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URTICARIA AND NICKEL

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Nickel is the commonest cause of contact allergy in Western countries.

Recently, nickel allergy - in a sample of Finnish university students - was encountered in 39% of all female students, in 14% without pierced skin and in 42% of females with pierced skin (regardless to the age of 1st skin piercing or to the number of piercing). The corresponding figures for males were 3%, 3% and 7%. In the multiple regression analysis, the risk factors for nickel allergy were female sex, current metal exposure at examination and skin piercing. Atopy (positive prick test or elevated IgE levels to common allergens) was not significantly associated with nickel allergy. During the last decades, the prevalence of nickel allergy has increased, particularly among females from 13% in 1986 to 39%; this prevalence among males has remained low at 3% (1).

Occupational nickel exposure occurs during nickel plating and electroforming of nickel. Other industries which use nickel compounds are battery production, some branches of enamel and glass production and chemical plants where nickel catalysts are used. Moderate exposure occurs in mechanical engineering and in many industrial plants where nickel alloy is worked up, or where metals are nickel plated.

Nickel is found in medicines, fungicides, nickel-plated objects, taps, coins, scissors, zippers, garter clasps, hairpins, eyelash curlers, metal frames for eye glasses and costume jewelry. Costume jewelry made of German silver can contain 10 to 20% of nickel and even jewelry made of white gold can contain up to 15% nickel. The use of jewelry is of special importance since exaggerated exposure occurs through the intimate and occluded contact with the skin. The wearing of wristwatches, tight fitting bracelets, clip-on earrings or earrings for pierced ears are typical examples of intimate skin contact. Ear piercing directly damages skin and exaggerates contact even further. Because of its special properties, nickel is often found in dental alloys or in implants such as joint protheses, plates and screws for fractured bones, surgical clips, etc..

Nickel is also found in kitchen utensils, e.g. cans and tins, pots and pans, electric kettles, cutlery, etc. Water taps, pipes, sinks and bath tubs can all contain and release nickel.

Minor amounts of nickel are found in food and drinking water. The proposed a nickel dietary requirement for humans is 50 μg per day. The normal daily intake of nickel through food has been estimated to between 200 and 600 μg.: most ingested nickel remains unabsorbed within the gastrointestinal tract; only 1-10% is absorbed. Nickel concentration in sweat is high, ranging from 7 to 270 mg per liter; sweating thus may provide an important route for the excretion of nickel from the body. In a healthy man, serum nickel concentrations vary from 1.6 to 7 μg/l and urinary nickel concentrations from 2 to 5 μg l per day. Nickel is found in many foods but common items with a high content, regardless of the nickel content of the soil in which they are grown, include whole wheat, rye, oats, cocoa, tea, gelatin, baking powder, kippered herrings, soy, red kidney beans, peas, peanuts, hazelnuts, sunflower seeds, strong licorice and dried fruits. Various other nickel food items and drinks can aggravate nickel eczema even though the nickel content of these foods may be low. Included among these are beer, wine (in particular red wine), herring, mackerel, tuna, tomato, onion, carrot and certain fruits, in particular apples and citrus fruits juice). The vegetables can usually be tolerated when cooked. (3)

Except for municipal water supplies coming from large open pit mines, the level of nickel in ground water in several countries is less than 10 ppb. Therefore, except for unusual cases the direct contribution of drinking water to nickel intake is small. On the other hand, drinking water may contain detectable nickel due to leaching from nickel-chromium plated pipes and boilers. Early morning hot water from household taps may contain up to 1.5 ppm nickel. This phenomenon may be attributed to corrosion of the tap or rusting of the lining of the boilers and pipes. (2)

The contribution made by 19 Cr/9 Ni stainless-steel cooking utensils to nickel in the diet is negligible: the amount of nickel (0 to 8 mg) derived from utensils in standard portions of various "aggressive" foodstuffs tested was less than that to be found occurring in 1 square of a bitter-sweet chocolate bar. New pans, if first used with acid fruits, can show a greater pick-up of nickel, which, in the worst case observed, amounted to approximately 1/5 of the normal daily intake for average person: this situation doesn't recur in subsequent usage. (4)

It is thought that the frequency of hypersensitivity reaction should increase in patients with prosthodontic or orthodontic appliances, especially those made of nickel-titanium alloys. Janson et al. patch tested

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patients before, during and after orthodontic treatment: they found an allergic reaction in 28.3% of the total sample without a statistically significant difference in the prevalence among the three groups, but with a positive association between nickel hypersensitivity and previous personal allergic history to metals as well as with the daily use of metal objects. This suggests that orthodontic therapy with conventional stainless steel appliance does not initiate or aggravate a nickel hypersensitivity reaction (5).

Contact dermatitis from nickel (distinct patch of eczema at a site where a nickel-plated item makes close contact with the skin) is as common as airborne nickel dermatitis is rare, 1 such case being due to a nickel-containing powder paint. The other cases of nickel patch test positivity were found in a man who inhaled nickel-containing aerosols during his Ist working day in an electroplating plant, developing an itchy papulo-erythematous rash on the limbs, chest and genital area (6) and in a seamstress that developed eczema on the face, neck and finger webs working in a sewing hall where the nickel is mainly rubbed off from nickel-plated trouser-hangers and parts of the sewing machines: in this last case important additional factors were high room temperature of 28-32° in the sewing hall and the constant sweating of the seamstress. In general, in nickel-allergic person, a threshold concentration of 10 g nickel/ions/cm is necessary to elicit contact dermatitis, the contact time needing to be at least 2 to 5 hours. (7)

Delayed allergy from nickel is common, but very few cases of immediate allergy have been reported: these reports are summarized in the following table.

