

# Improvement of cutaneous and gastrointestinal symptoms in Crohn's disease following a low-nickel diet: A case report and narrative review



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Nickel, a ubiquitous trace metal, is a common contact allergen that, for some people, can also be systemic, resulting primarily in cutaneous and gastrointestinal (GI) symptoms. This article presents a narrative review of the relevant literature on systemic nickel allergy syndrome and low-nickel diets (LNDs) and reports an autobiographical case of a 45-year-old male with a 25-year history of Crohn's disease (CD) and contact nickel allergy. The case details the identification of systemic nickel allergy and the treatment of symptoms related to CD with a LND, implemented using a nickel points scoring system. During the initial 4-week implementation period, considerable reductions in cutaneous (dyshidrotic eczema), GI symptoms and systemic pain were observed. Specifically, the frequency of bowel movements decreased from approximately six or more per day to around three or fewer, and back and neck pain severity dropped drastically from a baseline average of 8 (on a 1–10 scale) to < 2. These findings, along with ancillary improvements in mood and overall well-being, were concurrent with the use of the LND and have remained consistent and sustained at the time of writing, approximately 8 months later. Various diets that are, by nature, low in nickel content have shown promise for the treatment of CD, and this literature review and case report suggest a hypothesis that their efficacy may be related to reduced nickel intake.

**Keywords:** low-nickel diet; Crohn's disease; case study; autobiographical; dyshidrotic eczema; IBD; IBS; mood.

## Introduction

Nickel is a ubiquitous trace metal found commonly in jewellery, cooking utensils, surgical implants and in varying amounts in foods and drinking water. Allergic contact dermatitis to nickel is one of the most common allergies, with approximately 10% – 20% of the world's population exhibiting symptoms consistent with a contact nickel allergy.<sup>1,2,3</sup> Up to 20% of people with a contact nickel allergy might develop systemic nickel allergy syndrome (SNAS)<sup>1</sup> in which reactions, mostly cutaneous and gastrointestinal (GI), can occur to the nickel ingested in food and beverages.<sup>1,2</sup> Research from a cohort of people with allergy in Italy found that of 1696 patients presenting to allergy clinics, nearly 6% had verifiable SNAS, and of these, a statistically significant 16.3% presented immunoglobulin E (IgE)-mediated food allergy, suggesting underlying cross-facilitating pathways.<sup>4</sup>

## Aetiology and pathophysiology

The process resulting in SNAS begins with repeated exposure to nickel-containing items. Nickel is found in many everyday household items, including the stainless steel types used for cookware, cutlery and kitchen surfaces and sinks, which can contain up to 10% nickel; copper alloys used in plumbing and coinage; jewellery made from stainless steel, silver and gold and nickel-containing plating used for heating elements, bathroom fixtures and tools.<sup>5,6</sup> The progression of contact sensitisation and allergy to SNAS requires frequent, consistent contact exposure. Therefore, the nickel-releasing items most commonly causative of SNAS include jewellery, belt buckles, zips on clothing and surgical or dental implants.

When nickel ions are absorbed through the skin, they bind to proteins such as albumin, forming a hapten-carrier complex that can be recognised as an antigen, eliciting an immune response.<sup>7</sup> Langerhans cells in the epidermis, papillary dermis and mucosa take up the nickel-protein complex, subsequently migrating to the lymph nodes where the antigen is presented to

T-lymphocytes (T-cells), leading to the proliferation of *nickel-specific* T-cells.<sup>8</sup> This sensitisation process primes immune responses to nickel exposure, usually over several weeks. Subsequent exposures result in localised reactions involving memory T-cells that release inflammatory cytokines, leading to the classic symptoms of contact dermatitis: itching, redness, rash and pustules. While the classic contact dermatitis involves a Type IV hypersensitivity reaction, nickel has also been implicated in Type I, II and III hypersensitivity reactions.<sup>9</sup>

Sensitised individuals can become reactive to nickel from oral exposure. These ingested amounts are much lower than that required for toxicity. The average nickel uptake from diet is somewhere between 74 µg/day and 406 µg/day (for ages 20–25 years old and 40–50 years old, respectively),<sup>10,11</sup> which is less than ½ of the suggested upper limit for nickel intake in adults of 1.0 mg/day.<sup>11</sup> However, this amount is sufficient to elicit an immune response involving both Type 1 (Th1) and Type 2 (Th2) helper T-cells and cytokines and CD8- and CD4-positive T-lymphocytes.<sup>12</sup> Previously, sensitised T-cells encounter circulating nickel and trigger a widespread immune response, along with localised responses at the GI sites of contact.

