



HHS Public Access

Author manuscript

Int J Hyg Environ Health. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:

Int J Hyg Environ Health. 2018 May ; 221(4): 609–615. doi:10.1016/j.ijheh.2018.04.005.

Urinary metal concentrations among mothers and children in a Mexico City birth cohort study

Ryan C. Lewis, Ph.D.¹, John D. Meeker, Sc.D.², Niladri Basu, Ph.D.³, Alison M. Gauthier, M.S.P.H.¹, Alejandra Cantoral, Sc.D.⁴, Adriana Mercado-García, M.D., M.P.H.⁴, Karen E. Peterson, Sc.D.⁵, Martha Maria Téllez-Rojo, Sc.D.⁴, and Deborah J. Watkins, Ph.D.^{2,*}

¹Center for Health Sciences, Exponent, Inc., Oakland, CA, USA

²Department of Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, MI, USA

³Faculty of Agricultural and Environmental Sciences, McGill University, Montreal, QC, Canada

⁴Center for Nutrition and Health Research, National Institute of Public Health, Cuernavaca, MOR, Mexico

⁵Department of Nutritional Sciences, University of Michigan School of Public Health, Ann Arbor, MI, USA

Abstract

Personal care product use is a potential source of metals exposure among children, but studies have been limited. We measured urinary concentrations of 10 metals (aluminum, arsenic [As], barium [Ba], cadmium, cobalt [Co], lead [Pb], manganese [Mn], molybdenum [Mo], nickel, and zinc [Zn]) in third trimester pregnant women ($n=212$) and their children at 8-14 years of age ($n=250$). Demographic factors (child sex, age, socioeconomic status, and maternal education), body mass index (BMI) z-score, and child personal care product use in the 24 hours prior to urine collection were examined as predictors of urinary metal concentrations. Metals were detected in 80-100% of urine samples, with significant differences in maternal versus childhood levels. However, metal concentrations were not strongly correlated within or between time points. In linear regression models including all demographic characteristics, BMI z-score, and specific gravity, age was associated with higher Co (6% [95% CI: 2, 10]), while BMI z-score was associated with lower Mo (-6% [95% CI: -11, -1]). In addition, significantly higher metal concentrations were observed among users of colored cosmetics (Mo: 42% [95% CI: 1, 99]), deodorant (Ba: 28% [3, 58]), hair spray/hair gel (Mn: 22% [3, 45]), and other toiletries (As: 50%

*Corresponding author: Deborah Watkins, Ph.D., University of Michigan School of Public Health, Department of Environmental Health Sciences, 1415 Washington Heights, Ann Arbor, Michigan 48109, USA, debjwat@umich.edu, telephone: 1.734.647.1825.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest

Ryan Lewis, formerly of University of Michigan, and Alison Gauthier work for Exponent, Inc. (Exponent), a company that provides consultation on the potential human health risks posed by exposure to environmental agents, including metals. The opinions expressed in this manuscript are those of the authors only and not necessarily those of Exponent or other scientists that work for the company. All other authors declare no conflict of interest.

[9, 108]), as well as with an increasing number of personal care products used (As: 7% [3, 11]) after adjustment for child sex, age, total number of products used, and specific gravity. However, significantly lower metal concentrations were noted for users of hair cream (As and Zn: -20% [-36, -2] and -21% [-35, -2], respectively), shampoo (Pb: -40% [-62, -7]), and other hair products (Pb: -44% [-65, -9]). We found that personal care product use may be a predictor of exposure to multiple metals among children. Further research is recommended to inform product-specific exposure source identification and related child health risk assessment efforts.

