapid-Use Epicutaneous (T.R.U.E.) test (SmartPractice, Phoenix, Ariz) and the North American Extended Series (Dormer Laboratories, Toronto, Ontario, Canada). The T.R.U.E. test is the only Food and Drug Administration–approved, commercially available patch testing method in the United States and is often used by practicing allergists and dermatologists because of its ease of application.³ The T.R.U.E. test consists of 3 adhesive panels currently composed of 35 allergens, and 1 negative control. Additional allergens that have not been approved by the Food and Drug Administration can be obtained from other sources (AllergEAZE from SmartPractice and Chemotechnique from Dormer Laboratories).

Gold is a questionable hapten.⁵ For it to cause dermatitis, it needs to be solubilized, which does not happen spontaneously when in contact with the skin for any duration of time.⁶ The solubilization of gold happens most readily when dissolved by “aqua regia,” a mixture of nitric acid and hydrochloric acid.⁷ Gold allergenicity is evaluated by patch testing with gold sodium thiosulfate (GSTS). A few studies have reported on the interpretation of positive patch testing to gold.^{8,9} Here, we report high rates of clinically irrelevant positive patch testing to gold in

those undergoing evaluation of ACD at our academic allergy practice.

We performed a retrospective chart review of outpatient encounters at a single academic Allergy and Immunology practice between April 2010 and May 2016. A total of 588 patients underwent patch testing during this period. The patch testing was performed using the T.R.U.E. test alone, which includes GSTS (75 µg gold/cm² in hydroxypropyl cellulose gel vehicle; T.R.U.E. Test package insert) in its assay or in combination with the North America Contact Dermatitis Group Extended Series, which does not contain gold. Patch tests were applied by a small number of well-trained nurses and were interpreted by a board-certified allergist, and occasionally a second allergist, both with at least 15 years of experience in patch testing. Patch testing was read after 48 hours and again after 96 hours using International Contact Dermatitis Research Group criteria: doubtful (?+); mild reaction, possible erythema, infiltration, and papules (+); strong reaction, erythema, infiltration, papules, and vesicles (++); very strong reaction, intense erythema, infiltration, and coalescing vesicles (+++); irritant reaction, of various types (IR); or not tested (NT).¹⁰

Patient demographic characteristics are listed in Table I. Patient ages ranged from 4 to 92 years, with the average age of 51.9 years in the positive group and 48.2 years in the negative group. In those with positive test results, 53 (88.3%) were female, 54 (90%) were white, and the most common site of dermatitis was the head/neck (45%).

A total of 369 patients (63%) were positive to at least 1 allergen. Gold was the second most common allergen, after nickel, and was positive in 60 patients (10.3%). Patients were subdivided into those with positive or negative testing for GSTS. Of the patients who were positive for GSTS, 17 (30%) patients were also positive for nickel sulfate and 3 (5%) were positive for cobalt dichloride (Figure 1). Only 2 patients with positive patch testing for gold had history suggestive of clinical reactivity. One patient had dermatitis in a similar distribution to their gold jewelry, and the second patient had complained of “unspecified issues” with wearing gold jewelry in the past.

Of the remaining 58 patients who tested positive to gold, the reaction was determined to be clinically irrelevant; the most common reason was tolerance of wearing gold jewelry in the past without episodes of dermatitis or irritation from gold jewelry reported in 21 patients (36%). Seventeen (29%) patients had dermatitis in a location where they never had exposure to gold (such as a perioral rash or scalp rash), which could be better explained by being positive for other allergens. Ten (17%) patients had no history of any metal allergies but no explicit gold exposure. Five (8%) patients were positive on patch testing to chemicals in other products that were in contact with the location of the dermatitis. Two (3%) patients who thought they were reacting to their gold rings were determined to be sensitized to cleansing products they were using on their hands that were getting trapped under their rings. One patient on repeat patch testing was negative for gold. Finally, 1 patient was found to have chronic urticaria with eosinophilic dermatitis on punch biopsy.