## Clinical manifestations

The condition is characterised primarily by cutaneous manifestations of dermatitis, dyshidrotic eczema, pompholyx and urticaria and systemic symptoms such as headache, asthenia, pruritus and GI symptoms related to histopathological alterations of the mucosa<sup>13,14</sup> and possibly immunosuppressive actions.<sup>15</sup> However, Braga et al. found that only GI and cutaneous symptoms were elicited by an oral nickel challenge.<sup>1</sup>

Localised inflammation may result in other ancillary outcomes, such as lactose intolerance, because of impairment of brush border enzymes. In a trial comparing people with SNAS to healthy controls without GI symptoms, lactose intolerance (as measured by a lactose breath test) was found in 75% of those with SNAS, compared to 7% of those without.<sup>16</sup>

## The low-nickel diet

Nickel is ubiquitous in the diet, especially in plant-derived foods retaining the bran or germ (whole grains) and in nuts and seeds.<sup>17</sup> It is assimilated from the soil into plants and, from there, accumulates in plant tissues. Nickel can also accumulate in foods processed with stainless steel and other nickel-containing machinery and storage devices. Therefore, the nickel content of foods can vary widely and depends on the type of food, the soil in which it is grown and how it is processed, transported and stored. For example, puree from hydroponically grown tomatoes (a commonly high-nickel food) has lower nickel content due to the modifiability of the growing substrate and nutritional inputs and results in significantly lower GI symptoms than puree from conventionally grown tomatoes.<sup>18</sup>

Several iterations of a low-nickel diet (LND) have been developed, including the use of 'forbidden' (high-nickel) foods and simplified daily diet structures.<sup>1</sup> Mislanka and Zirwas have developed a simplified scoring system to quantify the average nickel content of common foods, making it easier to apply for those with SNAS. Using this scoring system, adults should consume no more than 15 'points' per day.<sup>17</sup>

## Efficacy of the low-nickel diet

The LND has been observed to significantly reduce systemic nickel (as measured by urinary excretion) to less than a suspected tolerance level of 1.7 µg/g creatinine,<sup>14</sup> and in a cohort of people who did not resolve symptoms by avoiding contact nickel exposure, an LND resolved symptoms in 80% of remaining participants.<sup>7</sup>

The diet has demonstrated efficacy for reducing dermatitis generally,<sup>19</sup> and dermatitis related to nickel exposure.<sup>20</sup>

In people with irritable bowel syndrome, LNDs have resulted in significant and consistent reductions in symptoms, such as bloating, pain, flatus, constipation, diarrhoea and nausea, along with significant improvements in body pain and perceived physical function.<sup>21</sup> Along with significant and meaningful reductions in cutaneous and GI symptoms resulting from an LND, sub-cohort ( $n = 87$ ) analysis found that the resumption of a 'normal' diet resulted in the return of symptoms.<sup>22</sup> Women with endometriosis also commonly experience irritable bowel syndrome symptoms, and these have been linked to allergic contact mucositis secondary to nickel allergy.<sup>23</sup> Three months of an LND significantly reduced GI, extra-intestinal and gynaecological symptoms in a small study of women with irritable bowel syndrome (IBS)-like disorders of endometriosis.<sup>23</sup> Additionally, a 2021 study also found that a telehealth intervention supporting a LND resulted in significant improvements in anthropometry and quality of life in people with SNAS.<sup>24</sup>

## Rationale for a low-nickel diet intervention

Nickel is the most common contact allergen, and repeated sensitisation can result in a substantial proportion of people who are allergic to contact nickel exposure developing a systemic allergy, with implications for diet-related pathologies.

