INTERNATIONAL JOURNAL
of PEDIATRIC DERMATOLOGY

Special Issue, 2025
ISSN 3035-1006 online

Review

Nickel Allergy in Children and Adolescents: Between Myth and Reality

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KEYWORDS

Allergic Contact Dermatitis,
Nickel sensitization,
Nickel allergy,
Patch test,
Systemic Nickel Allergy Syndrome

ABSTRACT

Nickel is a ubiquitous allergen found in many everyday objects. Hypersensitivity to nickel is the leading cause of allergic contact dermatitis in all ages, including pediatrics. Sensitization often begins in childhood and puberty, peaking between the ages of 12 and 20. Ear and body piercing have consistently been identified as the most significant risk factor for nickel sensitization in young people. The authors illustrate the main legislative regulations governing the presence of nickel in many manufactured products and cosmetics.

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Introduction

Nickel (Ni), a silvery-white transition element, ranks as the fourth most widely used metal worldwide, after iron, chromium, and lead. With atomic number 28, it belongs to group 10 of the periodic table and is commonly found in the Earth's crust in various mineral forms such as garnierite and niccolite. It is also present in soils as a contaminant from industrial processes. Nickel's unique physicochemical properties—including low atomic mass, high chemical reactivity, and pronounced hydrophobicity—render it a highly potent hapten. As such, it can bind covalently to endogenous proteins, creating immunogenic complexes capable of triggering a delayed-type hypersensitivity reaction mediated by T lymphocytes.

Approximately 65% of nickel is used in the production of stainless steel, while smaller percentages are employed in non-ferrous alloys, surface plating (nickel plating), and various other sectors including construction, electronics, automotive components, and medical instrumentation. The pervasive presence of nickel in everyday items—ranging from jewelry and clothing accessories to coins, orthodontic materials, and even cosmetics—has resulted in widespread environmental exposure. This ubiquity underlies its status as the most prevalent contact allergen in both pediatric and adult populations, representing a major concern in dermatological and allergological practice.

Allergic Contact Dermatitis: incidence, pathogenesis, and clinical expression

Nickel-induced allergic contact dermatitis (ACD) is a prototypical form of Type IV hypersensitivity, as classified by Gell and Coombs. It is characterized by the development of pruritic, eczematous lesions following dermal exposure to the metal in sensitized individuals. Unlike irritant contact dermatitis (ICD), which results from direct cytotoxic effects without immune involvement, ACD reflects an antigen-specific, cell-mediated immune response. Sensitization occurs when antigen-presenting cells such as Langerhans cells internalize nickel-protein conjugates and migrate to the regional lymph nodes, where they activate naïve T cells. Re-exposure elicits clonal expansion of memory T cells and the release of pro-inflammatory cytokines, most notably interferon gamma (IFN-γ) and tumor necrosis factor alpha (TNF-α), culminating in the cutaneous inflammatory cascade.

Percutaneous absorption of nickel is facilitated by a number of cofactors including humidity, perspiration, mechanical friction, elevated temperature, and occlusion, all of which compromise the integrity of the epidermal barrier, particularly the stratum corneum. Clinically, ACD due to nickel presents as acute erythema, vesiculation, and edema or, in chronic forms, lichenification, desquamation, and fissuring (Fig. 1). Involvement of visible or functionally important areas such as the hands can significantly impair quality of life, leading to functional limitations, occupational disability, and psychosocial distress.

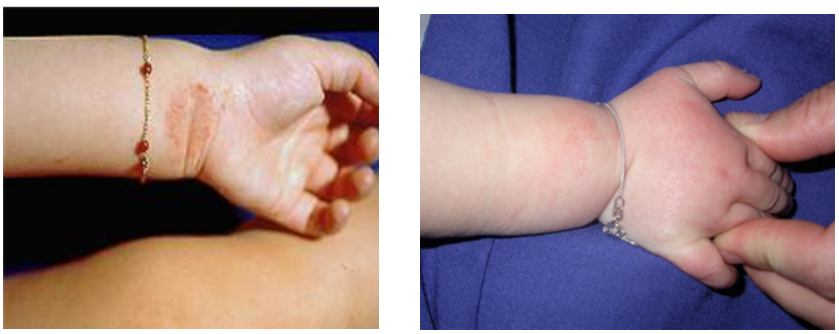

Fig. 1. *Allergic contact dermatitis caused by nickel-containing costume jewelry worn on the wrist.*

Epidemiological insights and risk determinants

Epidemiological surveys conducted across Europe estimate the prevalence of nickel sensitization in females to range from 8% to 15%, while in males it remains lower, between 1% and 3%. The gender disparity is attributed to behavioral and cultural factors, particularly the early and frequent use of nickel-containing jewelry among adolescent girls. Sensitization often begins in childhood, with several studies reporting increasing prevalence during puberty, peaking between the ages of 12 and 20.

