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Nickel allergy

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Nickel [chemical symbol: Ni] is a so-called transition metal that is a component of numerous iron alloys (stainless steels) and is found in galvanic coatings on metal objects. Nickel can be found in earrings, rings, watches, buttons, zippers, coins, keys, scissors, batteries, musical instruments (metal strings, brass instruments), dyes, dentures and dental implants, orthopedic fixations and endoprostheses, razor blades and razors, eyeglass frames, kitchenware, tools, machine parts, and many other metal objects. The presence of free nickel ions on the surface of metal objects can be detected using the Chemo Nickel Test™ (Chemotechnique). Nickel can accumulate in used cooling and lubricating fluids and metalworking fluids.

Synonyms and names in other languages

Blue salt; Carbonyl nickel powder; Nickel; Nickel; Nickel(II) sulfate hexahydrate; Nickel acetylmethionate; Nickel bis(hydroxydiphenylmethylpyrrolidinomethyl)pyridinediyl t-butylisocyano perchlorate; Nickel bis(hydroxydiphenylmethylpyrrolidinomethyl)pyridinediyl t-butylisocyanoate perchlorate; Nickel chloride; Nickel gluconate; Nickel monosulfate hexahydrate; Nickel sulfate; Nickel sulfate hexahydrate; Nikiel; Nikkel; Single nickel salt; Sulfuric acid, nickel (2+) salt hexahydrate

Clinical symptoms of nickel allergy

In most cases, nickel causes skin inflammation (allergic contact dermatitis or eczema) limited to areas directly exposed to nickel. Typical symptoms of nickel allergy include patches of itchy rash in the area of contact with metal objects that release nickel, like fashion jewellery, metal buttons, rivets, zippers, buckles of garments, or areas exposed to contact with nickel-releasing tools, coins, keys, doorknobs, etc. Nickel can cause skin lesions resembling erythema multiforme and airborne eczema. Systemic reactivation of allergic contact dermatitis, i.e., dermatitis due to systemic exposure via ingestion or inhalation, e.g. from orthodontic appliances is possible, but infrequently reported. The possible role of nickel in food and drinking water is discussed below. Hematogenous eczema due to absorption of

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nickel at the primary contact site and redistribution to other skin areas via the bloodstream is also possible, but seems very rare.

Sources of nickel sensitization

The primary causes of nickel sensitization are metal objects that come in contact with the skin and release nickel. In the EU, consumer products intended for prolonged contact with the skin, e.g., fashion jewellery, wristwatch cases and metal fittings in garments, are regulated at the manufacturing level by the REACH Regulations, which specify the upper limit of allowable nickel release (less than 0.5 µg/cm²/week). Note, however, that coins are not subject to this regulation – the Euro, as well as the British Pound, the Polish Złoty and numerous other coins do release substantial amounts of nickel. The same is true for coins circulated in the USA, where one particular denomination is referred to as a "nickel" in common language.

Nickel in cosmetic products / toiletries

In the European Union, Regulation (EC) No 1223/2009 on cosmetic products lists over 100 nickel compounds that are prohibited for use, having been banned because of their allergenic and carcinogenic potential. However, some do have registered INCI names:

- INCI: Nickel Acetylmethionate (Nickel salt of N-acetylmethionine)
- INCI: Nickel Chloride
- INCI: Nickel Gluconate
- INCI: Nickel Bis (Hydroxy Diphenyl Methyl Pyrrolidino Methyl) Pyridinediyl T-Butylisocyano Perchlorate

Note that in the EU, nickel dichloride [= nickel chloride] is a banned substance under Regulation (EC) No 1223/2009 on cosmetic products!

No nickel-containing cosmetic products and toiletries are to be found listed on INCIDecoder

INCI: International Nomenclature of Cosmetic Ingredients — In the UK, the European Union, and in other global regions, manufacturers of cosmetic products are legally required to list ingredients on product labels / packaging using standardised INCI nomenclature. The Personal Care Products Council cautions that "The designation of an INCI name for a cosmetic ingredient is an essential part of ingredient identification; however, the assignment of an INCI name does not mean that the ingredient has been approved for cosmetics."

Nickel in food

The "low-nickel diet", also known as the "nickel diet" or "nickel-free diet", is a very popular topic. Some doctors (including, unfortunately, some dermatologists and allergists) uncritically recommend such diets to every patient with a positive nickel patch test. Online, you can find lists of foods that people with nickel allergies should supposedly avoid. Such lists should be treated with a great deal of skepticism. Scientific studies indicate that although the consumption of foods with high nickel content (e.g., canned food, seafood) may be a risk factor for the development of symptomatic nickel allergy (Boonchai et al. 2014), only 1-11% of all nickel-allergic patients experience skin problems caused by nickel in food (Jensen et al. 2006, Antico & Soana 2015). It is worth realizing that oral doses of nickel capable of causing symptoms in allergic individuals are at least 1 mg and significantly exceed the typical daily exposure to nickel from food (0.22-0.35 mg Ni/day) (Veien & Andersen 1986). In a study of Polish nickel-allergic patients, in some cases as much as 11 mg of nickel was necessary to induce symptoms (Rudzki et al. 1991). Such a dose is difficult to achieve through the consumption of even the most "high-nickel" foods. An estimated 65 million Europeans are allergic to nickel (Spiewak et al. 2007), highlighting the scale of the problem and the social and economic consequences of uncritically recommending a low-nickel diets to every patient with a positive patch test result to nickel.

