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Update on Systemic Nickel Allergy Syndrome and Diet

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Key words

Allergic contact dermatitis; diet; nickel; systemic

Abbreviations

ACD - allergic contact dermatitis
SCD - systemic contact dermatitis
SNAS - systemic nickel allergy syndrome

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Dear editor,

We read with interest the Pizzutelli article on the relationship of systemic nickel hypersensitivity and diet, and find this an extremely immunologically complex and fascinating subject (1). We attempt to further elaborate on the differentiation of systemic nickel allergy syndrome (SNAS) and systemic contact dermatitis (SCD), as well as update the readers on recent developments in dietary nickel avoidance literature.

SCD, first described by Jadassohn in 1895, is a subset of allergic contact dermatitis (ACD) in which dermatitis is elicited from allergen exposure via routes other than trans-cutaneous contact (2) (see **table 1**). Cases have been reported to mercury, sulfonamide antibiotics, cinnamon oil, potassium dichromate, and thiamine, among others, and specifically to balsam of Peru, chromium and nickel following oral exposure (3,4). Nickel is the culprit behind systemic nickel allergy syndrome (SNAS) (3), which is reported to present with a multitude of symptoms, most commonly studied of which is vesicular hand eczema; however, SNAS can also present with generalized systemic (eg: fibromyalgia, headache), respiratory, generalized cutaneous and gastrointestinal symptoms (3).

Table 1 *- Routes of Systemic Exposure for SCD.*

Oral
Intravenous /Endovascular/ Subcutaneous/Intradermal/ Intramuscular
Intranasal/pulmonary inhalation
Subconjunctival
Dental
Intrauterine
Arthroplastic

Pizzutelli reported that the "therapeutic low-nickel diet is controversial" for the many manifestations of SNAS. While we agree that there is little data to suggest dietary impact of a low nickel diet on the respiratory and neurologic signs and symptoms, avoidance diets have been consistently studied for their preventive effect on cutaneous and gastrointestinal manifestations of SNAS (3, 5-8). In 1989, Veien proposed elimination diets as beneficial to decrease chances of repeat dermatitis (4), and corroborating this Jensen et al. demonstrated a dose-response between nickel-ingestion and dermatitis flares in 2003 (9). As nickel-elimination diets are commonly criticized for their adherence difficulty and variability, Mislankar et al. proposed a simplified point-based nickel-limitation diet for patients trying to limit daily intake and avoid systemic flares (10) (see **table 2**). The point-based nickel diet assigns individual foods point values that correspond to nickel content, and patients are instructed to limit the total point value to 15 per day (equivalent to 150 μg). This system is algorithmic and reproducible, making it a prime tool for patients, and clinical investigations.

Table 2 *- Foods with > 100 μg / serving of nickel [10*].*

Sunflower seeds
Cereal, oat ring
Beans (lima, pinto, refried, chili, with pork, canned)
Chocolate cake with icing

*Serving sizes based on average American portion consumption

SNAS pathophysiology involves both Th2 (typically associated with atopic dermatitis (AD)-related response) and Th1 (typically associated with the ACD-related response), and is thus complex in nature. It is plausible that expressed features may vary depending on the predominating immunologic milieu. While Th2 response to nickel dominates initially, respiratory symptoms such as rhinitis and asthma as well as cutaneous manifestations similar to AD would be expected (11,12). However, chronic exposure to nickel leads to a change in T cell expression with a reported Th1 secondary predominance and possibly predisposing to ACD, similar to the immunologic pathophysiology seen in chronic AD patients (13). Such immunologic response is seen clinically in non-atopic nickel allergic patients who develop indistinguishable-from-AD dermatitis after chronic continuous exposure to cutaneous nickel, a presentation known as "chemical atopic dermatitis" (13).

Di Gioacchino et al. assessed the effect of oral nickel desensitization in SNAS patients with both cutaneous and extra-cutaneous manifestations (gastrointestinal, cough, headache) (14). Notably, no cough or headache patients received the nickel oral challenge, but since they were enrolled, they were included in the analysis under "intention to treat". Patients who were both nickel-patch test and nickel-oral challenge positive were randomized into three groups receiving different doses of oral nickel for a year. When the dietary nickel was progressively reintroduced, the highest nickel-dosed group showed statistically significant control of cutaneous and gastrointestinal manifestations of SNAS, as assessed by subjective symptoms and individual visual analogic scale ratings (14). The development of oral nickel tolerance was theorized to be due to a proliferation of nickel-specific T regulatory lymphocytes (a distinct T cell promoted by IL-10 and which functions to inhibit general T cell responses) (14). These results suggest that chronic exposure to sensitizing allergens can lead to an immunologic loss of a "danger" signal, possibly via T cell class switching, summing to a gain of control over systemic response triggers.

In summary, although dietary avoidance and desensitization techniques utilizing oral nickel are not appropriate for all patients with contact sensitization to nickel, it is not controversial that it may be extremely helpful in a subset of patients with SNAS.

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