

technique but a more precise analytical method, may not be significant and could fall within experimental error.

However, human sweat does contain a substantial proportion of amino acids, which are not present in the composition of artificial sweat used by Lidén et al. According to Brown et al. (2), amino acids will complex gold ions, but the relevance of their study to gold contact dermatitis is not at all clear, since (a) the absence of data on surface area of the gold metal/alloy specimens tested does not permit calculation of rates of release, (b) the solutions used contained only amino acids and none of the other constituents occurring in human sweat, (c) the concentrations of amino acids used were greater than those found in human sweat, while the pH values were outside the normal range, and (d) hydrogen was often used as a cathodic stimulant.

The reported cases of allergic contact dermatitis due to gold metal almost certainly refer to gold alloys, since fine gold is too soft and is rarely used in jewellery, at least in Europe. The alloying constituents in yellow gold alloys are most commonly silver, zinc and copper. The latter 2 constituents will dissolve preferentially from gold alloys exposed to sweat, so that zinc and copper ions must also be considered. Zinc ions are thought to be non-allergenic but contact dermatitis due to copper alloys has been reported (1). Further, the effect that the alloying constituents could have on release of gold in human sweat is not known, although the results from Brown et al. (2) indicate that low carat gold alloys are more likely to suffer corrosion.

Thus, the data are not yet available on which it would be possible to make a definitive statement on whether gold ions can be released from metallic

gold and alloys in contact with the skin, in sufficient quantity to provoke an allergic reaction. Further tests are necessary, as recommended by Lidén (ref. (1), previous *Letter*), and the parameters that should be studied are:

- (i) the effect of varying additions of different amino acids to artificial sweat of the composition used by Lidén et al. (ref. (1), previous *Letter*) on the release of metal ions from gold and its alloys;
- (ii) the determination of the concentration and composition of amino acids in human sweats and especially determination of any differences in those persons reportedly suffering from gold contact dermatitis;
- (iii) the effect of alloying constituents on release of metal ions from gold alloys exposed to artificial sweat containing amino acids.

Yours sincerely

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References

1. Flint G N. A metallurgical approach to metal contact dermatitis. *Contact Dermatitis* 1998; 39: 213–221.
2. Brown D H, Smith W E, Fox P, Sturrock R D. The reaction of gold (0) with amino acids and the significance of these reactions in the biochemistry of gold. *Inorganica Chimica Acta* 1982; 67: 27–30.

The frequency of mercury intolerance in patients with chronic fatigue syndrome and healthy controls

Dear Sir

Percutaneous provocation with patch test doses of mercury has enabled us to define a subgroup of patients intolerant to low doses of mercury, reacting with subjective psychosomatic symptoms (1). Neutrophils from this group have a low superoxide anion production when exposed to mercury in vitro (2), which we believe to be an effect of superoxide dismutase (3). Furthermore, data suggesting dysregulation in the serotonergic system in this group have been presented (4). Various sleep disturbances constituted a salient finding among the mercury-intolerant patients (1). These

symptoms were also registered to a large extent among the patients claiming side-effects of metals in dental restoration alloys (5). In addition, we found widespread allergy to nickel, gold and palladium (5).

Recently, we completed a study on chronic fatigue syndrome (CFS) and contact allergy to metals (6). We patch tested for 8 metals or metal salts (potassium dichromate, metallic mercury, cobalt chloride, nickel sulphate, gold sodium thiosulphate, palladium dichloride, tin and silver nitrate) (6), and discovered an extremely high prevalence of nickel allergy, especially in females. To get

Table 1. Number of subjective symptoms in the CFS patients and controls in relation to patch testing and removal of old amalgam

Patient material (no. subjects)	Subjective symptoms during removal of old amalgam (no. patients (%))	Subjective symptoms during the epicutaneous test (no. patients (%))
patients (50)	10 (20)***	13 (26)***
controls (73)	2 (3)***	2 (3)***

*** $p < 0.001$.

Table 2. Symptoms recorded during removal of amalgam and during patch testing

Subjective symptoms during removal of old amalgam	Subjective symptoms during patch testing
joint ache, headache, loss of stamina, general malaise, bed-ridden, exhausted, pain in the lymphoid glands, tiredness, general feeling of upper respiratory infection.	general body ache, headache, vertigo, general malaise, back ache, general feeling of illness, malaise, disturbance of sleep, aching teeth and jaws, loss of stamina, aching muscles, fever, palpitations, early wakening.

an idea of whether mercury intolerance could be overrepresented in the CFS group, and whether the frequency of mercury intolerance was increased in a healthy control group, 2 key questions were posed to the 50 patients and 73 unrelated controls participating in the study, the same as used when selecting patients for the study of mercury intolerance (1), namely: (i) How do you feel during the days following removal of old dental amalgam? (ii) How did you feel during and after the patch test procedure?

Table 1 shows that 20% of the CFS patients and 3% of the controls ($p < 0.001$) responded affirmatively to the first question. Malaise in connection with the patch testing was recorded for 26% of the patients and 3% of the controls ($p < 0.001$). The various symptoms recorded are shown in Table 2. 4 CFS patients recorded symptoms in the 2 situations, which was not the case with the controls.

It is therefore quite clear that anamnestic intolerance to dental mercury and to the metals in the patch test series used is found to a greater extent

among the CFS subjects, compared to the control group, suggesting that mercury intolerance might be included in the CFS category. The findings imply that mercury is the most likely culprit, but the possibility that other metals might be involved is not excluded. However, for exact definition of mercury intolerance, a double-blind provocation needs to be done (1). From the previous investigation, it is evident that 22% of the patients with a positive history of malaise after dental treatment or patch testing with metals were mercury-intolerant after percutaneous provocation (1). Extrapolating these figures to the control group will show that less than 1% of the normal population would be mercury-intolerant. The upper limit would be 3%. Similar calculation would give us a prevalence of mercury intolerance in the CFS group of 5–6%. I consider these figures to be important when estimating how often one might expect to encounter the mercury intolerance problem in a patch test clinic dealing with metal allergy.

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References

1. Marcusson J A. Psychological and somatic subjective symptoms as result of dermatological patch testing with metallic mercury and phenyl mercuric acetate. *Toxicol Lett* 1996; 84: 113–122.
2. Marcusson J A, Jarstrand C. Oxidative metabolism and human mercury intolerance. *Toxicology in vitro* 1998; 12: 383–388.
3. Marcusson J A, Jarstrand C. Mercury intolerance in relation to superoxide dismutase, glutathione peroxidase, catalase and the nitroblue tetrazolium test (NBT). Submitted.
4. Marcusson J A, Cederbrant K, Gunnarsson L G. Serotonin production in lymphocytes and mercury intolerance. Manuscript form, submitted.
5. Marcusson J A. Contact allergies to nickel sulphate, gold sodium thiosulphate and palladium chloride in patients claiming side-effects from dental alloy components. *Contact Dermatitis* 1996; 34: 320–323.
6. Marcusson J A, Lindh G, Evengård B. Chronic fatigue syndrome and nickel allergy. *Contact Dermatitis* 1999; 40: 269–272.