# Avoidance of Nickel Contact Alleviate Respiratory Recurrent Symptoms in Asthmatic Patient

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**Abstract**

The frequency and expenses of allergic diseases (AD) worldwide in recent times are increasing. In some cases, these diseases affecting multiple organ systems, while the proper diagnosis and complexity to treat these patients is difficult. In many allergic patients, co-morbidity is present in different manifestation forms, but only in a few cases, the same patient had allergic contact dermatitis, respiratory symptoms and delayed allergy to nickel.1 According to Schmidt and al, allergic contact dermatitis (ACD) induced by nickel (Ni2+) affecting 10% to 12% of all populations.2 However, concomitantly asthma and other respiratory symptoms with Ni2+ allergy have been reported only in few cases, either to the rarity of these clinical conditions or due to difficulties to formulate the correct diagnosis.3 In this co-morbidity case, we hypotheses that unbalance between Naïve Th0, with direct interaction with T-helper CD4+, could be considered as possible the same or similar pathophysiological mechanisms, and any therapy that can contribute in this correction might improve health conditions of patients overall, including dietary therapy to avoid Ni2+ contacts. Hence, the aim of our study was to evaluate the possible interrelation between asthma and Ni2+ allergy.

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## Introduction

Despite endeavor efforts on healthcare settings the frequency and expenses of allergic diseases (AD) worldwide in recent times overcome our understanding. In many cases these diseases affecting multiple organ systems.[4] The complexity to treat the patient with AD sometimes requires a comprehensive physical examination linked with appropriate objective measures and in depth-history to have a proper diagnosis and to exclude the differential one.[5]
Among allergic diseases, asthma prevalence is rising dramatically in highly developing countries, as well as in low- and middle-income countries. To date, globally, 300 million people suffer from asthma and according to the World Health Organization, this number is expected to increase to 400 million, by 2050.[5] In many allergic patients, co-morbidity is present in different manifestation forms, but only in a few cases, the same patient had allergic contact dermatitis, respiratory symptoms and delayed allergy to nickel.[1] According to Schmidt and al, ACD induced by $Ni^{2+}$ affecting 10% to 12% of all populations.[2] However, concomitantly asthma and other respiratory symptoms with $Ni^{2+}$ allergy have been reported only in few cases, either to the rarity of these clinical conditions or due to difficulties to formulate the correct diagnosis.[3]
Based on our clinical database, this is our first report, where the same patient had respiratory symptoms (rhinitis and asthma) and ACD caused by delayed allergy to $Ni^{2+}$.

The patient gave her informed consent to participate in the study.

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## Case Report

A 30-year-old woman referred to our Institute by the family doctor for further examination for respiratory recurrent symptoms. She denied positive family history for any allergic diseases including atopic disease, while she

confirms that respiratory problems (sneezing, cough, and dyspnea during physical activity) have become worse 2 months ago. According to the clinical protocol, the patient undergone to the detail examinations, including blood tests (WBC, Eosinophilia > 0.82 x $10^9$L), pulmonary function testing (FVC=3.26L; FEV1=3.26L; PEF=5.49L; FEV1%=76.6), bronchoprovocation test ($PC_{20}$ >) and assay of total serum immunoglobulin E (IgE < 175 IU/mL). Furthermore, we expand our clinical examination doing auscultation, noted a prolonged expiration and decreased the lung sounds, but also reveal some minor sings for contact dermatitis in the neck. Hence, we advise prick testing for $Ni^{2+}$ (with 1 mg/ml and 10 mg/ml nickel sulfate) as more reliable methods for $Ni^{2+}$ allergy reaction[6] and the testing shown us the positive result.

## Results

To relieve the symptoms until next visit we ordered salbutamol inhalations and per-orally (PO) theophylline and advice maximal avoidance in direct or indirect contacts with $Ni^{2+}$ (metal alloys-costume jewelry, body piercings, coins, keys, clothes accessories, all foods canned or cooked in inox steel). After 4 weeks of diet and as-needed medication therapy, the patient reported a significant improvement of her symptoms and the last result for pulmonary function testing to confirm this (FVC=3.78L; FEV1=3.92L; PEF=6.12L; FEV1%=79.8).
We propose the patient to plan a nickel oral immunotherapy as a method to hyposensitize her systemic allergy to $Ni^{2+}$.