Keywords

Biomarkers; children; exposure; metals; personal care products; pregnancy

1. Introduction

Metals are present naturally in the environment and have a wide range of industrial, medical, and consumer applications (Centers for Disease Control and Prevention, 2009; World Health Organization, 1996). Consequently, humans regularly experience multi-source, multipathway exposures to metals voluntarily from naturally fortified foods and nutritional supplements and involuntarily from contaminated air, food, and water. Biomarkers of metals exposure have been measured among children and adults (Centers for Disease Control and Prevention, 2009), including pregnant women because of the trans-placental metals transfer from mother to fetus (Callan et al., 2014; Chen et al., 2014; Punshon et al., 2016). Some metals have fundamental roles in human physiology across all life stages, but virtually all can be toxic at certain levels depending on chemical form, route, frequency, and duration of exposure (Centers for Disease Control and Prevention, 2009; Hanna et al., 1997; World Health Organization, 1996). Several metals are known neurotoxicants, such as lead (Pb) and mercury, while others are identified as human carcinogens, including arsenic (As) and cadmium (Cd) (Andrade et al. 2017; Tchounwou et al. 2012; Villarreal and Castro, 2016). Various metals have also been shown to induce oxidative stress, which plays a role in many health outcomes, including cardiovascular, metabolic, and renal disease (Valko et al. 2016). A number of metals have also been shown to disrupt the endocrine system, with implications for thyroid function, reproduction, metabolism, and many other health endpoints (Iavicoli et al. 2009; Rana 2014).

Personal care products are consumer goods that are intended to cleanse or beautify, such as shampoo and lipstick, or prevent and treat health conditions, such as sunscreen and acne cream (Kessler, 2015). Metals are common additives in personal care product formulations because they impart certain desired properties to products. For example, manganese (Mn), molybdenum (Mo), zinc (Zn), and, occasionally in certain countries, Pb compounds provide pigment to cosmetics, whereas aluminum (Al) compounds are used as antiperspirants and topical astringents (Agency for Toxic Substances and Disease Registry, 2005b, 2007c; 2008, 2012b; Food and Drug Administration, 2016; Personal Care Product Council, 2017; Titenko-Holland et al., 1998). These and other metals, such as Cd and As, may also be impurities in personal care products due to their natural presence in raw materials (Environmental Defence, 2011). Use of most personal care products results in direct skin contact where,

occasionally, localized health effects can occur under the appropriate exposure conditions (Marinovich et al., 2014). For example, use of eye shadows with nickel (Ni) has been reported as a risk factor for allergic contact dermatitis in pre-sensitized individuals (Bocca and Forte, 2009; Sainio et al., 2000). However, exposure to metals through personal care product use may lead to systemic toxicity should skin penetration occur (Marinovich et al., 2014).

Given the prevalent use of personal care products among children, they may be exposed to metals through the application of various items such as cosmetics (e.g., fingernail polish) and those that are intended for general hygiene (e.g., liquid soap), hair styling (e.g., conditioner), and skincare (e.g., face and body lotion) (Environmental Protection Agency, 2008; Manová et al., 2013; Wu et al., 2010). Child characteristics, such as age, sex, and body mass index (BMI), and parental socioeconomic status (SES), such as income and education, may modify exposures due to their influence on product use patterns (Manová et al., 2013; Wu et al., 2010). To our knowledge, no published studies have considered childhood exposure to metals in relation to the use of personal care product despite the value of relevant research in exposure-source identification and child health risk assessment.

The objectives of this long-standing birth cohort study in Mexico City were to: (1) characterize urinary metal concentrations among pregnant women in their third trimester as an index of their children's exposure in utero, and among their children between the age of 8 to 14 years; and (2) evaluate potential associations between children's recent personal care product use and urinary metal concentrations.

2. Materials and methods

2.1 Study participants

Participants were recruited as part of the Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) project, a longitudinal cohort study of pregnant women and their children. The present analysis includes women who were recruited in 1997-2004 from public maternity hospitals during their first trimester and followed throughout pregnancy. At their third trimester prenatal visit to the study clinic, mothers provided a second-morning void urine sample and completed a nurse-administered questionnaire. In 2010, a subset of children was contacted at 8-14 years of age to participate in follow-up studies. Each child provided a spot urine sample and anthropometry, and completed a nurse-administered questionnaire with assistance from their primary caregiver. The present study includes children who had archived maternal third trimester urine samples ($n=212$) and/or their follow-up child urine samples ($n=250$) available for metals analysis. The ethics and research committees of the Mexico National Institute of Public Health and the University of Michigan approved the research protocols and participants provided informed consent before enrollment.