The population prevalence of SNAS could be as high as 4%, but recognition of the condition is often lacking in clinical nutrition practice. To put this in perspective, coeliac disease, commonly screened for in practice, has a population prevalence nearly 3-fold lower than this upper limit, at 1.4%.<sup>25</sup>

The demonstrable benefits of an LND, especially to GI and cutaneous symptoms, offer not just a tantalising treatment option for people with conditions involving these symptoms

but also hints at the possibility that specific diets suspected of being of benefit to GI disorders, and eczema might provide some of their benefits due to an inadvertent reduction in nickel intake. Of particular interest are lower-carbohydrate, ketogenic and carnivore-style diets, which, by their nature, are likely to be low in nickel due to the avoidance of the most common high-nickel foods (especially whole grains and legumes) and the reduction of other higher-nickel foods such as seeds, nuts and foods containing cocoa. If one of the reasons for the case successes of diets like the carnivore diet in inflammatory bowel disease patients,<sup>26</sup> or other conditions of GI or cutaneous pathologies are related to nickel exclusion, this might allow for more targeted dietary approaches and those that include a larger compendium of foods. This could provide further health benefits due to improved dietary adherence resulting from less rigid diet styles, as well as additional benefits from the inclusion of low-nickel foods higher in fibre and phytochemicals.

Students at the Auckland University of Technology are currently undertaking further research to explore the nickel content of different dietary approaches under the author's supervision, and additional trials are necessary to determine whether lower-nickel diets have broader application in treating specific pathologies.

## Autobiographical case report

At the time of this experiment, I was a 45-year-old fit and active, 85 kg, 176 cm, relatively lean (~15% bodyfat), *Pākehā* (New Zealand European) male with diagnoses of Crohn's disease (ICD), diagnosed in 2000 by colonoscopy) and bipolar disorder, neither of which are treated with medications, except for occasional use of analgesics. I also have a contact nickel allergy identified by eczematous reactions to jewellery and confirmed by patch-testing approximately 27 years ago.

Symptomatic expressions of these conditions include GI disturbances, pain and urgency to defecate and mood swings, depression and hypomania, respectively. I also experienced other symptoms commonly comorbid with these conditions including recurrent muscle aches and tension, arthritis and back and neck pain, along with dyshidrotic eczema, primarily affecting the feet.

I was seeking to lose body fat and began changing some dietary choices from more processed options, such as white bakery goods, white noodles and pasta and white bread, to more unprocessed or 'whole' options, prioritising legumes, nuts and seeds and wholegrain versions of foods. Thus, I was choosing ostensibly 'healthier' versions of discretionary foods, i.e. preferring high-cocoa-content chocolate (a common after-dinner treat) over milk or white chocolate. I noticed within days, despite what *should* have been a healthier diet, many symptoms, especially pustular dyshidrotic eczema, back and neck pain, mood and frequency of bowel motions, were worsening, not improving. This led me to suspect

SNAS, given my preexisting contact nickel allergy and the food substitutions I had made, which were consistent with a shift from lower- to higher-nickel foods.

## Application of a low-nickel diet

A LND was implemented for the purpose of verification and experimentation. For ease of use, I used the nickel points scoring system as devised by Mislanka and Zirwas<sup>17</sup> using modified tables reflecting the nickel content of foods available in New Zealand (Rebelytics Research and Development Inc.),<sup>27</sup> choosing only foods that are 'green' on the nickel foods list, with 0–1 'nickel point'.

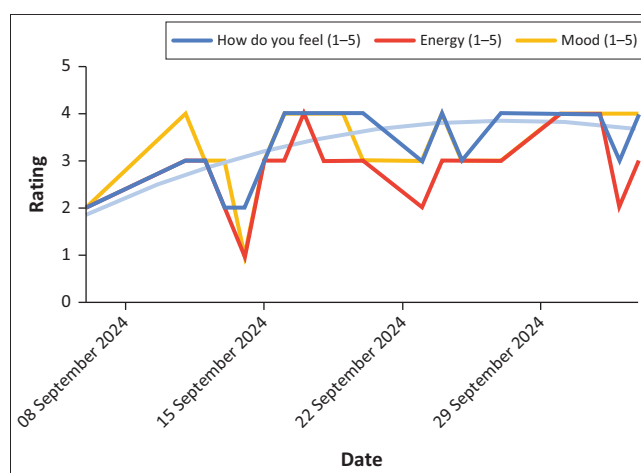
To eliminate, as best I could, the potential for other dietary influences to affect these results, I applied the diet without consideration for other factors, such as foods that may increase the likelihood of symptom exacerbation in some people with CD (such as dairy and wheat or gluten)<sup>28</sup> – nor did I attempt to eat 'healthier' versions of foods or make any substantive changes to exercise or other lifestyle factors. This meant that the LND I adopted could reasonably be construed as less 'healthy' than the diet I was previously following and was unrestricted in intakes of sugar, ultra-processed foods and gluten and casein.