In the 1970s, some authjors (9) noted that a considerable number of nickel-sensitive patients have dermatitis at sites other than those that have been in direct contact with nickel-plated items. This led Christensen (9) to consider this type of eczema a secondary rather than a primary type of eruption; he, in fact, suspected that ingested nickel could be responsible for these reactions. In recent years, particular attention has been paid to the influence of dietary nickel on the clinical course of nickel-induced dermatitis.

The diagnosis of hypersensitivity is based on clinical history and on the patch test to nickel sulfate (5% petrolatum); some authors proposed intradermal testing at immediate and delayed reading, but the sensibility is the same of the patch test. The lymphocyte proliferation test was able to differentiate nickel-sensitive patients from those without nickel contact allergy in 86% of the cases and gave false positive results in 9% of the cases. (10,11)

In order to confirm the diagnosis of endogenous Ni-induced dermatitis, the patients must underwent a challenge test with 10 or 20 mg nickel sulfate (Test Dose, Laboratorio Farmaceutico Lofarma s.r.l., Milan, Italy)

Results of recent studies have clearly shown that animals can be made more tolerant to nickel with oral doses of nickel. Induction of tolerance to nickel sensitization in mice has been shown by Van Hoogstraten et al, who demonstrated that tolerance can be induced by administering non toxic doses of nickel sulfate in drinking water or intragastrically. (12) The oral administration of allergens may induce systemic suppression of subsequent humoral and cell-mediated responses. Administration of the allergens onto the oral mucosa was actually most effective in the induction of immune tollerance.

There are few report of desensitization of nickel: Sjovall et al. (13) with doses of 5.0 mg nickel sulfate taken once a week for 6 weeks showed that the degree of contact allergy was significantly lowered, measured as patch test reactions before and after nickel administration. Panzani et al. treated 51 patients over 30 years with oral doses of 0.1 ng nickel sulfate per day: among the 30 cases who went through

Reference	N° of cases	Gender	Prick/ Scratch test	Patch	Contact Urticaria	Asthma	RAST	NPT/ BPT	Occupa tional	Exposure
Patient with asthma:										
-McConnel et al	1	M	+	+	-	Temporal	ND	ND	+	Metal plating
-Malo et al.	1	M	+	ND	-	Immediate	+	ND	+	Metal plating
-Block&Yaung	1	M	+	-	-	Immediate	ND	ND	+	Metal polishing
-Novey et al.	1	M	-	ND	-	Late	-	ND	+	Metal electroplating
-Malo et al.	1	M	-	ND	-	Dual	+	ND	+	Metal electroplating
-Davies	3		ND	ND	-	Immediate/late	ND	ND	+	Manufacturing of nickel catalyst
Patient with contact urticaria:										
-Osmundsen	1	F	+	+	+	-	ND		-	Jewellery
-Tosti et al.	1	F	+	-	+	-	ND		-	Jewellery
-Valsecchi & Cainelli	1	F	ND	+	+	-	ND		-	Jewellery
	1	F	+	+	+	-	ND		-	Jewellery
Patient with asthma and contact urticaria:										
-Estlander et al.	1	F	+	+	+	+	+	+/+	+	Metal casting

** 30 min patch test*
ND, not done
(modified from Estalnder et al. 1993)

e whole follow-up, symptomatology totally disap-
ared in 29 cases (14); Bagot et al. gave to their 30
itients 5 mg of nickel once a week for 7 weeks with
significant reduction in the number of circulating
mphocytes responding to nickel, but no other ef-
ct could be demonstrated for the clinical and bio-
gical parameters studied (15). On the other hand,
had a successful desensitization in 15 of the 16
r patients: oral provocation test showed an overall
crease of tolerance in all the 15 patients; patch
ts showed no variation in 2 cases, a reduction in
and were negative in 3. We used 1 μg of oral
kel sulfate (Laboratorio Farmaceutico LoLarma
.I., Milan, Italy): the active principle $NiSO4.6H_20$
been crumbled in a mortar in order to obtain a
e powder; the active principle has been diluted in
as inert excipient in a proper proportion to
ain the concentration of 1 μg of nickel per cap-
e. The capsules were of rigid gelatin, contained
) mg of excipient each, and were filled with a
nual capsule filling machine (Zuma, Milan, Italy).
have followed this desensitization regimen, dur-
the patient follows a low-nickel diet:

1 capsule daily for 15 days;

2 capsules daily for 15 days;

2 capsules daily to alternate days for several
ths, reintroducing gradually the offending foods:
n the patient is able to follow a free diet, we
luate the reached tolerance with patch test and
llenge test. If the patients is able to tolerate
ost 10 mg of nickel sulfate, the desensitization
de stopped, on the contrary the desensitization
t de prolonged until this goal is obtained.

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