

## A study of nickel allergy

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Nickel is a potentially allergenic material. It is one of the most common causes of allergic contact dermatitis, particularly in women.<sup>1-5</sup> Nickel can also be considered an occupational allergen. Nickel contact dermatitis is common among industrial workers, especially in those industries that use nickel as a raw material. It has been demonstrated that U.S. 5-cent coins contain approximately 25% nickel and that they can induce eczematous contact dermatitis.<sup>6-8</sup> A great number of daily use objects that contain nickel and can therefore cause contact dermatitis have been reported.<sup>5, 6, 9, 10</sup>

It has been demonstrated also that nickel-containing metallic orthopedic implants are linked to the production of sensitization dermatitis.<sup>11-13</sup> The "nickel itch" dermatitis caused by jewelry worn on the body or by occupation in nickel industries such as electroplating represents about 5% of all eczema in humans.<sup>14</sup>

As these alloys become more popular in dentistry, the frequency of allergic reactions should become more significant in the susceptible population and may result in inconvenience and expense for the patient who wears a prosthesis that contains the allergenic substances.

The ability of a metal to induce dermatitis appears to be related to its pattern and mode of corrosion. All base metals corrode. *In vitro* investigations have shown that most nickel-based alloys have relatively high rates of corrosion compared with dental gold alloys. Products that result from this corrosion could produce a soft tissue inflammation reaction and thereby initiate a sensitization dermatitis. Implants that contain nickel and chromium, with the exception of those fabricated from stainless steel, corrode in tissue fluids and facilitate migration of nickel and chromium to the surrounding tissue.<sup>11-13</sup>

Many studies concerning nickel hypersensitivity

have been reported.<sup>14-17</sup> Numerous authors agree that there is a great variety of factors that can influence the development of hypersensitivity to nickel. The most important are mechanical irritation, skin maceration, individual susceptibility, temperature, climate, and intensity and duration of exposure.<sup>1, 3, 4, 9, 18</sup> Mechanical irritation and skin maceration promote sensitivity. An increase in temperature causes increased sweating and the chloride ion present in perspiration ionizes the nickel present in the alloys. In this way nickel salts are formed that induce skin hypersensitivity reactions.<sup>9</sup>

### IMMUNOLOGIC MECHANISM

Allergenic contact dermatitis is a prototype of the delayed hypersensitivity reaction, mostly a cellular one.<sup>19</sup> This disorder has two phases: the induction phase and the elicitation phase. The induction phase is the period from initial contact with a chemical until the lymphocytes recognize and respond to the chemical. The elicitation phase is the period from reexposure to the chemical until the appearance of the dermatitis. Nickel compounds stimulate this type of immune response by their entrance through the connective tissue of the host on direct contact with the skin or mucosa.

The diagnosis of nickel allergy is usually based on patient history, clinical findings, and results of patch testing.<sup>20</sup> Some authors<sup>21</sup> have proposed a lymphocyte transformation test (*in vitro* method) to complement the patch test to detect nickel sensitivity.

Because of the increased price of gold, new alloys have been developed as alternatives to gold alloys and many of them contain nickel in large amounts (60% to 80%). Persons who wear prostheses that contain nickel may develop allergic reactions to the material. Many patients do not know if they are allergic to nickel. If nickel is to be used in dental practice, a study to determine the incidence of allergic responses to the material is indicated.

The purposes of this study were as follows:

1. To determine the incidence of an allergic response to nickel by patch testing in a group of

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**Table I.** Distribution of study population

Department	Absolute frequency	Relative frequency (%)
Public Health	82	20.3
School of Dentistry	52	12.9
Pharmacy	24	6.0
School of Medicine	6	1.5
Allied Health Professions	20	5.0
Nonstudents	219	54.3
Total	403	100

**Table II.** Patch test results of allergic reaction to nickel

Reaction	Absolute frequency	Relative frequency (%)
Negative	288	71.5
Positive	115	28.5
Total	403	100

students, faculty members, and employees of the Medical Sciences Campus of the University of Puerto Rico

2. To investigate if differences exist in the incidence of nickel hypersensitivity between sexes

3. To determine if there is a relationship between incidence of nickel hypersensitivity and age

4. To determine if there is a relationship between previous allergic history and nickel hypersensitivity

## MATERIAL AND METHODS

The patch test is used routinely by dermatologists and allergists to determine allergic responses. It is a well established and approved method for detection of sensitivity to different substances, and it is a helpful procedure to start the elicitation phase of the delayed hypersensitivity reaction previously described. The procedures for patch testing for this project were as follows.<sup>13, 20, 22, 23</sup>

A small amount of 5% nickel sulfate on a petroleum base was applied in the center of a test patch (A1 Test Patch, Imeco AB, Sweden; distributed by Dome Hollister Stier International, Spokane, Wash.) that was free from sensitizers and provided air tight occlusion. The patch was covered by a 5 × 5 cm piece of tape (Scanfor, Norgesplaster, Norway; distributed by Dome Hollister Stier International). The patch was applied to the medial aspect of the upper arm, which had been cleaned with alcohol. A control patch without reagent

**Table III.** Patch test results of allergic reaction to nickel according to degree of reaction

Degree of reaction	Absolute frequency	Relative frequency (%)
No reaction	263	65.3
Erythema	25	6.2
Erythema and papules	76	18.9
Erythema, papules, and vesicles	32	7.9
Marked edema with vesicles	7	1.7
Total	403	100

**Table IV.** Classification of allergic reaction to nickel according to sex

Sex	Negative	Positive	Relative frequency (%)
Men	96	25	20.7
Women	192	90	31.9
Total	288	115	52.6

Chi square = 5.26;  $p < .05$ .

was placed next to the first patch. The patches were left in place undisturbed for 48 hours. Subjects were instructed not to wet the arm or remove the patch during this time, with the exception of those who develop extreme itching or pain.

