



Baseline blood levels of manganese, lead, cadmium, copper, and zinc in residents of Beijing suburb

Long-Lian Zhang^{a,*}, Ling Lu^a, Ya-Juan Pan^b, Chun-Guang Ding^b, Da-Yong Xu^a,
Chuan-Feng Huang^b, Xing-Fu Pan^b, Wei Zheng^{c,**}

^a Department of Occupational Diseases Control and Prevention, Fengtai Center for Disease Control and Prevention, Beijing 100071, PR China

^b Institute for Occupational Health and Poison Control in China Center for Disease Prevention and Control, Beijing 100050, PR China

^c School of Health Sciences, Purdue University, West Lafayette, IN 47907, USA



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ABSTRACT

Baseline blood concentrations of metals are important references for monitoring metal exposure in environmental and occupational settings. The purpose of this study was to determine the blood levels of manganese (Mn), copper (Cu), zinc (Zn), lead (Pb), and cadmium (Cd) among the residents (aged 12–60 years old) living in the suburb southwest of Beijing in China and to compare the outcomes with reported values in various developed countries. Blood samples were collected from 648 subjects from March 2009 to February 2010. Metal concentrations in the whole blood were determined by ICP-MS. The geometric means of blood levels of Mn, Cu, Zn, Pb and Cd were 11.4, 802.4, 4665, 42.6, and 0.68 $\mu\text{g/L}$, respectively. Male subjects had higher blood Pb than the females, while the females had higher blood Mn and Cu than the males. There was no gender difference for blood Cd and Zn. Smokers had higher blood Cu, Zn, and Cd than nonsmokers. There were significant age-related differences in blood levels of all metals studied; subjects in the 17–30 age group had higher blood levels of Mn, Pb, Cu, and Zn, while those in the 46–60 age group had higher Cd than the other age groups. A remarkably lower blood level of Cu and Zn in this population as compared with residents of other developed countries was noticed. Based on the current study, the normal reference ranges for the blood Mn were estimated to be 5.80–25.2 $\mu\text{g/L}$; for blood Cu, 541–1475 $\mu\text{g/L}$; for blood Zn, 2349–9492 $\mu\text{g/L}$; for blood Pb, < 100 $\mu\text{g/L}$; and for blood Cd, < 5.30 $\mu\text{g/L}$ in the general population living in Beijing suburbs.

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1. Introduction

Environmental and occupational exposure to metals is a growing concern, as industrial, agricultural and natural sources have continued to release metals in air, soil and water in developed as well as developing countries (Kristiansen et al., 1997). In China, the geological background levels of heavy metal are generally low; however, recent human activities have rendered soil, water, air, and plants more prone to the pollution by heavy metals; in some cases, these pollutions have caused severe human health

Abbreviations: Mn, manganese; BMn, Mn concentration in the whole blood; Cu, copper; BCu, Cu concentration in the whole blood; Zn, zinc; BZn, Zn concentration in the whole blood; Pb, lead; BPb, Pb concentration in the whole blood; Cd, cadmium; BCd, Cd concentration in the whole blood

* Correspondence to: Beijing Fengtai District CDC, No. 3 Xian Street, Fengtai District, Beijing 100071, PR China. Fax: +86 10 6386 8056.

** Correspondence to: School of Health Science, Purdue University, 550 Stadium Mall Drive, CIVL 1173, West Lafayette, IN 47907, USA. Fax: +1 765 496 1377.

E-mail addresses: Longlian57@163.com (L.-L. Zhang), wzheng@purdue.edu (W. Zheng).

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problems (Cheng, 2003). Thus, the risk of metal exposure has been and will continue to be a major public health concern. To assess the risk and monitor exposure, there is a need to establish the reference values for metals of concern in the normal, healthy population for comparison purpose.

Reliable reference levels for individual metals are a prerequisite for evaluating metal exposure in both occupational and environmental exposure settings (Kristiansen et al., 1997; Wilhelm et al., 2004). Countries around the world set their own reference values for specific populations. For example, in the United States, the National Report on Human Exposure to Chemicals published by the Centers for Disease Control and Prevention (U.S. CDC) has documented the exposure data in an ongoing basis. The fourth report, which was published in 2009, has already been updated in September 2013, providing new representative biomonitoring data (CDC, 2013). In Germany, the Human Biomonitoring Commission of the German Federal Environmental Agency, which was established in 1992, has developed a set of scientifically based criteria for human biomonitoring; the criteria have recently been updated with newly recommend reference values (Wilhelm et al., 2004).

The Czech Republic has one of the earliest national surveillance systems. The biological monitoring of metal exposure has been in practice under the guideline of the System of Monitoring since 1994 (Cerná et al., 2001). In addition, there has been an ongoing EURO-TERVIHT project (Trace Element Reference Values in Human Tissues), aiming at establishing and comparing the trace metal reference values in inhabitants among different European community countries (Sabbioni et al., 1992).

Among metals of health concern, manganese (Mn), copper (Cu) and zinc (Zn) are nutritionally important, and yet their deficiency or overload is detrimental to human health. Lead (Pb) and cadmium (Cd), on the other hand, are toxic metals commonly present in environment and working places with no beneficial health effects. There are studies in literature to establish the reference values for these metals in various developed countries such as in Canada (Clark et al., 2007), Korea (Lee et al., 2012), Czech Republic (Batářiiová et al., 2006; Benes et al., 2005), Spain (Izquierdo-Alvarez et al., 2008; Moreno et al., 1999), Italy (Alimonti et al., 2005; Bocca et al., 2011; Pino et al., 2012), and Sweden (Bárány et al., 2002). However, the reliable reference values among Chinese general population remained uncertain.

