# Allergic Patient Response to Low-Nickel Epidermal Contact

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**Statement of Purpose:** Nickel is the most frequent allergen on a worldwide basis [1]. Hierholzer et. al. [2] found a higher rate of osteosynthesis complications for allergic patients who had Ni containing implants. The objective of the present study was to patch test nickel sensitized patients to determine the minimum $NiSO_4 \cdot 6H_2O$ concentrations in Vaseline that provoked a positive epidermal reaction. Standard implant quality 316L and low-nickel Biodur® 108 (Carpenter Technology, Reading, PA) stainless steel discs were also applied to the subject's backs in order to demonstrate whether a positive patch test reaction was triggered by skin contact.

**Methods:** Test solution were formulated with 5%, 1%, 0.1%, 0.001%, and 0.001% $NiSO_4 \cdot 6H_20$ in Vaseline. The negative control plaster consisted of Vaseline ointment with no additions of nickel sulfate. Metal discs 8 mm in diameter x 1 mm thick were machined from implant quality 316L stainless steel bar, heat 525735, containing 14.68% nickel and Biodur 108 stainless steel, heat 991309, containing 0.034% nickel. The discs were machined from bar, manually deburred to round the edges, and electropolished. The Biodur 108 specimens were laser etched with "108" on one side before electropolishing for positive identification.
Six men and forty four women volunteer subjects aged between 22 and 68 years with known nickel allergies were enrolled in the study. The protocol was approved by the Ethics Commission of the Technical University of Munich and all subjects were insured throughout the study. The nickel sulfate plasters, alloy discs, and negative control plasters were taped to the back if each patient for 48 hours. Each patient was tested with 20 negative control plasters. The test plasters and discs were removed and the skin was assessed after 48 and 72 hours. Skin reactions were documented according to the guidelines of the German Contact Allergy Group. Nickel sensitivity reactions within the test area were graded as (+) papules and infiltration; (++) vesicles; (+++) confluent blisters. Ionic nickel release from the alloy discs was evaluated with a immunoselect test (Squarix Biotechnology, Elbstr. 10, D-45768 Marl). In this test, the metal discs were treated with a drop of high purity water and indicator strip that contained a reagent for detecting nickel ions. The test was positive when the color of the paper changed from white to pink or red. The lowest concentration of nickel ions detected in this test is $0.01 mg/cm^2$.

**Results / Discussion:** None of the patients elicited a sensitivity response to the Vaseline negative control preparation. The nickel sulfate positive test results were summarized independently of the reaction grade, thus providing an overview of the allergic patient response.

Patch test results for the nickel sensitized 50 patient group are shown in Table 1.

Table 1. Patient group response to $NiSO_4 \cdot 6H_2O$ patch test

| $NiSO_4 \cdot 6H_2O$ (%) | 0.001 | 0.01 | 0.1 | 1 | 5 |
|---|---|---|---|---|---|
| Allergy Response (%) | 2 | 12 | 30 | 24 | 32 |

The minimum nickel sulfate patch test concentration that provoked a positive nickel sensitivity reaction was significantly different for the individual patients that were evaluated in this study. About half of the subjects (56%) reacted to a 5% and 1% nickel sulfate solution while 44% reacted to a concentration within a range of 0.1% to 0.001%. Epidermal contact results with the alloy discs were negative in all patients. The free-nickel ion tests were negative for both alloy disc compositions and this indicated that the nickel ion concentrations at the alloy surfaces were less than $0.01 mg/cm^2$.
Sensitized patients who demonstrated a reaction to nickel sulfate patch test solutions did not demonstrate nickel allergy reactions to the alloy discs. This suggests that the inherent corrosion resistance of the high and low nickel implant alloys is sufficient to prevent a positive nickel contact epidermal response.

**Conclusions:** Nearly 70% of a group of 50 **s**ensitized patients exhibited a positive allergic response to $NiSO_4 \cdot 6H_2O$ solutions that were 5 to 5000 times less concentrated than the standard 5% patch test formulation. No conclusions can be established regarding whether low nickel Biodur 108 stainless steel will reduce the incidence of nickel allergy reactions in sensitized patients. Taping implant specimens to patients is not a useful predictor of nickel sensitization response.

**References:** [1] Brasch J, Hautarzt, 1998;49:184-191 [2] Hierholzer S, Internal Fixation and Metal Allergie, Thieme Medical Publishers, New York, 1992:28.

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