Mild itching and erythema were determined as inadequate primary criteria for patch test reactions. Therefore, the presence of erythema alone was considered a negative reaction. Patch testing was avoided in skin that was infected, macerated, or gave evidence of any rash.

The preparation of the 5% nickel sulfate petroleum base, the categories used for recording the test reactions, and the dimethylglyoxime test were described previously.<sup>23</sup> The population studied consisted of 403 subjects of which 121 were men (30%) and 282 were women (70%), who were students, personnel, and faculty members of the University of Puerto Rico, Medical Sciences Campus (Table I).

## RESULTS

Results of the patch test survey are presented in Table II. One hundred fifteen subjects developed an allergic response to nickel. Therefore, the incidence of

**Table V.** Relationship of previous allergic history and reaction to nickel

Reaction to nickel	No allergic history	Jewelry	Penicillin	Aspirin	Other	Raw total
Negative	201	7	26	6	48	288
Positive	58	30	10	2	15	115
Total	259	37	36	8	63	403

Chi square = 55.63;  $p < .001$ .

**Table VI.** Classification of previous allergic history according to sex in subjects with positive patch test reaction to nickel

Sex	No allergic history	Allergic history	Relative frequency (%)
Men	19	6	10.5
Women	39	51	89.5
Column total	58	57	100

Chi square = 8.35;  $p < .01$ .

positive patch test reactions to nickel was found to be 28.5%; conversely, 288 persons (71.5%) showed no positive reactions.

Table III shows results of the patch test by the degree of reaction. The number of subjects with no reaction was 263 (65.3%); those with erythema, 25 (6.2%); erythema and papules, 76 (18.9%), erythema, papules, and vesicles, 32 (7.9%); and marked edema with vesicles, 7 (1.7%).

In classifying patch test reactions as positive or negative the following criteria were considered. Erythema alone (redness) was considered a negative reaction. This was done to eliminate false positives that might be due to primary irritant reactions. Primary irritant reactions are not due to allergy but are caused by direct inherent skin-damaging properties of the substance that is applied or the tape that is used. Erythema and papules, as well as erythema, papules, and vesicles, were regarded as positive reactions. The interpretation of the patch test was based on the severity of the inflammatory reaction of the skin.

When the incidence of nickel hypersensitivity was compared by sex, it was found that women had a higher rate than men. Table IV shows that there was a striking difference in nickel hypersensitivity by sex. Of all women tested, 31.9% showed a positive reaction to nickel, while 20.7% of the men tested showed the same reaction. This difference in the incidence of nickel hypersensitivity between sexes was analyzed by the chi square test and was found to be statistically significant ( $p < .05$ ).

**Table VII.** Distribution of population according to age

Age group (yrs)	Absolute frequency	Relative frequency (%)
17 to 20	25	6.2
21 to 30	220	54.6
31 to 40	101	25.1
41 to 50	37	9.2
51 to 65	20	5.0
Total	403	100

Table V shows that 81.1% of the subjects who had a history of allergy to jewelry were hypersensitive to nickel, while only 18.9% of the subjects who had a history of allergy to jewelry were not. This table shows that in the population studied there is a significant relationship ( $p < .001$ ) between a history of allergy to jewelry and nickel hypersensitivity. In other words, individuals with a history of reaction to jewelry are more likely to have a positive reaction to a nickel patch test than those with no such history.

Table VI shows the classification of previous allergic history according to sex in subjects with a positive patch test reaction to nickel. From the total subjects with a previous allergic history, including 21 different categories of allergies, 89.5% were women while only 10.5% were men; thus, women are more likely to have an allergic history than men. This difference was analyzed by the chi square test and found to be statistically significant ( $p < .01$ ).

The age range in the study population varied from 17 to 65 years of age. The mean or average was 30.196 years, the median was 27.083 years, and the mode 22 years. Table VII shows the distribution of the population according to age. No definite age-related patterns of patch test reactivity were found. A linear regression analysis was performed, which demonstrated that there is no relationship between age and nickel hypersensitivity.

In regard to medications taken by the subjects during the study, only nine (2.2%) were taking corticosteroids.

## DISCUSSION

It has been shown that nickel is a potential allergen and is one of the most common causes of allergic contact dermatitis. Nickel is present in most jewelry, and there are a great number of objects in daily use that contain nickel; therefore, nickel may be considered a potential hazard to the public health. With the use of nickel in dental restorations, the hazard is increased considerably.

The incidence of positive patch test reactions to nickel was found to be 28.5% in the population studied. This suggests that the true incidence of nickel hypersensitivity in the general population is sufficiently high as to encourage further attention to this problem. The finding that nearly three of 10 individuals were sensitive to nickel is disturbing.

There is a striking difference in the incidence of nickel hypersensitivity between sexes. Of all the women tested, 31.9% showed a positive reaction to nickel, while 20.7% of the men showed the same reaction. This is possibly due to the fact that women contact nickel more by wearing jewelry that contains this metal, so they have been sensitized at an early age.

There is no relationship between age and nickel hypersensitivity. Some investigators have postulated that nickel hypersensitivity increases with age, but in this study no such relationship was found.

There is a positive correlation between a previous allergic history and nickel hypersensitivity. Of the subjects who had a previous history of allergy to jewelry, 81.1% were hypersensitive to nickel, while only 18.9% were not. This suggests that the histories were valid and useful in that they were in a sense predictive to contact sensitivity to nickel.

## CONCLUSION

A standardized patch test should be performed on every patient who is to be treated with a prosthesis that contains nickel to detect nickel sensitivity. A patch test should also be performed on industrial workers or employees who may be exposed to nickel.

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