Effects of the diet were quantified by the number of bowel movements in the morning (as I had noted increased urgency and frequency at this time) and overall per day.

Data were recorded electronically in a spreadsheet (Google Sheets) that facilitated immediate data visualisation and analysis. Additionally, I rated 'How do you feel', energy and mood on a 1–5 scale (1 being worst and 5 being best) and back and neck pain on a 1–10 scale of severity, every day for 4 weeks, along with a baseline reflection on my overall impression of the month before starting the diet.

## Clinical course

Upon adoption of the LND, mood, energy and overall well-being increased, with a trend upward over the month (Figure 1). Most evidently and unexpectedly, there were



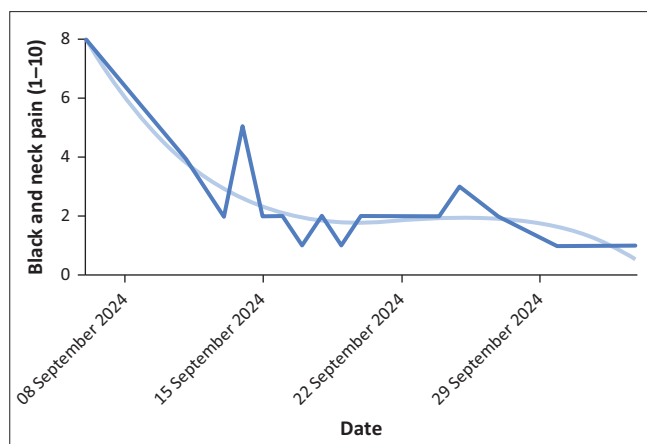
Note: 1-5 scale: 1 = worst, 5 = best.

FIGURE 1: Daily recording of mood, energy and 'How do you feel' on a 1–5 scale.

drastic reductions in neck and back pain from a baseline average of around 8, which was a near-debilitating level of chronic pain, down to < 2 (Figure 2). Large reductions in the frequency of bowel motions and subjectively a substantial decrease in 'urgency', both key hallmarks of CD,<sup>29,30</sup> also occurred. This had previously been around six events or more per day and was reduced to around 3 or fewer (Figure 3).

Some transient lifestyle factors affected the overall results, and when these confounding influences like a bout of food poisoning, poorer sleep due to children waking and mood and possible physiological effects from lack of sleep, stress and a cold (and use of vitamin C that increased bowel frequency) are considered, the beneficial effects of the LND could be even more pronounced than these results suggest. There was also a clear reduction in dyshidrotic eczema of the feet, especially the total elimination of pustules, which had previously caused considerable pain and discomfort (Figure 4).

At the time of writing, approximately 8 months after initiating and sustaining the use of an LND, pustular expressions of peripheral eczema have not returned, nor has back and neck pain returned to the previous levels, remaining at a similar



Note: 1-10 scale: 1 = least severe, 10 = most severe.

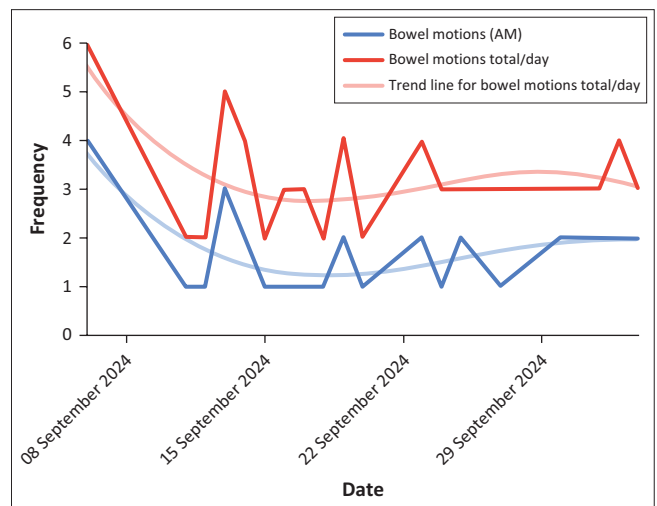
**FIGURE 2:** Daily recording of the severity of back and neck pain on a 1–10 scale.

