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Low Nickel Diet: A Patient-Centered Review

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Abstract

Nickel allergic contact dermatitis (ACD) has become a more widely recognized disease process over the last three decades in the United States. A subpopulation of ACD patients will manifest with systemic contact dermatitis (SCD). Specifically, those cases of widespread recalcitrant nickel ACD with only partial clinical relief after strict nickel avoidance, suggest SCD. Evidence indicates that application of the low nickel diet has the highest efficacy in patients with SCD, and that a targeted, points-based approach is most meaningful. Furthermore, as the immunologic pathways of how oral nickel provokes cutaneous dermatitis are complex, involving interplay between the Th2 and Th1 response, more specific investigative work in this area is much needed.

Keywords: Systemic Contact Dermatitis (SCD); Systemic Nickel Allergy Syndrome (SNAS); Nickel allergy; Low nickel diet

Introduction

Prevalence of nickel contact dermatitis is estimated to be 19.5% in adults and 25.6% in children patch tested within the US [1,2]. The exact prevalence within the general, non-patch tested, US population is largely unknown, as the last study to evaluate healthy US volunteers took place over 30 years ago [3]. At that time, Prystowsky et al. showed that 5.7% of an asymptomatic study population had been (unknowingly) sensitized to nickel [3]. The reported rates of nickel sensitization are on the rise, suggesting a large proportion of the US population continues to be exposed and sensitized to nickel [4].

The relationship between allergic contact dermatitis (ACD) and nickel is undisputed and widely confirmed in literature. Systemically-induced contact dermatitis (SCD) is a cutaneous manifestation secondary to allergen exposure via the oral, per rectum, intravesical, transcutaneous, intravenous, or inhalation routes [5]. While SCD is often considered a cutaneous form of systemic nickel allergy syndrome (SNAS), it is important to recognize that SNAS is a broader syndrome. In addition to cutaneous symptoms, SNAS often presents with a host of systemic symptoms including heartburn, abdominal pain, nausea, vomiting, constipation, abdominal distension rhinitis, asthma, headache, chronic fatigue syndrome, arthralgia, fibromyalgia, and fever [6,7]. SCD may also be a misleading term, because skin contact with nickel is not a requirement for disease elicitation though reactivation of previous nickel contact sites may be seen, clinical presentation also includes generalized skin manifestations, such as urticaria and eczema [6,7]. Fabbro et al. remark that the typical clinical presentation of SNAS may be a severe recurring ACD despite proper treatment and avoidance [8]. The most common clinical presentation of SNAS is often refractory vesicular hand dermatitis, with possible pruritic papules on the elbows [8].

The prevalence of SCD in the population of patients with ACD is largely unknown. In one recent study, SNAS alone was identified in up to 6% of patients presenting to allergy clinics in Europe, implying that SCD may be under-identified in the dermatitis population [9]. Additionally, Jensen demonstrated that up to 10% of nickel sensitized patients exhibit SCD due to the amount of nickel found in a normal diet [10]. SCD to nickel is one of the most commonly reported and described forms of dietary SCD, consistent with the fact that nickel is one of the most common contact allergens ingested due to its ubiquitous nature [8,11].

Food Source	mg/kg	Nickel content (µg)	Serving Size (g)
Mussels	1.033	154	1 cup (150)
Spirulina	2.7	151	1 cup (56)
Canned Refried Beans	0.541	131	1 cup (242)
Oatmeal	0.354	83	1 cup (234)
White beans	0.329	82	1 cup (250)
Wheat germ	0.713	82	1 cup (115)
Oat ring cereal	2.124	59	1 cup (28)