Implementing a truly nickel-free diet is not only unjustified for most patients, but also simply impossible, as nickel is a common element in water and food. The most rigorous "nickel-free" diets reduce the daily nickel intake by 50% at best, but even among patients who have successfully reduced serum and urinary nickel concentrations using a very restrictive diet, not all experienced improvement in their skin condition (Burrows 1992). Therefore, implementing nickel-restricted diets should be reserved for carefully selected cases in which there is actual evidence that the patient will benefit from such a diet, and its effectiveness should be critically assessed after 4 weeks. In my practice, I have frequently encountered patients who, at the recommendation of their physicians, maintained a "nickel-free diet" for many years, at the cost of significant financial outlay and personal sacrifice, without achieving any noticeable benefit. Therefore, the decision to implement the diet should be based on the results of a placebo-controlled, double-blind trial [DBPCT; see Macchia et al. 2015]. In the study reported by Veien et al. (1993), approximately two-thirds of patients with a positive DBPCT result actually benefited from a low-nickel diet. In this group, patients who had strong nickel patch test reactions were less likely to experience improvement after a nickel-restricted diet. Due to the possibility of false-negative results, a positive nickel patch test result is not an absolute requirement for provocation, and patients with negative test results do respond to oral provocation (Hindsén 1999). However, such cases require particularly cautious interpretation.

Performing a DBPCT in routine medical practice is quite cumbersome, therefore, if systemic nickel allergy is strongly suspected, a dietary nickel elimination and re-exposure test is sometimes used instead of a DBPCT. Any assessment of the effectiveness of a low-nickel diet should be performed after at least one month of consistent use (Veien et al. 1993). It is important to realise that determining which foods actually contain less nickel is very difficult, as the content of this element depends not only on the type of product, as suggested by the authors of various lists of foods supposedly "rich" or "low" in nickel, but also on the concentration of nickel in the soil and water at the place of cultivation or breeding, and the propensity of the plant or animal to accumulate the element (Antico & Soana 1999). In a Danish study, relatively high nickel content has been found in shrimp, mussels, beans, peas, kale, leek, lentils, lettuce, spinach, pea and alfalfa sprouts, cereal products, buckwheat, millet, oatmeal, bran, muesli, multigrain bread, figs, pineapples, raspberries, plums, chocolate, cocoa, marzipan, almonds, baking powder, linseed, hazelnuts, peanuts, soy products, sunflower seeds, and licorice (Veien & Andersen 1986). Furthermore, patients are advised to avoid dietary supplements containing nickel, as well as acidic foods cooked in steel vessels, canned food and hot drinks from vending machines and dispensers. Veien & Andersen (1986) suggested maintaining a nickel-restricted diet for a month, after which a critical assessment of its effectiveness should be performed. Individuals who have not noticed improvement in their skin condition after a month of a low-nickel diet are not advised to continue it! Those who have experienced improvement are advised to gradually reintroduce the restricted foods to make the diet more tolerable, and in the event of a recurrence of symptoms, eliminate the offending foods. Due to the possibility of periodic spontaneous improvement in skin condition and the subjective nature of assessing disease severity, the effectiveness of such elimination diet can only be confirmed by complete resolution of the disease or significant improvement of eczema persisting for at least 4 weeks after discontinuing pharmacotherapy, and a relapse after returning to the previous diet (Śpiewak 2015). If a DBPCT is not carried out, it is rarely possible to establish a cause-and-effect relationship solely based on elimination and re-exposure, especially because cases of "positive reactions", i.e., worsening of skin condition has been also reported during DBPCT after consuming placebo, i.e., food containing very low amounts of nickel.

Accordingly, in the absence of conclusive confirmation of dietary nickel hypersensitivity, it is safer to assume that the presence of this metal in food does not cause symptoms in a given patient. Such an assumption carries a significantly lower risk of error than the opposite assumption. Moreover, it does not entail burdensome and costly interventions, restrictions, and sacrifices that would reduce the patient's quality of life.

Available diagnostic methods and materials

At present, the only validated method of detecting nickel allergy is patch test performed in line with the current guidelines by national or international scientific societies, e.g., European Society of Contact Dermatitis. Patch test material available for testing includes:

- Nickel(II) sulfate hexahydrate 5% pet. [Chemotechnique Diagnostics, cat. number N-002A] – recommended by the author, part of the European Baseline Series and most other national and regional series
- Nickel(II) sulfate hexahydrate 2.5% pet. [Chemotechnique Diagnostics, cat. number N-002B] – recommended by some authors as suitable for testing in children
- Nickel(II) sulfate 200 µg/cm² is included in Panel 1.3 of T.R.U.E. Test® – comparative studies have shown that its detection rate is lower than for nickel sulfate 5% pet.; see Lazarov et al. (2007)

Please note: Blood tests for nickel allergy (mostly advertised as "lymphocyte transformation tests"), although popular in some countries, have not been approved as a diagnostic tool, and their use in allergy diagnosis is controversial.

Positivity rate

Although it varies between countries around the world, and there is a greater prevalence in females over males, 13.4-29.5% of [female] patients scheduled for routine patch testing will be found to have developed sensitivity to nickel (Schuttelaar et al. 2018).

Cross-reactivities, co-positivities, and co-sensitizations

Palladium is the most frequent and best-known cross-reactant of nickel. In the past, positive reactions to palladium were considered to be cross reactions secondary to nickel allergy, due to the similar atomic structures and chemical properties of both metals (Santucci et al. 1996). There are also patients in whom allergy to palladium seems to be the primary clinically relevant event who show cross-reactivity to nickel. Nowadays, however, palladium is increasingly present in the everyday environment and isolated allergy to palladium with a concomitant negative test to nickel is being found (Faurschou et al. 2011).

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