level to that observed after a month on the LND. Subjectively, I feel my mood, energy and overall well-being have improved. Most quantifiably, bowel motions remain mostly around one to three times per day compared to the six or more in the period before initiating the LND. Additionally, the requirement for analgesia is less, although I did not quantify this outcome.

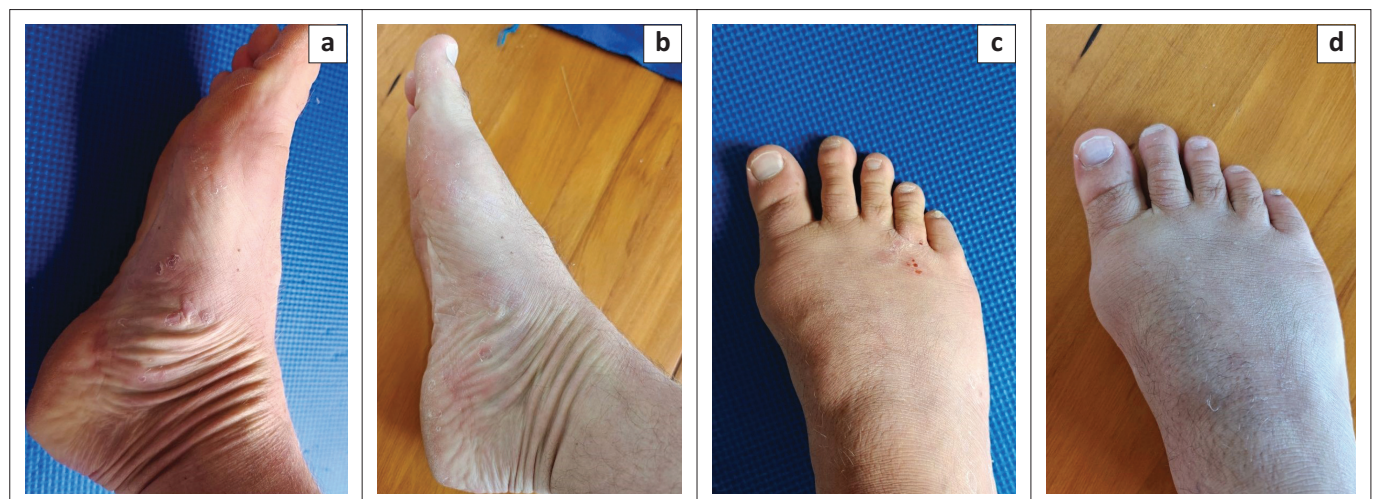
## Discussion

Crohn's disease can be both physically and socially debilitating due to pain, urgency and frequency of bowel motions,<sup>29</sup> even when in remission.<sup>30</sup> It can also lead to serious complications and, in rare cases, result in medical emergencies such as fistulae and bowel perforations.<sup>31,32</sup>

While it is common, in the author's experience, for the potential benefits of nutrition for CD treatment to be dismissed in medical settings, evidence demonstrates that shifts to healthier, nutrient-dense diets, such as a specific carbohydrate diet or a Mediterranean diet, are similarly effective for reducing inflammation and CD symptoms.<sup>33</sup> The Crohn's disease exclusion diet (CDED) has also been demonstrated to



**FIGURE 3:** Number of bowel motions per day.



**FIGURE 4:** (a, c) Pre-diet and (b, d) post-diet comparison of the right foot, showing reduced eczema and elimination of pustular dyshidrotic eczema.