Pinto beans	0.578	46	1/2 cup (80)
Lima beans	0.062	45	1/2 cup (72)
Avocado	0.315	43	1 avocado (136)
Granola with raisins	0.946	41	1 bar (43)
Milk chocolate	0.921	41	1 bar (44)
Lasagna with meat	0.129	38	1 serving (297)
Chocolate cake	0.521	37	1 piece (71)
Prune juice	0.136	35	8 Oz (256)
Peanuts	0.494	35	1/2 cup (70)
Chocolate milkshake	0.142	35	8 Oz (244)
Pineapple juice, from concentrate	0.128	32	8 Oz (250)
Tomato salsa	0.13	32	1 cup (245)
Green beans	0.077	28	1 cup (240)
Iceberg lettuce	0.118	28	1 cup (240)
Spaghetti with meat sauce	0.09	25	1 cup (283)
Pork sausage	0.111	25	1 sausage (227)
French Fries	0.196	23	1 medium serving (117)
Canned tomato soup	0.086	22	1 cup (250)
Clam chowder	0.084	21	1 cup (245)
Canned Pineapple	0.082	21	1 cup (250)
Sweet potatoes	0.089	21	1 large potato (200)
Tomato sauce	0.096	20	1 cup (212)
Peas	0.203	20	1/2 cup (98)
Chocolate milk	0.0792	20	1 cup (244)
Tomato juice	0.078	20	8 Oz (250)
Canned fruit cocktail	0.065	17	1 cup (253)
Potato	0.058	15	1 large potato (250)
Peanut butter	0.481	15	2 tbsp (32)
Catfish	0.105	15	1 fillet (143)
Brownie	0.622	15	1 brownie (24)
Cocoa powder	0.98	15	3 tbsp (15)
Doughnut	0.244	15	1 doughnut (60)
Asparagus	0.112	15	1 cup (134)
Pumpkin pie	0.102	14	1 piece (133)
Taco/tostada with beef and cheese	0.13	13	1 taco (99)
Cantaloupe	0.071	13	1 cup (177)

Peach	0.078	12	1 cup (154)
Corn/tortilla chips	0.195	12	1 cup (63)
Canned chicken noodle soup	0.045	11	1 cup (250)
Raisins	0.068	11	1 cup (165)
Presweetened cereal	0.397	11	1 cup (28)
Fast-food quarterpound cheeseburger	0.056	10	1 cheeseburger (186)
Pizza, cheese and pepperoni	0.084	10	1 slice (120)
Winter squash (Hubbard/acorn)	0.087	10	1 cup (113)
Chicken nuggets	0.131	10	5 pieces (75)

Table 1: Nickel Content by Food Source Following a point based diet 10 μg= 1 point. Daily goal is less than 15 points [20]. Amounts of dietary nickel were gathered from literature review [17,20,22].

The specific non-cutaneous dose of nickel required to evoke a hypersensitivity reaction has been in question due to variance of the nickel dose reported in oral challenge tests. A meta review by Jensen specifically assessed elicitation of SCD due to nickel ingestion, and found that 1% of those sensitized to nickel react to the nickel content of a "normal" diet, defined as 0.22 mg, 0.35 mg, or 0.53 mg [12]. Furthermore, a dose-response relationship was revealed showing 10% of nickel sensitized patients responding to exposures between 0.55 mg and 0.89 mg. Such low exposures can be easily attained by consuming foods high in nickel content (see Table 1, Figure 2 and Figure 3) [12].

Figure 1: Nickel Survey QR Code: link to take the survey. https://emg.wufoo.com/forms/nickel-allergic-contact-dermatitis-survey.

However, many patients sensitized to nickel are unaware that dietary exposure may play a role in their morbidity. Recent data from the first self-reporting nickel allergy patient registry study showed that within 280 participants endorsing a self-reported history of nickel allergy, only 37% recognized nickel could be found in foods (Loma Linda University, Nickel Allergy Alliance, and Dermatitis Academy™) (Figure 1).

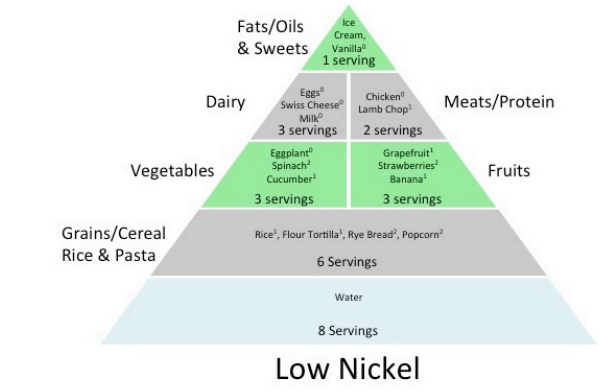

Figure 2: Points Based Low Nickel Diet Food Pyramid: Schematic of lower nickel foods with points in superscript. Suggested for nickel-sensitized patients with recalcitrant ACD due to nickel, despite standard nickel avoidance measures.

