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# Influence of Nickel on Reactivity of *Dermatophagoides pteronyssinus* and *Staphylococcus aureus* Antigens in Atopic Dermatitis

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**Abstract**

Allergy to house dust mite (HDM) such as Dermatophagoides pteronyssinus, nickel and infection by *Staphylococcus aureus* are frequent in atopic dermatitis. Understanding molecular mechanisms responsible for pathological reactivity of immune cells on these substances may enable to individualize and consequently improve treatment of atopic patients. Furthermore, better understanding of nickel action can also prevent from postoperative complications in patients sensitive to nickel with atopic dermatitis.

## Introduction

Atopic dermatitis is heterogenetic disease concerning its phenotype, genetic background and clinical manifestation. Acitivation of T cells, dendritic cells, macrophages, keratinocytes, mastocytes and eosinophiles are consequences of genetic background and interaction of environmental factors with the immune cells in atopic dermatitis [1]. Reactivity of peripheral blood mononuclear cells *in vivo* on different substances such as nickel presented in water, food and in the air, Derp1 proteinase of *Dermatophagoides pteronyssinus* and enterotoxins of *Staphylococcus aureus* may depend on co-operation of these allergens through induction of different cytokines by these substances in inflammed tissue. Consequently, reaction to the same allergen may be different in patients with atopic dermatitis [2]. Knowledge on intracellular mechanisms and interaction of cells with allergens can be useful for better treatment and enable to design therapies promoting molecular processes directing towards remission of atopic dermatitis [3].

## Material and Methods

Twenty female patients and six male patients with diagnosed AD treated in the Department of Clinical and Environmental Allergology of the Medical College of the Jagiellonian University in Krakow, Poland and ten female and six male healthy volunteers participated in the study as a control group. The control group consisted of volunteers with no clinical symptoms of allergic diseases and all with a negative history of allergic diseases and with negative results of tests to nickel, *Dermatophagoides pteronyssinus* and infection by *Staphylococcus aureus*. The median age of AD group and control group was comparable 36.8 ± 14.2 in AD group and 36.8 ± 11.2 in control group. The diagnosis of atopic dermatitis was confirmed following the Haifin and Rajka criteria. Briefly, the patch test to nickel was performed with 5% NiSO4 petrolatum in IQ Ultimate chamber (Chemotechnique Diagnostics, Creutzwald, France) and the test was read after 3 and 5 days in remission of atopic dermatitis. Der p1 allergen for prick test to *Dermatophagoides pteronyssinus* were obtained from Allergopharma GmbH & CO and result of this test was analysed in 15 min after allergen application on the skin in remission of atopic dermatitis. Levels of antigen specific antibodies for SEA, SEB, Derp1 were measured by UNICAP 100 (Pharmacia& Upjohn, Bringwater, NJ, USA) in the acute phase of atopic dermatitis. All procedures for *Staphylococcus aureus* identification were detailed described in our previous paper. Briefly, tests for microbiological indentification were obtained from bioMerieux (Marcy l'Etoile, France) and were performed in accordance to EUCAST (European Society of Clinical Microbiology and Infectious Diseases). Secretion of cytokines (IFNγ, IL-2, IL-13) by PBMC *in vitro* in acute phase and remission in atopic dermatitis and healthy controls was measured by Enzyme-linked Immunospot assay according to manufacturer's guidelines (Sanquin, Amsterdam. Netherlands). Data were analyzed and graphed with GraphPad Prism 5.01 (Graphpad Software Inc., La Jolla, CA, USA). Data are shown as individual participants with medians and were analyzed with Spearman correlation and D'Agostino and Pearson omnibus normality test for a Gaussian distribution. Differences were considered statistically significant at a p value less than 0.05. The study was accepted by the Ethics Committee of the Jagiellonian University in Krakow, Poland and performed in accordance with the ethical standards of the Helsinki Declaration (approval number: KBET/61/2009) and informed written constent had been obtained from patients and controls.

## Results

As it is listed in Table 1, allergenic components are 3 times more frequent than bacterial component in atopic dermatitis. Interestingly, staphylococcal infections in the skin often corresponds to allergy of the upper respiratory and digestive systems. Thus, bacterial component may systemically influence to clinical manifestation of allergy in skin, upper respiratory and digestive system.

