

Gold trichloride and gold sodium thiosulfate as markers of contact allergy to gold

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The usefulness of a trivalent gold salt, gold trichloride (GTC), was evaluated as a marker of contact allergy to gold. Patients patch test-positive or patch test-negative to gold sodium thiosulfate (GSTS), 13 subjects of each, were patch tested with dilution series of GTC and equimolar concentrations of GSTS. In order to avoid false-positive and false-negative test reactions, the salts were buffered and placed on polypropylene chambers. Allergic reactions were registered in 9/13 gold-allergic patients with GSTS and in 2/13 with GTC. The sum of positive reactions was 18 with GSTS and 5 with GTC. Irritant reactions were none with GSTS and 2 with GTC in the gold-allergic patients. It is concluded that GTC can elicit positive patch test reactions in patients with gold allergy but to a lesser degree when compared with GSTS. Thus, GTC cannot be recommended in patch testing, and GSTS is still the test agent of choice.

Key words: buffered solution; gold sodium thiosulfate; gold trichloride; patch test material.
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When patch testing to demonstrate contact allergy to gold, the monovalent salt gold sodium thiosulfate (GSTS) is nowadays recommended (1, 2). In early reports on contact dermatitis to gold, testing was usually performed with metallic (elemental) gold, which with few exceptions tested negative, and/or with the trivalent gold chloride (GTC). However, many authors (3–6) have pointed out the difficulties in interpreting test reactions from GTC because of suspected primary toxic reactions. Nevertheless, more than 20 publications can be found in which this chemical has been tested and the reaction considered positive, in many cases without considering the possibility of false-positive results or without using proper controls.

In the present study, we wanted to evaluate the efficacy of GTC as a marker of contact allergy comparing it – in equimolar concentrations – with that of GSTS. The test agents were buffered to counteract the acidity of the solutions, and chemical reactions with metallic aluminium were avoided by substituting plastic test chambers.

Materials and Methods

Patients

Patients who had earlier shown positive or negative patch test reactions to GSTS were recalled

for the study. There were 13 gold-positive patients (2 males and 11 females, mean age 60 years) and 13 gold-negative patients (1 male and 12 females, mean age 49 years). Informed consent was obtained from the patients, and the study was approved by the Ethics committee of the Lund University Medical Faculty.

Chemicals

GSTS was obtained from Chemotechnique Diagnostics, Tygelsjö, Sweden, and GTC from Acros Organics, Morris Plains, NJ, USA. In order to avoid irritant test reactions, all the aqueous preparations were buffered (7). To make the solutions equimolar, the highest concentration for GSTS was 1.6%, for GTC 0.93%. A dilution series in 5 steps was prepared with $\sqrt{10}$ as a dilution factor.

Patch testing

Testing was performed using van der Bend[®] polypropylene chambers fastened with Scanpor[®] tape. The patches were applied on the back for 48 hr. Each dilution series was placed with the steps kept together in falling concentration. The location on the back between the two chemicals, however, changed in a randomized way from one patient

to another, which allowed for a blind reading. On D3 and D7, the test reactions were read according to the International Contact Dermatitis Research Group recommendations (8).

Results

The results of patch testing with GSTS and GTC in 26 patients are summarized in Table 1. Among 13 gold-positive patients, there were 9 subjects with ≥ 1 allergic reaction to GSTS and 2 patients with ≥ 1 allergic reaction to GTC on D7 ($P = 0.016$, MacNemar's test, two-sided). These two latter subjects were positive to GSTS as well. Among the originally gold-negative patients, there were 2 subjects reacting allergically to GSTS and none to GTC. If not making any distinction between allergic and irritant reactions in individual test and control patients, the sensitivity and specificity were 69% and 69%, respectively, for GSTS, and 23% and 92%, respectively, for GTC.

Counting the total number of allergic reactions in the dilution series on D7, there were 18 such ones to GSTS and 9 to GTC among the gold-positive patients, and 2 such ones to GSTS and none to GTC among the gold-negative patients.

There was an obvious increase of patients with allergic reactions to GSTS from D3 to D7, not so with regard to GTC.

There were 4/26 patients with irritative reactions, 2 for GSTS and 2 for GTC.

Discussion

In our early studies on contact allergy to gold, it was found that the allergy could be demonstrated not only with GSTS but also with the monovalent salts potassium dicyanoaurate and gold sodium thiomalate (9, 10). In the present paper, we have compared the efficacy of GSTS with that of a previously popular trivalent salt, GTC, as a test agent, and we found that contact allergy could be demonstrated with both salts. However, many more patients with a previously known contact allergy to gold reacted to GSTS than to GTC, and when results of testing serial dilutions were

counted, twice as many reactions were found to GSTS than to GTC. Two of the control patients who had tested negatively to GSTS during the last years were now test-positive which must be interpreted as a later sensitization. Alternatively, it might be due to a change of reactivity of an old contact allergy to gold but with a degree of reactivity to GSTS below the detection level at the previous patch testing (11).