Thus, further patient and provider education regarding non-cutaneous nickel exposures, specifically in diet, are necessary.

Underlying Immunology

The immunologic response to oral provocation of nickel allergy is complex and diverse. The cytokine profile of SNAS involves both a Th1 and Th2 response. The delayed cytotoxic cellular immunity shared by SNAS and ACD is mediated through a predominant Th1 reaction, evident by elevations of IFN-γ, IL-2, and TNF-α [13]. An observed rapid cutaneous response following oral nickel provocation, suggests a complex interplay within SNAS between Type IV (cellular) and III (humoral) hypersensitivity reactions [13,14]. Jensen et al. demonstrated a statistically significant rise in IL-5, a Th2 response, within 24 hours after oral challenge, highlighting the role of the Th2 response in the initial elicitation phase of SNAS [13]. Of interest, the

Th2 response that is shared with atopic dermatitis and asthma, offers a plausible explanation for the cutaneous and extra cutaneous manifestations of SNAS [15]. The immunological complexities extend to include underlying cross-facilitating pathways, demonstrated by Ricciardi et al. where 16 out of the 98 SNAS patients (16.3%, p<0.001) presented with an IgE-mediated food allergy [9]. Ultimately, SNAS exhibits Th1 and Th2 responses with clinical presentation dictated by the predominating immune response.

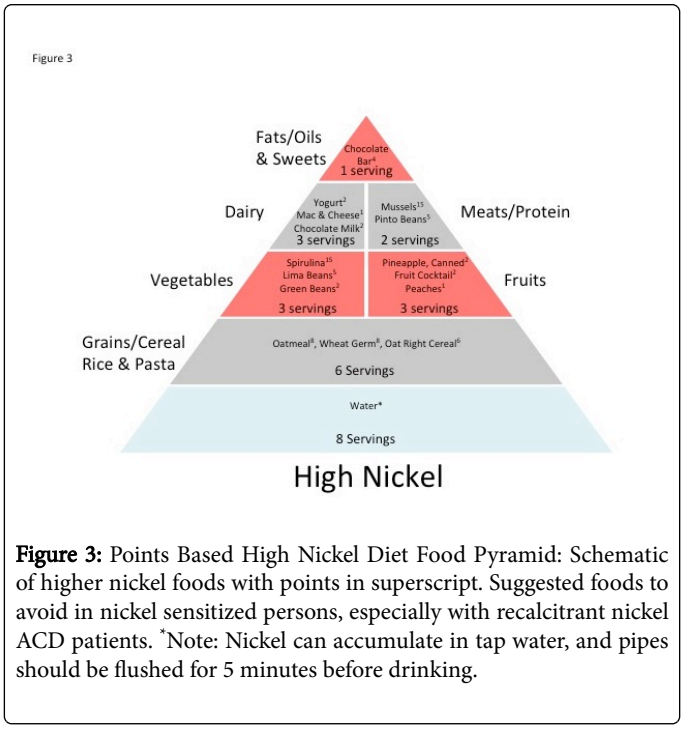

Figure 3: Points Based High Nickel Diet Food Pyramid: Schematic of higher nickel foods with points in superscript. Suggested foods to avoid in nickel sensitized persons, especially with recalcitrant nickel ACD patients. *Note: Nickel can accumulate in tap water, and pipes should be flushed for 5 minutes before drinking.

All oral nickel exposure does not result in SCD, and in fact if repeated oral exposure occurs prior to topical prolonged contact, immunologic tolerance may be conferred. In a study from Denmark, adolescent girls with dental braces before ear piercings exhibited a lower prevalence of nickel allergy compared to those girls with ear piercings before dental braces [16]. A more recent study by Di Gioacchino et al. showed that nickel oral hyposensitization also resulted in immune tolerance [17]. Nickel oral hyposensitization is a mechanism of immune tolerance, in a nickel-sensitized patient, through the ingestion of low dose nickel. When comparing nickel oral hyposensitization to placebo in patients with SNAS, those patients exposed to oral low dose nickel for one year exhibited dose-dependent improvement in gastrointestinal symptoms and cutaneous visual analog scores [17]. Those taking the highest dose of 1.5 μg Ni/week demonstrated increased tolerance as seen by the higher challenge dose of oral allergen needed to elicit cutaneous symptoms. Additionally, a statistically significant number of hyposensitized patients had a negative patch test when retested at the conclusion of the study. The hypothesized mechanism is an active cellular suppression through a Th2 response regulating nickel-specific T lymphocytes [17,18].