be effective for the induction of remission in CD.<sup>34</sup> The CDED features a 12-week induction phase that includes mostly whole unprocessed foods such as fruits and vegetables, chicken, eggs, rice and potatoes, all of which, incidentally, are low-nickel foods.<sup>17,34</sup> Lower-carbohydrate interventions have also been suggested, and it has been theorised that a low-starch diet could help improve disturbances in the microbiota in CD.<sup>35</sup> A recent case series found universal, large improvements of 72–165 points on the Inflammatory Bowel Disease Questionnaire resulting from the application of a carnivore-style very-low-carbohydrate ketogenic diet.<sup>26</sup>

As noted earlier, lower-carbohydrate, ketogenic and carnivore-style diets are, by their nature, low in nickel due to the avoidance of many higher-nickel foods. But if they are achieving benefits in some cases due to nickel reduction, they might also be unnecessarily restrictive. Evidence shows that higher intakes of fruit-derived fibre are considered protective against CD,<sup>36</sup> and active cases of the disease are characterised by lower intakes of vegetables and fruit and have lower levels of serum micronutrients than healthy controls.<sup>37</sup> Therefore, if individuals benefitting from a low-carbohydrate or carnivore approach were found to have SNAS, they may be able to expand their available food choices and get the same symptom benefits with a larger array of available foods and resultant benefits to dietary adherence and health from inclusion of foods higher in fibre and phytochemicals.

With respect to the constellation of symptoms present in my case, Nickel is a known trigger or cofactor of intestinal and systemic symptoms in multiple conditions, and LNDs have demonstrated efficacy for reducing dermatitis generally<sup>19</sup> and dermatitis related to nickel exposure,<sup>20</sup> along with significant and consistent reductions in GI symptoms, such as bloating, pain, flatus, constipation, diarrhoea and nausea, and significant improvements in body pain and the perception of physical function.<sup>21</sup> There is also emerging research demonstrating that ingested nickel particles precipitate or exacerbate colitis in mouse models carrying mutations associated with inflammatory bowel disease (IBD) susceptibility by perturbing gut autophagy. This mechanism operates in addition to eliciting allergic responses, suggesting additional aspects of nickel ingestion specific to CD pathogenesis.<sup>38</sup>

## Conclusion

This case report demonstrated that in an otherwise functional and healthy 45-year-old male, the application of an LND resulted in large and sustained self-reported improvements in many symptoms related to CD.

Limitations of any case report, particularly an autobiographical one, are the potential for bias, subjectivity, the lack of any comparators to identify placebo effects and the 'n of 1' nature of the exploration. Hence, the results observed in this case are not generalisable and may have been unique to me, due to genetic, environmental or other factors within the physiological-cum-psychosocial milieu. They may also have resulted from regular cycles of relapse

and remission common to autoimmune conditions, the placebo effect, self-reporting biases or other lifestyle or dietary factors that were inadvertently not accounted for. However, the reduction in symptoms has persisted and appears to have been objectively worsened by the reintroduction, even acutely, of higher-nickel foods. This suggests that the LND was responsible for the improvements, especially as no effort was made to eat a 'healthy' diet.

The case suggests the hypothesis that LNDs offer a treatment option for CD, and that diets lower in nickel might exert some of their effects due to a reduction in nickel load, reducing local and systemic immune and inflammatory responses in sensitive individuals. Thus, further research using blinded, controlled trials is warranted to investigate this hypothesis.

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### Competing interests

The author declares that no financial or personal relationships inappropriately influenced the writing of this article.

### CRedit authorship contribution

Cliff J.D. Harvey: Conceptualisation; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Software; Supervision; Visualisation; Writing – original draft; Writing – review & editing. The author confirms that this work is entirely their own, has reviewed the article, approved the final version for submission and publication and takes full responsibility for the integrity of its findings.

### Ethical considerations

This manuscript presents a narrative review and autobiographical case report. As the sole participant in the research, any data presented and analysed is exclusively my own personal experience. The research was conducted with a commitment to ethical principles of honesty, transparency and integrity. All efforts were made to ensure the accuracy of the account and to avoid any misrepresentation. The manuscript does not contain any private or privileged information or data about other individuals. By submitting this work, I attest that the research was conducted responsibly, with full awareness of the potential for psychological distress, and that the narrative is presented with intellectual honesty.

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### Data availability

The author confirms that the data supporting the findings of this study are available within the article.

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