



Correspondence

Staphylococcal infections in atopic dermatitis and nickel allergy: Immunologic implications and elemental opportunities



We commend Bogdali et al. for bringing to attention the complex associations between nickel allergy, atopic dermatitis (AD), and *Staphylococcus aureus* [1]. *S. aureus* is a common colonizer of human skin and mucosa with an ability to create biofilms that resist antibiotic treatment and avert recognition by inflammatory cells. In combination with this survival mechanism, disturbances in the acid mantle in atopic skin enable further staphylococcal proliferation [2]. This increased colonization (and subsequent reduction in microbiome diversification) is clinically important in the context of the immunologic aberrancies found in AD patients, because resulting cytokine alterations may promote nickel sensitization.

The altered immunologic response in AD patients involves decreased subsets of TH1 and TH2 genes with increased expression of Th17, inconsistent upregulation of Th2 pathway products, and abnormal negative regulator levels [2]. This results in global attenuation and differential polarization with a subsequent potential for inconsistent responsiveness to contact provocation via skin patch testing. Furthermore, recent studies have found that nickel allergic contact dermatitis reactions involve several immunologic pathways that include Th17/IL-23, in addition to the classical Th1 reaction and direct activation of toll-like receptor 4 (TLR4) by nickel ions [2]. A study conducted by Jun et al. discovered that *S. aureus* membrane vesicles penetrate the epidermis to stimulate a mixed Th1/Th2 response [3]. This mechanism was found to exacerbate AD flares and may have implications in triggering allergies to nickel.

Bogdali et al. highlighted an increased IL-2 response following exposure to nickel sulfate in AD patients with *S. aureus* infections and nickel allergy [1]. This particular cytokine enhanced by *S. aureus* has important immunologic implications because it is critical in the initial phases of contact sensitization. Increased levels of IL-2 induce lymphocytic proliferation through autocrine feedback mechanisms. The resulting lymphocytic clonal expansion heightens the risk for sensitization when exposed to allergens such as nickel [2]. This immunologic process supports the relationships found between nickel allergy and *S. aureus* infections in AD patients.

Several methods may be used to reduce skin colonization of *S. aureus*. Anti-staphylococcal antibiotics may decrease levels of skin colonization; however, this therapeutic arm alternatively increases the potential risk of antibiotic resistance and further impairs the reduced diversity of the microbiome seen in AD [2]. Disturbances in the lipid layer, elevated transepidermal water loss, and increased pH all contribute to the proliferation of *S. aureus* in the skin of patients with atopic dermatitis. Acidification of skin leads to a reduced bacterial load with the additional clinical benefit of limiting AD flares [2]. Alkaline soaps, diluted vinegar soaks, and colloidal oatmeal emollients have been shown to decrease the pH of the skin [4]. That said, elemental-based options for restoration and maintenance of the acid mantle are still needed.

Aseptic soaks with diluted sodium hypochlorite have shown in *in vitro* studies to reduce staphylococcal concentrations and biofilms but *in vivo* antibacterial effects still need to be studied [5]. Of note, these bleach baths may actually raise skin pH and their use should be partnered with acidification measures [4]. Vitamin D supplementation may also decrease the risk of nickel sensitization in AD patients by activating cathelicidin in the skin which then blocks activation of TLR4 by nickel ions [2]. While the exact mechanisms correlating *S. aureus* infections and nickel allergy in AD patients have yet to be fully understood, the available treatment options that help limit *S. aureus* overgrowth have shown to decrease AD flares and potentially reduce the risk of sensitization to nickel.

Conflicts of interest

None.

References

- [1] A.M. Bogdali, A. Grazyna, D. Wojciech, O. Aleksander, B. Anna, K. Andrzej, et al., Nickel allergy and relationship with *Staphylococcus aureus* in atopic dermatitis, J. Trace Elem. Med. Biol. 33 (2016) 1–7, <http://dx.doi.org/10.1016/j.jtemb.2015.06.009>.
- [2] C.W. Rundle, D. Bergman, A. Goldenberg, S.E. Jacob, Contact dermatitis considerations in atopic dermatitis, Clin. Dermatol. (4) (2017) 367–374, <http://dx.doi.org/10.1016/j.clindermatol.2017.03.009>.
- [3] S.H. Jun, J.H. Lee, S.I. Kim, C.W. Choi, T.L. Park, H.R. Jung, et al., Staphylococcus aureus *Staphylococcus aureus*-derived membrane vesicles exacerbate skin inflammation in atopic dermatitis, Clin. Exp. Allergy 47 (2017) 85–96, <http://dx.doi.org/10.1111/cea.12851>.
- [4] S. Eriksson, M.J.A. van der Plas, M. Morgelin, A. Sonesson, Antibacterial and anti-biofilm effects of sodium hypochlorite against *Staphylococcus aureus* isolates derived from patients with atopic dermatitis, Br. J. Dermatol. (February) (2017), <http://dx.doi.org/10.3390/jcm4050970> (Epub ahead of print).
- [5] S.E. Jacob, N. Brankov, Nickel sensitization in children with atopic dermatitis and its relationship to *Staphylococcus* infection, Pract. Dermatol. 13 (2016) 42–66.

Brittanya A. Limone

MSIV, School of Medicine, Loma Linda University, Loma Linda, CA, United States

Sharon E. Jacob*

Department of Dermatology, Loma Linda University, Loma Linda, CA, United States

E-mail address: sjacob@contactderm.net

* Corresponding author at: Department of Dermatology, Loma Linda University, Faculty Medical Offices, 11370, Anderson St, Suite 2600, Loma Linda, CA 92354, United States.