## Discussion

Our results show ameliorates of clinical condition and improvement of spirometry results after avoidance the $Ni^{2+}$ contacts. This finding match with conclusion of Novey et al which declared that in $Ni^{2+}$ exposure of patients produced an exacerbation of asthma.[7]
Others scientific evidence shows an proven association between $Ni^{2+}$ and contact allergy, and according to these findings the European Union and other countries has implemented the standards of reduction of $Ni^{2+}$ exposure in order to prevent any possible allergy reactions.[8,9,10]
Contrary to this, the association between $Ni^{2+}$ allergy and asthma is not definitively documented and several publications support this statement and in this cause-effect relation they describe other contributing factors.[11,12]

Some other authors mention the sensation mechanism of $Ni^{2+}$ in contact allergy is different from mechanism of $Ni^{2+}$ allergy and asthma.[13,14] Initially, the scientific findings concluded that IgE-mediated Type I immunologic mechanisms are attributed to asthma and $Ni^{2+}$ allergy.[7] Recently, other mechanisms, not mediated by IgE are described as cause for $Ni^{2+}$ allergic reaction linked with asthma. Lutz and al, show the basic pathophysiology mechanisms for chronic inflammatory diseases involving airways is attributed to the many cells and meditators that play a crucial role.[15] The latest scientific results shows that there are three modalities of induction of sensitivity reaction in $Ni^{2+}$ exposure: 1) the $Ni^{2+}$ serve as a hapten and binds to carrier protein and together with antigen presenting cell (APC) activates CD4+ lymphocytes;[16] 2) $Ni^{2+}$ in circulation blood penetrates into the different cells and binds to intracellular proteins. This binding structure is presented in the context of major histocompatibility complex (MHC) class I molecules, which subsequently activates CD8+ lymphocytes;[17] and 3) $Ni^{2+}$ express analogy as superantigen and can introduce the MHC molecule through TCR receptor on lymphocyte without activation the antigen-binding site.[18]

Nevertheless, research data introduced other possible complementary mechanisms of $Ni^{2+}$ in induction of asthma. Besides atopic and exposure to specific living conditions, for the allergic inflammatory disease, a common disease mechanism could be considered also the unbalance between Naïve T-helper lymphocyte (Th0), cell differentiation into either Th1 or Th2 phenotypes [15]. Indeed, at the core of this process especially during the acuter phase of hypersensitivity response are T-helper CD4+ that produces an array of cytokines (IL3, IL4, IL5) and IgE. The Th2 cells play also an important role during the late-phase response in allergic inflammatory diseases [19]. In light of our case, we are trying to give a reasonable explanation of the crosslink between allergic inflammatory diseases involving airways and $Ni^{2+}$ induced allergic reaction. Some subsequent studies in humans reveal that $Ni^{2+}$ induced ACD can be elicited by both the innate and adaptive immune systems involve toll-like receptor 4/complex or T-helper lymphocytes. Especially for adaptive immune

systems, the key factor is considered a direct interaction with T-helper CD4+ and CD8+.[20]

In this co-morbidity case, we hypotheses that imbalance between Naïve Th0, with direct interaction with T-helper CD4+, could be considered as same or similar pathophysiological mechanisms, and any therapy, including dietary therapy to avoid $Ni^{2+}$ contacts, can contribute to correct the dysregulation of these mechanisms and might improve health conditions of patients overall.

## Conclusions

In summary, our results were found a clinical and testing improvement of asthma after $Ni^{2+}$ withdrawal exposure of patient. These facts indicate a possible association between $Ni^{2+}$ exposure and worsening of asthma. We assume that further investigations are needed to clarify the predisposition factors and induction of immunological mechanism of asthma linked with $Ni^{2+}$ exposure reactions.

## Declaration of Interest

The authors report no conflict of interest.

| PFTs | FVC | FEV1 | PEF | FEV1% |
|---|---|---|---|---|
| 1st Visit | 3.26 L | 3.26 L | 5.49 L | 76.6 |
| 2d Visit | 3.78 L | 3.92 L | 6.12 L | 79.8 |

**Table 1. Results of pulmonary functional testing during laboratory examination.**

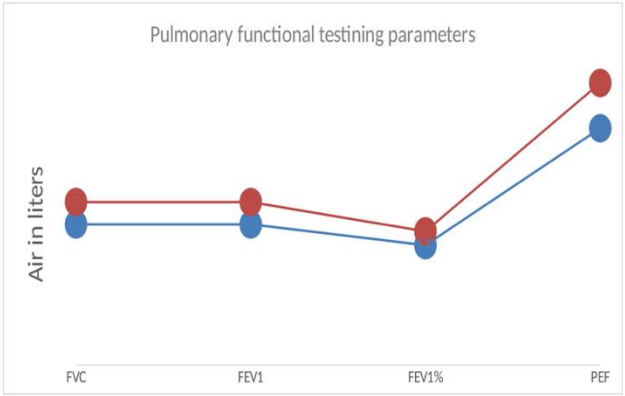


**Fig.1. Pulmonary functional testing values during 1st and 2d visit.**

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