Low Nickel Diet—does it work?

In the recent literature there have been many documented cases of SCD linked to diet. Jacob et al. reported dramatic improvement in cutaneous symptoms of four pediatric patients with refractory nickel ACD after following strict avoidance measures including diet modification [19]. The case study outlined four children with known nickel allergy who had a 60%-80% improvement of their dermatitis following avoidance strategies and a low nickel diet. However, all children developed acute generalized dermatitis exacerbations after ingestion of chocolate—a nickel-rich food. After educating the patients and parents regarding foods to avoid, the patients' symptoms of generalized dermatitis resolved by the next follow-up appointment.

A retrospective case series by Antico and Soana showed that low nickel diets dramatically improved dermatitis symptoms in nickel sensitive patients [14]. The study analyzed 339 patients sensitized to nickel via patch testing. Simple avoidance of nickel contact resulted in a 15% recovery rate. However, 80% of the patients who combined a low nickel diet with avoidance of nickel contact had a complete or nearly complete resolution of skin symptoms. A double-blind placebo-controlled oral nickel challenge was then conducted on the improved patients, with an 89% recurrence or worsening of symptoms, which accounted for 10% of the total patient population.

Nutraceuticals and functional food ingredients (such as the plant-based Mediterranean meal plan) have been highly used as alternative care treatments, especially in reducing cardiovascular risk in patients that cannot tolerate statin therapy to decreased morbidity and mortality [20]. Notably, many of these diets contain high nickel foods such as legumes and grains. As a result, subpopulations of patients with nickel sensitization using nutraceuticals and functional food ingredients may be at increased risk of SNAS or SCD.

The literature continues to expand the understanding of nickel allergy, specifically the complexities related to oral exposure. Patient-centered education is key when explaining these complex pathophysiological processes and applying them to pragmatic guidelines. Table 1 provides a streamlined reference for practitioners offering information regarding food groups and nickel content in order to council patients suffering from recalcitrant nickel-allergic contact dermatitis or SCD. Of note, "detox" and "fad" diets must be scrutinized closely as often nickel content may remain high despite the "healthy" food options. Thus, a systematic points-based diet may be instituted to specifically avoid high nickel intake in exquisitely sensitized individuals.

Discussion

Nickel diets have been highly criticized due to adherence difficulties. However, Mislankar et al. proposed a simple point-based low nickel diet [21]. The overall goal of a low-nickel diet is to not exceed 150 μg of nickel per day, or equivalent to 15 "points" as calculated by the simple algorithm. Such dietary plans may help patients avoid SCD flares (see Figures 2 and 3).

It should be noted that diligence with a low nickel diet should be followed for at least 1 to 3 months to determine the efficacy and impact of the dietary restriction on SCD expression. Factors that may compromise the effectiveness of a low nickel diet could include kitchenware such as pots, pans or eating utensils that release free nickel in the presence of acidic foods. Also, tap water used to cook foods may also contain significant amounts of nickel and should be considered when preparing various food items [22]. SCD from food ingestion is becoming recognized as a distinct disease process, and should be suspected in nickel-sensitized patients whose dermatitis partially improves with contact avoidance strategies [23]. In such cases a trial of a low nickel diet may be an appropriate therapeutic option.