Positive patch testing to gold can be challenging to interpret. In our small retrospective study, gold was the second most

TABLE I. Patients' demographic characteristics (n = 585)

Characteristic	Positive to GSTS (n = 60)	Negative to GSTS (n = 525)
Age (y)	5.9	48.2
Range	5-89	4-92
Sex, n (%)		
Female	53 (88.3)	365 (69.5)
Male	7 (11.7)	160 (30.5)
Ethnicity, n (%)		
White	54 (90)	401 (76.4)
Black	1 (1.7)	28 (5.3)
Asian	2 (3.3)	21 (4)
Hispanic	0 (0)	6 (1.1)
Other	3 (5)	62 (11.8)
History of atopy,* overall	39 (65)	297 (56.6)
Distribution of rash/symptoms, n (%)		
Head or neck	27 (45)	172 (32.8)
Trunk	17 (28.3)	113 (21.5)
Extremities	26 (43.3)	190 (36.2)

*Eczema, allergic rhinitis, or asthma.

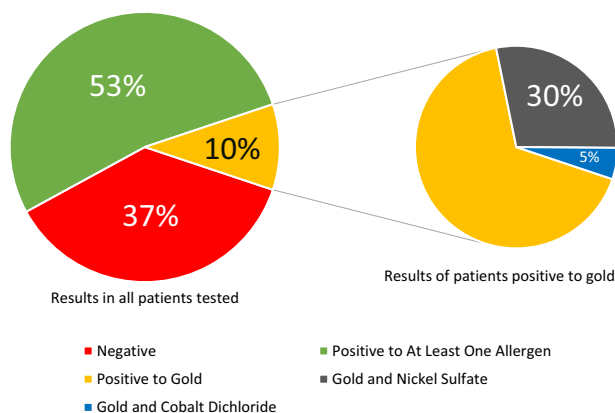


FIGURE 1. Proportion of positive and negative patch test results in all evaluated patients, including the percentage positive to gold. In the subset positive to gold, the proportion of those positive to other metals including cobalt dichloride and nickel sulfate was also included.

positive allergen on patch testing; however, after careful review of patient history, in most cases it was determined to be clinically irrelevant. A previous review has highlighted the controversies associated with gold contact allergy, and recommended to screen for gold allergy in cases of dermatitis involving the face, eyelids, ears, hands, and neck or when jewelry allergy is suspected.⁵ Our study demonstrates that although gold is often positive on patch testing, it should be a diagnosis of exclusion. A thorough history is imperative in establishing clinical relevance, and patients should be counseled appropriately to prevent unnecessary avoidance.

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REFERENCES

1. Beltrani VS, Beltrani VP. Contact dermatitis. *Ann Allergy Asthma Immunol* 1997;78:160-73. quiz 74-76.
2. Fonacier LS, Sher JM. Allergic contact dermatitis. *Ann Allergy Asthma Immunol* 2014;113:9-12.
3. Fonacier L, Bernstein DI, Pacheco K, Holness DL, Blessing-Moore J, Khan D, et al. Contact dermatitis: a practice parameter—update 2015. *J Allergy Clin Immunol Pract* 2015;3:S1-S9.
4. Schalock PC, Dunnick CA, Nedorost S, Brod B, Warshaw E, Mowad C. American Contact Dermatitis Society Core Allergen Series: 2017 update. *Dermatitis* 2017;28:141-3.
5. Chen JK, Lampel HP. Gold contact allergy: clues and controversies. *Dermatitis* 2015;26:69-77.
6. Bjorkner B, Bruze M, Moller H. High frequency of contact allergy to gold sodium thiosulfate. An indication of gold allergy? *Contact Dermatitis* 1994;30:144-51.
7. Sheng PP, Etsell TH. Recovery of gold from computer circuit board scrap using aqua regia. *Waste Manag Res* 2007;25:380-3.
8. Fleming C, Lucke T, Forsyth A, Rees S, Lever R, Wray D, et al. A controlled study of gold contact hypersensitivity. *Contact Dermatitis* 1998;38:137-9.
9. Lee AY, Eun HC, Kim HO, Moon KC, Lee CH, Kim GJ, et al. Multicenter study of the frequency of contact allergy to gold. *Contact Dermatitis* 2001;45:214-6.
10. Fregert S, International Contact Dermatitis Research Group. Manual of contact dermatitis: on behalf of the International Contact Dermatitis Research Group. Copenhagen: Munksgaard; 1974.