In order to study relation between two frequent allergies to *Dermatophagoides pteronyssinus* and nickel allergy in atopic dermatitis results of diagnostic tests were compared with cytokines

secretion by PBMC *in vitro* (Figure 1). We found negative correlation between patch test result to nickel and secretion of IL2 under stimulation with 0.4 μg/ml of Derp1 in remission of atopic dermatitis (Figure 1A) (P<0.05).

| | |
|---|---|
| DE | 0.67 |
| (+) family history | 0.65 |
| (+) Ni patch | 0.63 |
| (+) prick Derp1 | 0.64 |
| (+) tests for *Staphylococcus aureus* presence | 0.21 |
| Other diseases in patients infected with *Staphylococcus aureus* | |
| Contact allergy | 0.57 |
| Allergic rhinitis | 0.57 |
| Food allergy | 0.57 |
| Allergic asthma | 0.29 |

**Table 1:** Clinical characteristics of patients concerning frequent allergenic and bacterial components in atopic dermatitis

We did not find such correlations for other studied cytokines (IFN-gamma and IL-13) and when higher concentration of Derp1 (1 μg/ml) was used for stimulation of PBMC. Furthermore, no correlation between prick tests to Derp1 and cytokines secretion under 25 μM and 50 μM of nickel sulfate was found in our patients (data not shown). Interestingly, secretion of IL-2 by PBMC stimulated with 0.4 μg/ml of Derp1 in patients with diagnosed allergy to *Dermatophagoides pteronyssinus* was similar to secretion of this cytokine by PBMC from controls and simultaneously decreased in comparison to patients without this allergy (Figure 1B). These results suggest that secretion of IL-2 Derp1 - dependent is antagonistic to the skin immune system response to nickel. Furthermore, secretion of IL-2 protects against occurrence of allergic symptoms to Derp1 in acute phase of atopic dermatitis.

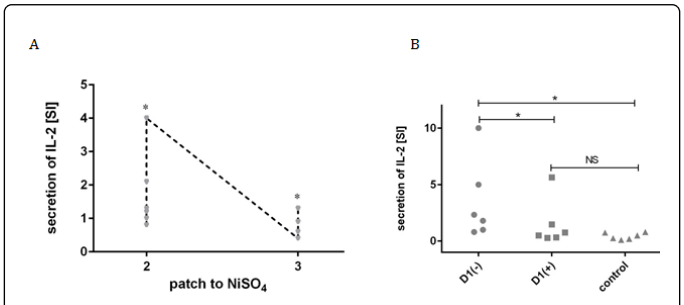


**Figure 1:** *Dermatophagoides pteronyssinus* and nickel allergy in atopic dermatitis, (A) Remission of atopic dermatitis, (B) *Dermatophagoides pteronyssinus* comparison.

## Discussion

It has been shown that infection by *Staphylococcus aureus* play a role in bronchial asthma in patients sensitive to house dust mite [4]. Furthermore, mites harbour a variety of bacterial species often associated with human skin and house dusts contain bacteriolytic enzymes that may be mite-derived [5]. It is known that predisposition to infection by *Staphylococcus aureus* may be related with the influence of nickel to secretion of TGFβ by T reg cell. TGFβ influence to expression of fibronectin that is bound by *Staphylococcus aureus* [6]. We did not see any correlation between clinical manifestation of atopic dermatitis and corresponding diseases and presence of nickel allergy, allergy to house dust mite and infection by *Staphylococcus aureus*. Nevertheless, it may be the result of high heterogeneity of clinical manifestation of the disease and population studies are required to understand if such correlation can be found. Nevertheless, as it has been published previously by our group nickel allergy and infection by *Staphylococcus aureus* can be linked in atopic dermatitis [7].

Atopic eczema presented not only in areas of the nickel contact with skin is the proof of systemic allergy to nickel. It has been proven that in contact allergy to nickel this metal provokes secretion of IL12 promoting differentiation towards Th1 and IL-10 promoting differentiation towards Th2. In turn, secretion of Th1 and Th2 cytokines in systemic allergy is unclear [8-10]. Thus, nickel does not direct Th0 cells towards one subpopulation during differentiation of Th0 cells in contact and systemic allergy to nickel. We discovered that cytokine milieu and especially secretion of IL-2 responsible for normalization of antigen presentation for T cells influenced by nickel in systemic manner can regulate response to *Dermatophagoides pteronyssinus* in atopic dermatitis. Thus, small haptens may have tendency to become systemic regulators of allergic mechanisms as opposed to aeroallergens such as HDM. It can be explained in such a way that haptens require proteins to trigger effect and therefore can migrate in the skin, respiratory and digestive systems and bind with proteins that become allergenic. Whereas, proteins such as Derp1 are themselves allergenic and trigger effect immediately. Thus, Der p1 works more locally not systemically like haptens [11]. Such explanation help to understand why in our diagnostic tests only correlation between test to nickel was linked with PBMC response to Derp1 and such correlation was not found for result of tests to Derp1 and PBMC response to nickel *in vitro*. Consequently, nickel may mask tendency to house dust mite allergy in patients with atopic dermatitis with genetic predisposition to develop allergy to *Dermatophagoides pteronyssinus via* normalization of secretion of IL-2 and consequently regulation of antigen presentation for T cells [12]. It is known that in remission of atopic dermatitis Th1 mechanisms predominate [13]. Thus, nickel may be important factor to promote remission in patients sensitive to *Dermatophagoides pteronyssinus* with atopic dermatitis.

