

A controlled study of gold contact hypersensitivity

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1203 patients attending for routine patch testing at 3 hospitals and 105 volunteers were tested with 0.5% and 0.05% gold sodium thiosulfate (GST). 38 patients (3.2%) and 5 volunteers (4.8%) had positive patch tests to GST. There were no significant differences between volunteers and patients with respect to age, sex, atopy or exposure to gold in dental restorations, jewellery or through occupation. There were no significant differences in prevalence of GST hypersensitivity in the 3 hospitals, or between patients and controls. This is the 1st controlled study of hypersensitivity to GST, and suggests that routine patch testing to gold is of limited clinical benefit.

Key words: allergic contact dermatitis; contact hypersensitivity; gold; gold sodium thiosulfate; patch testing; delayed hypersensitivity; controlled study, multicenter study, metal hypersensitivity.
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A number of recent studies have suggested that cutaneous hypersensitivity to the gold salt, gold sodium thiosulfate (GST), is common in patients who are routinely patch tested (1–4). However, the prevalence of gold hypersensitivity in the normal population is not known, and the clinical significance of a positive patch test to GST in patients with eczema is therefore unclear. We have examined the prevalence and clinical relevance of hypersensitivity to GST in patients attending for diagnostic patch testing in 3 hospitals in Central Scotland, and in a group of volunteers. This was done by addition of GST to the European standard series, and questionnaire assessment of gold exposure.

Patients and Methods

The study was approved by the local ethics committees. Patients attending the Dermatology Departments of the Western Infirmary, Glasgow (WI), Glasgow Royal Infirmary (GRI) and Edinburgh Royal Infirmary (ERI) for patch testing were tested to 0.5% and 0.05% GST (Chemotechnique, Malmö, Sweden) in petrolatum (pet.) in addition to other investigations. Staff of the Glasgow Dental Hospital, who had volunteered to be patch tested to the European standard series as controls

for a separate study, were also invited to be patch tested to 0.5% and 0.05% GST. 15 of the volunteers worked with gold in dentistry and the others were not in contact with gold through their job. The control group was of similar ethnic origin to the patients.

The tests were attached using Finn Chambers and Scanpor tape. Patches were removed after 2 days and read after 2 and 4 days. Reactions were scored as recommended by the International Contact Dermatitis Group (5).

All volunteers and patients attending 1 hospital (WI) were invited to complete a questionnaire (modified from Bruze (1)) prior to patch testing, and the presence of eczema and possible sources of contact with gold were determined.

Results

1203 patients and 105 volunteers were patch tested. 373, 640 and 190 patients were patch tested at GRI, ERI and WI, respectively. 38 patients (3.2%) and 5 volunteers (4.8%) had positive patch tests to either 0.5% or 0.05% GST, or both. The mean age of patients was 42 years (range 16–88 years) and the mean age of controls was 32 years (range 18–59 years). The prevalence of positive patch tests to GST at each of the centres was 2.1% (WI), 4.1%

Table 1. Details of patients and volunteers derived from questionnaire

	Patients (n=190)	Volunteers (n=105)
mean age (years)	41	32
female: male	3.6:1	2.5:1
presence of eczema	99%	14%
presence of atopic disease	24%	17%
gold jewellery normally worn	66%	67%
mean age of ear-piercing (years)	17	15
history of gold therapy	none	none
gold dental restorations	17%	18%
contact with gold through occupation	1%	14%
patients or volunteers suspecting gold allergy before testing	3%	none
history of resolution of eczema after gold avoidance	2%	none
positive patch test to GST	2.1%	4.8%

(ERI) and 2.2% (GRI). There were no significant differences amongst the 3 patient groups and the control group (χ^2 , $p=0.298$) or between the combined patient group and controls (χ^2 , $p=0.212$). Detailed analysis of patients patch tested to GST at GRI has been published elsewhere (6).

The questionnaire responses in the patient and control group are shown in Table 1. The mean age of patients and volunteers was 41 years, and 32 years, respectively. The female: male ratio was 3.6:1 in patients and 2.5:1 in the control group. There were no significant differences in responses to questions regarding atopy, exposure to gold jewellery, dental gold and therapeutic gold (χ^2 , $p>0.05$, $p>0.01$, $p>0.01$, $p>0.01$, respectively). 15 volunteers (14%) had a history of exposure to gold in their occupation but none of these had a positive patch test to GST. No volunteers suspected gold allergy, and none gave a history of eczema resolving after gold avoidance.

Discussion

There has been much recent debate concerning patch testing with GST (1–4, 6–12) (also, 7 related presentations at the Jadassohn Centenary Congress, London, 1996). Bruze et al. noted 10% of patients patch tested were positive to the salt, the 2nd most common allergen after nickel sulfate in their population (1). Other investigators have found 4.6% (2) and 13% (3) of patients attending for patch testing had positive responses to GST, and that 12.4% of dental patients had a positive patch test to GST (4). It is difficult to assess the relevance of positive patch tests to GST, since the majority of patients have no detectable relationship between the test result and clinical events. Previous studies have lacked control groups of individuals without skin disease, and we hypothesized

that if GST was a marker of clinically relevant gold allergy, then it should occur with a greater frequency in patients referred with suspected cutaneous contact allergy than in individuals without skin disease.

Patients were patch tested in 3 centres in 2 cities, to obtain an impression of the variation between centres. Antigens, procedures and readings were standardized. The prevalence of positive responses to GST were 2.2%, 2.1% and 4.1%, and there was no significant difference in prevalence between patients and volunteers. This implies that gold allergy is unlikely to be involved in the pathogenesis of eczema in patients with positive patch tests to GST.

The control group had a lower mean age than the study groups, with a higher proportion of males, but were of similar ethnic background. GST hypersensitivity is commoner in females and there was no particular age preference in our population (6), so these differences do not explain the high prevalence of GST hypersensitivity in the control group. The control group did have some individuals with skin disease. 14% of the control group reported eczema and were included for study as it was felt this was representative of the general population. Possible sources of exposure to gold were determined from the questionnaire and were similar in both groups. There were no significant differences in reported exposure to dental gold, therapeutic gold or gold jewellery between patients and volunteers. The control group could be criticized as appearing to have a high exposure to gold, but 86% of this group were administrative or clerical workers with no history of occupational gold exposure. In addition, none of those reporting occupational contact with gold had positive patch tests to GST, suggesting that occupational contact with gold is not an important factor in development of GST hypersensitivity.

The patch test response to GST appears to represent true contact allergy, rather than an irritant contact reaction (10, 11). GST therefore seems to be a "hidden allergen", analogous to thimerosal (13), and a positive reaction may result from a previous subclinical sensitization. There is little structural similarity between thimerosal and GST, and the sulfur group in the 2 molecules is in a different oxidation state, so the reaction pattern does not appear to be due to a chemical similarity. An alternative explanation of GST hypersensitivity is that it is a cross-reaction common to transition metals, as patients are often sensitive to other metals (12).

There are few studies of patch testing using individuals without significant skin disease as controls. Previous studies have compared routinely patch tested patients with positive and negative results

to GST (1, 3). We have also examined part of the population described in this study in this manner and found no association between a positive patch test to gold and dental or therapeutic gold, or ear-piercing (6). Patch testing alone is an imprecise method of determining allergic contact hypersensitivity, but it should be possible to gain additional evidence-based insight into the use of this investigation with further studies of populations without significant skin disease.

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