References

1. Fransway AF, Zug KA, Belsito DV, Deleo VA, Fowler JF Jr, et al. (2013) North American Contact Dermatitis Group patch test results for 2007-2008. Dermatitis 24: 10-21.
2. Zug KA, Pham AK, Belsito DV, DeKoven JG, DeLeo VA, et al. (2014) Patch testing in children from 2005 to 2012: results from the North American contact dermatitis group. Dermatitis 25: 345-355.
3. Prystowsky SD, Allen AM, Smith RW, Nonomura JH, Odom RB, et al. (1979) Allergic contact hypersensitivity to nickel, neomycin, ethylenediamine, and benzocaine: relationships between age, sex, history of exposure, and reactivity to standard patch tests and use tests in a general population. Arch Dermatol 115: 959-962.
4. Goldenberg A, Vassantachart J, Lin EJ, Lampel HP, Jacob SE (2015) Nickel Allergy in Adults in the U.S.: 1962 to 2015. Dermatitis 26: 216-223.
5. Veien NK (2011) Systemic contact dermatitis. Int J Dermatol 50: 1445-1456.
6. Braga M, Quecchia C, Perotta C, Timpini A, Maccarinelli K, et al. (2013) Systemic nickel allergy syndrome: nosologic framework and usefulness of diet regimen for diagnosis. Int J Immunopathol Pharmacol 26: 707-716.
7. Thyssen JP, Maibach HI (2008) Drug-elicited systemic allergic (contact) dermatitis--update and possible pathomechanisms. Contact dermatitis 59: 195-202.
8. Fabbro SK, Zirwas MJ (2014) Systemic contact dermatitis to foods: nickel, BOP, and more. Curr Allergy Asthma Rep 14: 463.
9. Ricciardi L, Arena A, Arena E, Zambito M, Ingrassia A, et al. (2014) Systemic nickel allergy syndrome: epidemiological data from four Italian allergy units. Int J Immunopathol Pharmacol 27: 131-136.
10. Jensen CS, Menné T, Johansen JD (2006) Systemic contact dermatitis after oral exposure to nickel: a review with a modified meta-analysis. Contact Dermatitis 54: 79-86.
11. Sharma AD (2013) Low nickel diet in dermatology. Indian J Dermatol 58: 240.
12. Jensen CS, Menné T, Johansen JD (2006) Systemic contact dermatitis after oral exposure to nickel: a review with a modified meta-analysis. Contact Dermatitis 54: 79-86.
13. Jensen CS, Lisby S, Larsen JK, Veien NK, Menne T (2004) Characterization of lymphocyte subpopulations and cytokine profiles in peripheral blood of nickel-sensitive individuals with systemic contact dermatitis after oral nickel exposure. Contact Dermatitis 50: 31–38.
14. Antico A, Soana R (2015) Nickel sensitization and dietary nickel are a substantial cause of symptoms provocation in patients with chronic allergic-like dermatitis syndromes. Allergy Rhinol (Providence). 6: 56-63.
15. Babi L, Picker L, Soler M, Drzimalla K, Flohr P, et al. (1995) Circulating allergen-reactive T cells from patients with atopic dermatitis and allergic contact dermatitis express the skin-selective homing receptor, the cutaneous lymphocyte-associated antigen. The Journal of experimental medicine 181: 1935-1940.
16. Mortz CG, Lauritsen JM, Bindslev-Jensen C, Andersen KE (2002) Nickel sensitization in adolescents and association with ear piercing, use of dental braces and hand eczema. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis (TOACS). Acta Derm Venereol 82: 359-364.
17. Di Gioacchino M, Ricciardi L, De Pità O, Minelli M, Patella V, et al. (2014) Nickel oral hyposensitization in patients with systemic nickel allergy syndrome. Annals of medicine 46: 31-37.
18. Weiner HL (1997) Oral tolerance: immune mechanisms and treatment of autoimmune diseases. Immunol Today 18: 335-343.
19. Jacob SE, Hamann D, Goldenberg A, Connelly E (2015) Easter Egg Hunt Dermatitis: Systemic Allergic Contact Dermatitis Associated with Chocolate Ingestion. Pediatric Dermatology 32: 231-223.
20. Scicchitano P, Cameli M, Maiello M, Modesti P, Muiesan M, et al. (2014) Nutraceuticals and dyslipidaemia: Beyond the common therapeutics. Journal of Functional Foods :11-32.
21. Mislankar M, Zirwas MJ (2013) Low-nickel diet scoring system for systemic nickel allergy. Dermatitis 24: 190-195.
22. Kamerud K, Hobbie K, Anderson K (2013) Stainless Steel Leaches Nickel and Chromium into Foods during Cooking. J Agric Food Chem 61: 9495-9501.
23. Total Diet Study Statistics on Element Results based on 2006-2011 US Food and Drug Administration Market Baskets.