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# Association of toxic and essential metals with atopy markers and ventilatory lung function in women and men

*Alica Pizent*, Jelena Macan, Jasna Jurasović, Veda Marija Varnai, Sanja Milković-Kraus, Božica Kanceljak-Macan*

*Institute for Medical Research and Occupational Health, Zagreb, Croatia*

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ABSTRACT

The association of age, smoking, alcohol, superoxide dismutase (SOD), glutathione peroxidase (GPx), blood lead (BPb) and cadmium (BCd) levels, and serum levels of copper (SCu), zinc (SZn) and selenium (SSe) with atopic status and ventilatory function was examined in the groups of 166 women and 50 men with no occupational exposure to metals or other xenobiotics. Markers of atopy included serum total IgE, skin prick test (SPT) to common inhalatory allergens, non-specific nasal reactivity (NNR) and non-specific bronchial reactivity (NBR). Parameters of ventilatory function included forced vital capacity (FVC) and forced expiratory volume in the first second ($FEV_1$). Significantly higher BPb, SZn, IgE and prevalence of positive SPT, and lower SCu and NNR was found in men than in women. Fifteen women taking female sex hormones (HT) had significantly higher SCu than women without HT. Regression models showed significant inverse associations between IgE and SCu ($P=0.021$) and NNR and SCu ($P=0.044$) in women. When excluding women with HT, the association of SCu and total IgE became of borderline significance ($P=0.051$), association between SCu and NNR disappeared, and significant positive association between total IgE and BPb emerged ($P=0.046$). In men, significant inverse association was found between positive SPT and SSe, and between NBR and SSe. A decrease in FVC% and $FEV_1$% was associated with an increase in smoking intensity ($P<0.001$) and a decrease in SZn ($P=0.043$ and $P=0.053$, respectively). These results were observed at the levels of the metals comparable to those in general populations worldwide. The observed differences between men and women may partly be explained by different levels of relevant toxic and essential metals, and their combination. The role of female HT in associations of atopy markers and SCu should be further investigated.



## 1. Introduction

The incidence of allergic respiratory diseases is increasing in industrialized and developed countries due to inadequately elucidated reasons. Genetic predisposition, allergen exposure, environmental pollutants, decreased stimulation of the immune system during the critical period of development and lifestyle are concerned as the main risk factors (Ring et al., 2001; Macan et al., 2003; Cvitanović et al., 2007). A combination of these influences ultimately determines disease development and progression. Recent revision of nomenclature for allergy (Johansson et al., 2004) defines atopy as "a personal and/or familiar tendency, usually in childhood or adolescence, to become sensitised and produce IgE antibodies in response to ordinary exposures to allergens, usually proteins. As a consequence, these persons can develop typical symptoms of asthma, rhinoconjunctivitis, or eczema. Therefore, the term atopy or atopic disease should be used when typical respira-

* *Corresponding author*. Institute for Medical Research and Occupational Health, Ksaverska cesta 2, PO Box 291, HR-10001 Zagreb, Croatia. Tel.: +385 1 4673 188; fax: +385 1 4673 303.
*E-mail address:* apizent@imi.hr (A. Pizent).

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tory and/or skin symptoms are accompanied by elevated IgE levels and/or positive skin prick test to common allergens."

Immune cells, like all other types of cells, require an adequate supply of trace elements, especially zinc (Zn), selenium (Se) and copper (Cu), to express and preserve the structure and function of key metalloproteins that participate in important processes in the organism. For example, the continuous generation of immune cells in bone marrow and the clonal expansion of lymphocytes in response to antigenic stimulation require the availability of sufficient iron and Zn in the synthesis of deoxyribonucleotide precursors by ribonucleotide reductase and for the various nucleotidyl transferases and zinc-finger proteins that are required for DNA replication and cell division, respectively (Failla 2003). In addition, Zn, Se and Cu are also required to maintain the activity of a number of enzymes that directly participate in important defence processes (Shankar and Prasad 1998).