In conclusion, prevention from house dust mite, correction of reactivity to *Staphylococcus aureus* in patients with nickel allergy can be recommended. Furthermore, detailed understanding of interaction among allergies to different allergens in atopic dermatitis can be important not only for treatment by allergologists but also for safe surgery of patients with nickel allergy with nickel-containing tools.

## Conclusions

There is a negative correlation between secretion of IL-2 and intensity of patch test to nickel. Thus, increase of IL-2 secretion *via* treatment stimulus may normalize reactivity of skin to nickel in atopic dermatitis

Increase of IL-2 secretion may enable to normalize of antigens presentation of *Dermatophagoides pteronyssinus* and *Staphylococcus aureus*

Reduction of skin reactivity to nickel *via* medicines and patient's isolation from nickel may impair reactivity to *Dermatophagoides pteronyssinus* and *Staphylococcus aureus* and consequently promote remission.

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## References

1. Harskamp CT, Amstrong AW (2013) Immunology of atopic dermatitis: novel insights into mechanisms and immunomodulatory therapies. Semin Cutan Med Surg 32: 132-139.
2. Hoffjan S, Stemmler S (2015) Unravelling the complex genetic background of atopic dermatitis: from genetic association results towards novel therapeutic strategies. Arch Dermatol Res 307: 659-670.
3. Chase EP, Armstrong AW (2012) Advances in management of atopic dermatitis: new therapies and novel uses of existing treatments. Semin Cutan Med Surg 31: 17-24.
4. Riechelmann H, Essig A, Deutschle T (2005) Nasal carriage of *Staphylococcus aureus* in house dust mite allergic patients and healthy controls. Allergy 60: 1418-1423.
5. Tang VH, Chang BJ, Srinivasan A, Leslie T Mathaba, Gerald B, et al. (2013) Skin-associated Bacillus, staphylococcal and micrococcal species from the house dust mite, *Dermatophagoides pteronyssinus* and bacteriolytic enzymes. Exp Appl Acarol 61: 431-47.
6. Mollerup S, Rivedal E, Maehle L (1996) Nickel(II) induces alterations in EGF- and TGF-beta 1-mediated growth control during malignant transformation of human kidney epithelial cells. Carcinogenesis 17: 361-367.
7. Bogdali AM, Antoszczyk G, Dyga W, Obtulowicz (2016) Nickel allergy and relationship with *Staphylococcus aureus* in atopic dermatitis. Ja Trace Elem Med Biol 33: 1-7.
8. Ricciardi L, Gangemi S, Isola S (1999) Nickel allergy, a model of food cellular hypersensitivity? Allergy 2001; 56(67): 109-112. 9. Ring J & Thewes M. The clinical expression of allergy in the skin. Allergy 56: 192-197.
9. Purello D' Ambrosio F, Bagnato GF, Guarneri B, Dugo G, Ricciardi L, et al. (1998) The role of nickel in foods exacerbating nickel contact dermatitis. Allergy 53: 143-145.
10. Martin S, Weltzien HU (1994) T cell recognition of haptens, a molecular view. Int Arch Allergy Immunol 104: 10-16.
11. Waysbort N, Russ D, Chain BM, Friedman N (2013) Coupled IL-2-dependent extracellular feedbacks govern two distinct consecutive phases of CD4 T cell activation. J Immunol 191: 5822-5830.
12. Eyerich K, Novak N (2013) Immunology of atopic eczema: overcoming the Th1/Th2 paradigm. Allergy 68: 974-982.
13. Haudrechy P, Mantout B, Frappaz A (1997) Nickel release from stainless steels. Contact Dermatitis 37: 113-117.