

## NICKEL VACCINATION: TODAY AND TOMORROW

M. MINELLI

*1<sup>st</sup> Level Medical Executive - O.U. of General Medicine Presidio Ospedaliero "Vito Fazzi"  
Stabilimento di Campi Salentina, Lecce, Italy*

Nickel is considered the sensitising agent most frequently responsible of occupational (metalworkers, hairdressers, dental technicians, cashiers, tailors, shoemakers) and non-occupational contact allergic dermatitis. It is a pathology affecting a vast part of the population. Recent epidemiological studies show that 25 of young women and 5% of young men are affected from nickel allergy. Therefore, this problem has a great relevance both under the sanitary and the social point of view.

Many objects of common use contain nickel: metallic clothes fittings, earrings and in general piercing, metallic glasses frames, jewellery/trinkets, coins, keys, kitchenware, cosmetics, etc.

The coetaneous regions mainly interested by nickel contact allergy changed in last years in relation to changes in clothes and behaviours. In the thirties the region most frequently affected was the thigh's superior third, because of the use of suspender belts. In the seventies the blue-jeans buttons were responsible of 40% of contact dermatitis in young women, with a typical localization at the abdomen region. Afterwards, because of the spread habit to pierce the ears, the cases of nickel contact dermatitis consistently increased. In fact it is today well established that the piercing is a factor strongly favouring the appearance of this type of allergic sensitisation.

Besides the dermatitis in the described coetaneous regions, some episodes of eyelids oedema after the use of eye-liner and of solutions

for the cleaning of contact lenses, and dermatitis of fingers of musicians playing cord instruments have been described. The nickel sensitivity can be, besides, the cause of rejection of artificial cardiac valves, intrauterine medical devices, and of orthopaedic devices (plates, screws, arthroprosthesis), with clinical consequences in some cases very severe.

But contact dermatitis is not the unique clinical symptom of nickel allergy. In fact nickel can be responsible also of respiratory symptoms and/or systemic reactions, as urticaria with generalized itching, angioedema, diffuse erythema, and focal symptoms at gastro enteric level (gastritis and chronic colitis).

These pathologies are not due to the skin contact with objects containing nickel, but to the ingestion of foods and beverages containing traces of nickel. In fact this metal is practically ubiquitous and is present, with variable concentration, in almost all the components of our daily diet. Chocolate, soy, oats, peanuts, tomato, plums are some of the foods having high nickel content. Besides, the nickel contamination can also arise from the cans of canned foods and from cooking saucepans, especially in presence of acidic substances (like oxalic acid present in tomatoes) which favour the release of the metal. The daily dietary intake of nickel varies from country to country in relation both to the concentration of the metal in the soil and to dietary habits. In USA it is of about 300-600 micrograms

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*Mailing address: Mauro Minelli  
Ospedale di Campi Salentina, Unità Operativa di Medicina Interna  
Ambulatorio di Allergologia, 73012 Campi Salentina, Lecce, Italy  
Tel + 39-0832-790375  
e-mail: mauro.minelli@tiscali.it*

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per day (1 micrograms is the millionth part of one gram), while in Europe it is about 200 micrograms per day. It is therefore clear how the intake of nickel with the diet could be able to influence the course of the contact dermatitis lesions, e.g. by causing sudden and apparently inexplicable relapses. Besides, such intake can provoke diffuse and marked reactions at intestinal level, where the nickel, taken by ingestion, can induce chronic inflammatory reactions causing nausea, heartburn, meteorism, abdominal pain, diarrhoea or constipation.

The pathogenetic mechanisms of these symptoms are still poorly known. Besides the involvement of specific immunological and allergic reactions, also the role of toxic mechanisms has been hypothesised. The diagnosis of nickel allergy is performed by patch test, consisting in applying on the skin an ointment containing nickel, or by oral provocation test, consisting in administering small amounts of nickel. In the first test an eczematous skin reaction is observed, in the second a relapse of the symptoms referred by the patient in anamnesis.

As regards the strategy to keep under control these pathologies, good results are obtained in patients with skin diffuse reactions by recommending a diet avoiding foods at high nickel content.

Recently, furthermore, a remarkable interest has

been raised by the possibility to keep under control the symptoms of nickel allergic patients with a hyposensitizing treatment consisting in the administration by oral route of minute amounts of nickel sulphate. Something like a "vaccine" that, with an incremental posological schedule, reaches, after at least one year, a satisfactory clinical response, with a good tolerability and safety profile.

This therapeutical model arises from studies in animals, which showed that the repeated oral administration of nickel salts is able to induce an "immunological tolerance", linked to the appearance of T cells able to switch off the allergic response (T suppressor). Such studies have been performed also in humans, with encouraging results. On this basis an observational study has been carried out to evaluate the efficacy of an hyposensitizing therapy with nickel to induce the disappearance, or at least the consistent improvement, of the coetaneous symptoms (itching, urticarioid wheals) and of meteorism, constipation and/or diarrhoea or other related dyspeptic pathology, or both. The efficacy of this therapeutical model is checked with the gradual reintroduction in diet of foods containing high amount of nickel. It is opportune in this phase to keep the patients under frequent controls, in order to monitor the subjective and objective symptoms.