

## Clinical and Experimental Studies of Contact Allergy to Stent Metals with Focus on Gold

CECILIA SVEDMAN (WRITTEN ON BEHALF OF SUSANNE EKVIST WHO HAS LEFT HER POSITION)

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Susanne Ekqvist, research nurse from the Department of Occupational and Environmental Dermatology, Malmö University Hospital, defended her PhD thesis, on the 7 November 2008, in Malmö University Hospital, University of Lund, Sweden. The thesis was supervised by Professor Magnus Bruze and the opponent was Associate Professor Mats Berg, Eskilstuna, University of Uppsala, Sweden.

Implants are used increasingly in medicine, both for cosmetic and medical reasons. The number of patients that become sensitized or develop contact allergic eczema or other symptoms of contact allergy due to the use of foreign material is small compared with the total number treated. Various metals are used as alloys in dental material, in orthopaedic implants, and in stents. Many of these metals are known to cause contact allergy as ions under certain circumstances.

Today, percutaneous coronary intervention (PCI) and stenting is a routine procedure used to treat patients with cardiac attacks and angina due to stenosis of the cardiac vessels. Of those patients treated with "bare-metal" stents, 6–10% experience re-stenosis, requiring a second intervention. It has been argued that contact allergy could be a reason for re-stenosis. Gold is still used as a marker in stents, and was previously used as plating for bare-metal stents. Gold-plated stents have been known to cause re-stenosis to a greater extent, and their use has therefore diminished. Previous studies have shown that patients with contact allergy to gold who are given gold systemically develop systemic effects, including increased levels of cytokines. It has also been shown that in patients with contact allergy to gold there is a correlation between the concentration of gold in blood and the exposure to gold.

The thesis was based on a retrospective study performed in the south of Sweden. Over a period of several years data for patients who had undergone PCI and were stented were collected in a database. From this database, patients who had been stented with two stent types, identical in design and material (stainless steel), apart from the fact that one was gold-plated (with 99.9% pure gold) were selected and contacted. The patients thus came to represent two groups, those stented with a stainless steel stent (nickel stent) and those stented with a gold plated stent (gold stent). In this study 484 patients completed a questionnaire, blood samples were taken, and the patients were patch-tested. A total of 447 age- and sex-correlated patients with dermatitis were selected to serve as controls.



Susanne Ekqvist (right) with opponent Associate Professor Mats Berg to her right, supervisor Professor Magnus Bruze and assistance supervisor Cecilia Svedman.

In addition, an experimental study was performed to characterize further the effects of systemic exposure to gold in gold allergic patients.

It was found that the level of contact allergy to gold was significantly higher in both the stented groups compared with the controls ( $p < 0.001$ ). Of the gold-stented patients, 37% (54 of 146) were contact allergic to gold compared with 19% (85 of 447) of controls ( $p < 0.001$ ). With regard to re-stenosis there was a significant difference ( $p < 0.0016$ ) between nickel-stented patients ( $n=44$ , 13%) and gold-stented patients ( $n=42$ , 24.7%). Within the gold-stented group there was a significant difference ( $p=0.03$ ) between those who were gold-allergic and had re-stenosis ( $n=23$ , 33.8%) and those who were not gold-allergic ( $n=19$ , 18.6%).

The gold allergic patients with a gold stent also showed a higher degree of chest pain compared with the non-gold allergic patients.

Contact allergy in general, not including contact allergy to metals, was more common among the control patients, but

among the stented patients certain contact allergies, such as *Myroxylon pereirae* and *cainemix*, were more frequently found indicating perhaps both other exposure routes and exposure patterns.

With regard to the concentration of gold in blood, in the retrospective study this was found to correlate with the intensity of the patch test reaction to gold sodium thiosulphate. This correlation was not found regarding nickel.

The experimental study showed that the concentration of gold in blood is, to a high degree, influenced by topical exposure, and that the increase in concentration lasts for several weeks when a provocation has occurred. The study indicated a relationship between minimal elicitation concentration and the gold concentration in blood, thus indicating that systemic exposure to an allergen may be a factor that influences skin reactivity on topical exposure.