The practice of ear and body piercing has been consistently identified as the most significant risk factor for nickel sensitization in young individuals. During the post-piercing re-epithelialization phase, the prolonged occlusive contact between healing tissue and nickel-laden earrings fosters hapten penetration and immune priming. Notably, data from Italian dermatology clinics indicate a sensitization rate of 15% among pierced adolescents, compared to only 2% among those without piercings. Moreover, the risk increases with the number of piercings, demonstrating a dose-response relationship.

Regulatory policies and exposure thresholds

In an effort to curb the public health burden of nickel-induced contact allergy, the European Union enacted Directive 94/27/EC, later incorporated into the REACH regulation, which limits the permissible nickel release from items intended for prolonged skin contact to 0.5 μg/cm²/week, and 0.2 μg/cm²/week for objects intended to be inserted into pierced skin. Despite this regulatory framework, numerous sources of exposure remain unregulated or poorly controlled, particularly in non-industrial contexts.

Metallic currency, such as 1- and 2-euro coins composed of nickel-brass or nickel-copper alloys, have been shown to release quantities of nickel vastly exceeding regulated thresholds. In nickel-sensitized individuals, repeated contact with such objects, especially in the presence of sweat—can elicit flare-ups of dermatitis. Other unregulated items include metallic tools, buttons, keys, orthopedic devices, orthodontic appliances, and various electronic components. Additionally, cosmetics - especially those containing inorganic pigments like iron oxides - can be inadvertently contaminated with trace amounts of nickel. While the regulatory limit for nickel in cosmetics is 5 ppm, products such as children's toy makeup often fail to comply.

The dimethylglyoxime spot test, in combination with ammonium hydroxide, remains a reliable, simple, and cost-effective method for detecting free nickel release, producing a pink coloration upon contact with nickel concentrations exceeding 10 ppm.

Systemic Nickel Allergy Syndrome (SNAS)

In addition to localized ACD, sensitized individuals may exhibit systemic reactions to dietary nickel intake, a condition known as Systemic Nickel Allergy Syndrome (SNAS). In these cases, the ingestion of nickel-rich foods or the use of cookware that leaches nickel into food may provoke widespread symptoms. Clinical manifestations include dyshidrotic hand eczema, nummular and papulovesicular eruptions, urticaria, purpuric lesions, and extra-cutaneous symptoms such as headache, fatigue, pruritus, bloating, diarrhea, and other gastrointestinal disturbances.

The underlying immunological mechanisms are complex and likely involve both Type I (IgE-mediated) and Type IV (T cell-mediated) pathways. The daily oral threshold associated with symptom reactivation is estimated to range between 0.3 and 0.6 mg of elemental nickel. High-nickel foods include cocoa, legumes, nuts, soy, whole grains, spinach, tomatoes, and certain seafood.

Diagnosis and clinical management

The cornerstone of diagnosis is epicutaneous patch testing, typically performed with 5% nickel sulfate in petrolatum (Fig. 2). For environmental sources, spot tests can identify nickel release from suspect items. In cases of SNAS, the implementation of a low-nickel diet, maintained under medical supervision for at least 8 to 12 weeks, may provide clinical benefit, though outcomes vary among patients.

In refractory or severe cases, experimental protocols involving oral desensitization with controlled micro-

doses of nickel have been proposed. These aim to induce immunological tolerance via gradual modulation of T-cell reactivity; however, such approaches remain investigational and are not yet standardized in clinical practice.

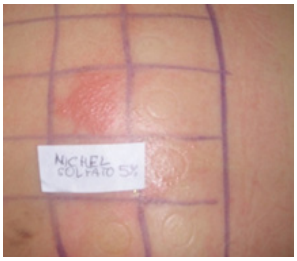

Fig. 2. *Positive patch test reaction to nickel sulfate 5%, indicating nickel allergy.*

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