

Letter to the Editor

Nomenclature and contact allergy to nickel and gold

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Dear Editor,

In a recent editorial (1), Lepoittevin, Midander, Thyssen and Lidén state the well-known prerequisites for pure metals and metal alloys to become sensitizers, that is, to act as allergens and induce a contact allergy, and thereby cause an allergic contact dermatitis. In both cases, the metal in contact with the skin needs to release ions, the quantity of which varies between different metals and metal alloys, but also between oxidation states of the metal and the presence of inorganic and organic chemicals in the solution. According to the authors, metallic nickel and cobalt and some of their alloys release significant amounts of ions upon skin contact, whereas, for example, metallic gold does not, at least not at levels sufficient to act as sensitizers. This is, of course, a surprising statement, as worldwide clinical and experimental studies on contact allergy to gold have been carried out during the last 20 years (2).

We, as well as many other test laboratories, have reported the occurrence of clinical cases of allergic contact dermatitis caused by metallic gold (3, 4), as demonstrated by patch testing with several monovalent and trivalent gold salts, and confirmed by an array of other methods (5) in order to disclose false-positive test results. Examples of indirect evidence for gold allergy have also been reported such as: (i) the flare-up of old sites of clinical contact dermatitis and of experimental contact dermatitis (patch test) after systemic provocation with ionic gold (6, 7); (ii) the allergen-specific action of this type of provocation, including cytokine release in the blood (8, 9); (iii) the distant effect of metallic gold on the skin (3); and (iv) the correlation of gold contact allergy with the presence of dental gold (10) and also such allergy in those with gold-coated intracoronary stents (11, 12). To our knowledge, there was no skin contact with gold sodium thiosulfate or other ionized gold preparations in the 'dental' or 'coronary' groups, only with elemental gold and gold alloys. Patients implanted

with a gold-coated stent have an increased risk of in-stent restenosis (13, 14).

Recently, Halwani et al. (15) showed that corrosion occurs *in vivo* in bare-metal stents, and is associated with the release of heavy metal ions into adjacent tissue, with ensuing 'vasculitis' and restenosis. Thus, it seems quite reasonable to assume that the local vascular inflammation leading to restenosis might at least partly be caused by a contact allergy to gold. The prerequisites for an allergic reaction, such as immunocompetent cells, do occur in the vascular wall (16).

Metallic nickel/nickel alloys readily release nickel ions in a salt solution ('artificial sweat'), whereas metallic gold does not (17), or only releases ions in small amounts (18). However, in 1982, Brown et al. (19), when testing several extraction media, found the release of gold ions in solutions containing sulfur-containing amino acids, cysteine in particular. We have confirmed that gold is released from metallic gold in such a solution, which is more similar to the skin surface environment than a simple salt solution (20, 21).

Consequently, metallic nickel and gold are both sensitizers, and can induce contact allergy and elicit allergic contact dermatitis in human skin when they release the specific ions binding to epidermal proteins. Metallic nickel can be patch tested as such, as it easily releases nickel in ionized form. However, during the patch test with a closed application of 48 hr, metallic gold does not release a sufficient number of ions, gold apparently being slower (e.g. as shown by a later crescendo of positive patch test reactions) and also requiring a more demanding micromilieu.

Finally, with regard to nomenclature, we agree that the present terms nickel allergy, cobalt allergy, gold allergy, etc. should be kept for clinical and experimental reports on patients with test reactions to elemental and ionic metal solutions; it should, of course, always be documented which type of test method and which test substance have been used. Terms such as nickel sulfate hexahydrate contact allergy and gold sodium thiosulfate contact allergy are too awkward to handle!

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