The risk of inducing false-positive patch test reactions with GTC is obvious: an aqueous solution of this salt turns acidic already in moderate concentrations as hydrochloric acid is formed. We found 23 papers from the literature on allergic contact dermatitis from gold, demonstrated by a positive patch test to aqueous GTC in concentrations 0.1–2.0%, most commonly 1.0% (Table 2). In most cases, GTC has been used, in a few, the monochloride, and in some, the valence is not clear. In the present paper, both GSTS and GTC were buffered, leading to a pH of 7.1 for GTC and of 7.0 for GSTS of our highest test concentrations. Thereby, irritant test reactions were few, occurring in only 4 of 26 patients (Table 1).

When interpreting positive patch tests as being of an allergic or irritative nature, traditional clinical criteria were followed. Such criteria have not, however, been fully established for D7 readings. For the present study, we chose to optimize the evaluation by using blind readings.

Another risk when using GTC in occlusive testing, leading to false-negative results, is a chemical reaction between the salt and metallic aluminium of the test material such as Finn chambers[®], as recently described (12). In the present study, the corrosion could be avoided by using polypropylene test chambers instead of aluminium. It was confirmed, at least with GSTS as a test agent, that gold patch tests in many cases develop late (13); at least two test readings are required.

One report on a clinical contact dermatitis to gold (14) was intriguing: during patch testing with gold sodium thiomalate, a flare-up of a previous, distant dermatitis was observed, and this was repeated when testing with gold chloride.

Table 1. Patch test reactions to gold salts in 13 gold-positive and 13 gold-negative patients

	Reading D3 (<i>n</i> patients)	Reading D7 (<i>n</i> patients)
Gold-positive		
Test with GSTS	6 AR, 0 IR	9 AR, 0 IR
Test with GTC	2 AR, 1 IR	2 AR, 1 IR
Gold-negative		
Test with GSTS	0 AR, 2 IR	2 AR, 2 IR
Test with GTC	0 AR, 1 IR	0 AR, 1 IR

GSTS = gold sodium thiosulfate; GTC = gold trichloride; AR = allergic reaction; IR = irritant reaction.

Table 2. Reports on positive patch tests to aqueous gold chloride/trichloride

First author, year (reference)	Concentration %	Reading	Positive control	Negative control
Fox 1961 (16)	2.0	D2 D3	GSTM	
Shelley 1963 (17)	1.0	Not given	GPC, i.d.	Yes
Malten 1966 (18)	2.0	Not given		
Bowyer 1967 (19)	1.0	D2 D7	GSTM	
Comaish 1969 (20)	2.0, 0.2	D2 D3		Yes
Schöpf 1970 (21)	1.0, 0.1	D2	<i>in vitro</i>	Yes
Elgart 1971 (14)	0.5	D1	GSTM	
Cooke 1973 (22)	1.0	D2 D7	GSTS	
Petros 1973 (23)	0.5	D3		
Fisher 1974 (24)	0.5	Not given		
Young 1974 (25)	1.0	D2 D5		Yes
Klaschka 1975 (26)	0.5	Not given		
Roeleveld 1975 (27)	2.0–0.5	D1 D2		Yes
Cronin 1980 (3)	0.5, 0.1	D2 D4		
Izumi 1982 (28)	0.5	Not given	GSTM, i.d.	
Wiesenfeld 1984 (29)	1.0	D2 D4		
Trathen 1985 (30)	1.0	D2 D3		
van Loon 1986 (5)	1.0	Not given		Yes
Dutrée-M. 1992 (31)	1.0	Not given		
Laeijendecker 1994 (6)	0.5, 1.0	D2 D4		
Osawa 1994 (32)	0.2	D2 D3	GSTM, GPMT, i.d.	
Nakada 1997 (33)	0.2	D3		
Nonaka 2003 (34)	0.2	D3		

D = test reading day; positive control = test positive with other chemical or reaction; negative control = negative tests in controls; GSTM = gold sodium thiomalate; GSTS = gold sodium thiosulfate; GPC = gold potassium chloride; i.d. = intradermal test; GPMT = guinea-pig maximization test.

We have recently been able to confirm this percutaneous absorption of ionized gold from occluded patch tests (15).

Because GTC does not seem to elicit as many allergic test reactions as GSTS and, in addition, may induce irritant reactions if not properly buffered, GSTS should be the test chemical of choice. If for some reason testing with GTC still might be of interest, the test solution should be buffered and polypropene chambers substituted.

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