There is evidence that deficiency of Zn and Se, and to a lesser extent Cu, can have adverse consequences for disease susceptibility and maintenance of optimal health (Walsh et al., 1994; Pizent et al., 1999; Rayman 2000; Arthur et al., 2003). Lead (Pb) and cadmium (Cd) are toxic metals pervasive in the human environment and accumulate in the human body over a lifetime. They can interfere with the metabolism of Cu, Zn and Se by affecting their absorption, distribution, and bioavailability in the organism, can contribute to oxidative stress, and can inhibit DNA repair (Nordberg 1978; Telišman 1995; Jurasović et al., 2000; Pizent et al., 2003). Harmful effects of Pb (Fischbein et al., 1993; Ündeger et al., 1996; Sata et al., 1997) and Cd (Jelovčan et al., 2003) on the immune status and pulmonary function in humans may be more expressed in individuals with relative Zn and Se deficiency caused by stress, inflammatory process and/or inadequate nutrition. Moreover, Cu, Zn, and Se are co-factors of enzymes Cu,Zn-superoxide dismutase (SOD), and Se-glutathione peroxidase (GPx) that play a key role in protecting cells against oxidative damage. It is known that oxidative stress is implicated in the pathogenesis of over 100 human diseases, including impaired immune and pulmonary function (Nair et al., 2003). On the other hand, Zn and Se may act as antagonists of Pb and Cd and thus mask the Pb- and/or Cd-related effects (Telišman 1995). In the general population, the most important sources of each of the above mentioned metals are food, water and air, and levels of blood lead (BPb), blood cadmium (BCd), serum zinc (SZn), serum copper (SCu), and serum selenium (SSe) depend on age, gender, stress, smoking habits and alcohol consumption.

The aim of the study was to evaluate possible association of BPb, BCd, SCu, SZn, SSe, SOD, and GPx with markers of atopy and parameters of ventilatory function, in women and men with no occupational exposure to metal or other xenobiotics.

## 2. Subjects and methods

### 2.1. Study population

The study was carried out in 216 white-collar office workers, consisting of 166 women and 50 men, who had never been occupationally exposed to metals. All subjects were recruited on a voluntary basis. Each subject was informed about the study protocol and required to sign a consent form. Subjects were free to stop their participation at any time. The study was designed in accordance with the Helsinki Declaration and approved by the authorized Ethical Committee.

A questionnaire including data on age, dietary habits, smoking, alcohol consumption, and medical and occupational history was completed by a physician for each subject. The main descriptive characteristics of the participants are presented in Table 1. All subjects lived in the urban area of Zagreb and declared mixed food consumption. Smoking intensity was expressed as the number of cigarettes smoked per day and as pack year (20 manufactured cigarettes (1 pack) smoked per day × number of years smoking). Alcohol consumption was expressed as the number of drinks per week, where one drink corresponds to 3 dL beer, 1 dL wine, or 0.3 dL brandy. Twenty-four out of 166 women and 6 out of 50 men reported taking some form of vitamin and mineral supplementation. There were no significant differences in blood concentrations of essential (Cu, Zn, Se) and toxic (Pb, Cd) elements between mineral supplemented and non-supplemented subjects of either sex. Fifteen women were taking female sex hormones (11 for the purpose of hormonal replacement therapy and 4 as oral contraceptives).

Contraindications for inclusion in the study were evaluated for each subject during the initial medical interview and physical examination.

### 2.2. Sampling and analyses

Venous blood was sampled between 0800 and 1000 hours after overnight fasting for each subject. All chemicals used for metal analyses were of analytical grade for spectroscopy (Merck, Darmstadt, Germany).

### 2.3. Trace element analyses

The BPb and BCd measurements were performed by electrothermal atomic absorption spectrometry (AAS) method with the Zeeman-effect background correction (Jurasović and Telišman 1993). The accuracy of both BPb and BCd measurements

**Table 1 – The main descriptive characteristics of participants**

| Variable | Women | | Men | |
|---|---|---|---|---|
| | N | Median (range) | N | Median (range) |
| Age (years) | 166 | 43 (19–67) | 50 | 45 (20.5–67) |
| Current smokers | 54/166 (32.5%) | | 18/50 (36%) | |
| Smoking exposure [a] (pack year) | 54 | 10.0 (0.2–45.0) | 18 | 16.5 (0.5–66.0) |
| Non-smokers | 112/166 (67.5%) | | 32/50 (64%) | |
| Smoking (cigarettes/day) | 166 | 0 (0–30) | 50 | 0 (0–40) |
| Alcohol consumers | 56/166 (33.7%) | | 35/50 (70%) | |
| Abstainers | 110/166 (66.3%) | | 15/50 (30%) | |
| Alcohol [b] (drinks [c]/week) | 166 | 0 (0–15) | 50 | 0 (0–32) |

[a] Pack year = 20 manufactured cigarettes (1 pack) smoked per day × number of years smoking; data given for smokers only.
[b] $P < 0.0001$.
[c] One drink = 3 dL beer, 1 dL wine, or 0.3 dL brandy.