This study was a sub-project of the “Establishing Biological Monitoring Index of Reference Values for Important Chemicals in Population”, carried out by the Institute for Occupational Health and Poison Control in China Center for Disease Prevention and Control (Chinese CDC) from March 2009 to February 2010. The parent project includes studies in seven provinces and municipalities in China. The current study had a unique focus on Beijing suburban population living in southwest of metropolitan Beijing city. The purpose of this study was to establish background blood levels of metals (Mn, Pb, Cd, Cu and Zn) in the healthy people living in Beijing area as a snap shot and to compare the values with literature data obtained from other developed countries. The outcomes shall be of importance for nutritional, environmental and/or occupational monitoring of these metals in human populations.

2. Materials and methods

2.1. Subject selection

This study was performed in the Fengtai District, the southwest of Beijing metropolitan area, which has a total surface area of 305.87 km². The distances from the east to the west and from the north to the south are 35 km and 14 km, respectively. There are 2.14 million people, among which 1.69 million are permanent residents with 0.447 million having lived in this area for more than 0.5 year. By using a cluster sampling method, we selected study participants in the following order. Initially, we divided the Fengtai District according to its geographical location into three regions, i.e., eastern (Fangzhuang and Nanyuan), central (Fengtai) and western (Yungang) regions (Fig. 1). We then randomly selected neighborhood communities and schools within each region, i.e., two communities and 2 schools (elementary and middle schools) from the eastern region, one each community from the central and western regions, one each elementary and high school from the central region, and one middle school from the western region. Finally, we randomly selected subjects in each community for this study. Thus, participants were selected from 4 communities, 2 elementary schools, 2 middle schools and 1 high school. A total of 648 subjects participated in this study.

The study subjects met the following requirements: (1) living in the Fengtai District for 5 years; (2) living in areas without any industries; (3) having no history of liver and kidney diseases, diabetes, hyperthyroidism, cancer, or chronic diseases; (4) having

not taken calcium, iron, Zn, and other trace elements in dietary supplements within the past 3 months; (5) age in the range of 12–60 years old. Out of 682 people enrolled in the study, 648 subjects accepted to participate, with a participation rate of 95.01%. The study subjects were recruited from the following areas (Fig. 2): 232 from the Yungang area, 157 from the Fengtai area, 88 from the Fangzhuang area, and 151 from the Nanyuan area. A total of 648 blood samples were collected from March 2009 to February 2010.

Participants were required to complete a questionnaire consisting of personal information, employment status, lifestyle, eating habits, and disease history. All participants were required to sign the consent forms, which was approved by the Ethical Censorship Committee of the Institute for Occupational Health and Poison Control at the China Center for Disease Prevention and Control (CDC). Participants agreed to use their blood samples for this biological monitoring research.

2.2. Sample preparation and analysis

Sample collection and processing were carried out in local clinics. A total of 6 mL of blood was collected in a tube containing lithium heparin monomers (BD, USA), and immediately transferred to 2 mL frozen pipe (Axygen, USA) after thorough mixing. All samples were stored at –80 °C freezer until analysis.

At the time of sample analysis, blood samples were brought to room temperature. An aliquot of 500- μ L blood samples was diluted with a solution containing 0.01% (V/V) Triton-X-100 (Sigma-Aldrich, USA) and 0.5% ultrapure concentrated nitric acid (Merck, Darmstadt, Germany) to a 5 mL total volume. The samples were vortexed in a table-top vortexer (Heidolph Multi Reax (XWT-204) for 1 min. The diluted samples were then quantified by ICP-MS. The detection limits for Mn, Cu, Zn, Pb and Cd were 0.11, 0.55, 4.3, 0.28 and 0.08 μ g/L, respectively.

2.3. Quality control

A previous report by Minoia et al. (1992) suggests that the contamination in the pre-analytical phase during sample collection may lead to the false outcomes, which has become the basis for rejection of scientific manuscripts in various cases. To minimize the contamination, we have pre-tested the heparin monovettes and frozen vials used in our blood collection. By soaking 20 monovettes and 20 vials with 1% (V/V) ultrapure nitric acid for 1 h, we determined the metal concentrations in the soaking solution by LCP-MS. The results showed that the concentrations of Mn, Pb and Cd in these monovettes and vials were lower than their respective detection limits.

All blood samples were analyzed in an authorized laboratory in the Occupational Health and Poison Control at Chinese CDC in Beijing. For internal quality assurance, The SeronormTM Trace Elements Whole Blood Control Level 1 (Sero AS, Billingstad, Norway) and the Blood Control Level 1–2 of China for Pb and Cd (GBW09139, GBW09140) were used. Control standards and reference materials were run together with collected blood samples on a daily basis. If the results of the reference materials were within the expected range, the results of that batch were accepted. The quality of laboratory instruments and procedures was also periodically checked to ensure the reproducibility and accuracy of the assays.

2.4. Statistical analysis

Results from the whole blood sample usually have the skewed distribution. Therefore, the metal concentrations were described in terms of percentiles (P25, P50 and P75), geometric mean (GM) and the 95% confidence interval (95% CI) for the geometric mean. A

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