2.2 Urinary metal concentrations

Urinary concentrations of the metals in this analysis generally reflect recent exposures (Agency for Toxic Substances and Disease Registry, 2004, 2005a, 2007a, 2007b, 2007c,

2008, 2012b; IARC, 2012; Novotny and Turnlund, 2007), and, therefore, are considered appropriate biomarkers of exposure among those who recently used personal care products. Maternal and childhood urine samples were collected in sterile cups, aliquoted within one hour after collection, frozen, and stored at -80°C until they were later analyzed for their metal content (i.e., the data presented here are based on archived urine samples). Urinary metals were measured using inductively coupled plasma mass spectrometry (ICPMS, Varian, Inc., Palo Alto, California) at McGill University (Montreal, Canada) as described previously (Basu et al., 2010; Srigboh et al., 2016). Accuracy and precision were measured using certified reference standards (Institut National de Santé Publique du Québec, or INSPQ), and each batch run in replicates and contained procedural blanks (Srigboh et al., 2016). The following 10 metals: Al, As, barium (Ba), Cd, cobalt (Co), Mn, Mo, Ni, Pb, and Zn were selected in this study based on their potential as additives and/or contaminants in personal care products (Breast Cancer Fund, 2016; Cosmetic Ingredient Review, 2014; Environmental Defence, 2011; Environmental Working Group, 2017; Personal Care Product Council, 2017).

In addition, urinary specific gravity (SG) was measured using a handheld digital refractometer (Atago Co., Ltd., Tokyo, Japan) to account for variability in metal levels due to urinary dilution (Pearson et al., 2009).

2.3 Predictors of metal exposure

During pregnancy, mothers were asked to report their total years of education. At one of their follow-up visits (2007-2011), mothers provided information regarding their household possessions as a surrogate measure of SES, from which a continuous score was created as previously described (Fortenberry et al., 2014; Watkins et al., 2016). Duplicate measures of child weight and height during the follow-up were taken by study personnel using an established research protocol (Lohman et al., 1988), and BMI z-scores were calculated using the 2007 World Health Organization (WHO) reference growth standard (de Onis et al., 2007).

Questionnaires administered to children at 8-14 years of age contained “yes/no” items regarding their use of the following personal care products/product categories in the past 24 hours: aftershave, bar soap, cologne/perfume, colored cosmetics, conditioner, deodorant, fingernail polish, hair cream, hair spray/hair gel, laundry products, liquid soap, lotion, mouthwash, shampoo, shaving cream, other hair products, and other toiletries (Lewis et al., 2013). If needed, mothers or other primary caregivers assisted their children in completing the questionnaire.

2.4 Statistical analysis

Urinary metal concentrations below the limit of quantitation (LOQ) were assigned a value of LOQ divided by the square root of 2 (Hornung and Reed, 1990). Distributions of maternal and childhood urinary metal concentrations were calculated and visualized via histograms. Maternal and childhood urinary metal concentrations were corrected for SG (normalized to the median urinary SG for the sample) for comparisons using Wilcoxon rank-sum tests and Spearman rank correlations of these levels at and between both time points. Distributions of

demographic characteristics and BMI z-score and frequency of personal care product use were calculated, and product use frequency stratified by sex was compared using Fisher's exact test.

Separate linear regression models were performed to assess demographic characteristics, BMI z-score, and the use of personal care products in the past 24 hours, as predictors of In-transformed concentrations of each metal (not corrected for SG) among children at 8-14 years of age. Predictors were first explored individually in models that were adjusted only for SG as a covariate, and then in fully adjusted models with covariates selected based on biological and statistical considerations (Kleinbaum et al., 1998). In analyses evaluating demographic characteristics and BMI z-score as predictors of metal levels, all models included child sex, age, BMI z-score, household SES score, maternal education, and SG. Models evaluating personal care product use as predictors of metal levels were adjusted for child sex, age, SG, and total number of personal care products used in the past 24 hours. Sex was not included in the two models that relied on data from girls only: cosmetics and fingernail polish

As personal care product use may differ among boys and girls, potentially leading to sex-based differences in the intensity, frequency, and/or duration of exposure to metals through the use of these items, we evaluated a sex*product use interaction term in models predicting metals exposure. However, there were no significant interactions between sex and product use (data not shown) and, consequently, this interaction term was not included in subsequent models. Effect estimates are expressed as percent change in urinary metal concentrations related to a specific demographic variable, BMI z-score, personal care product used, or a total number of personal care products used (equation: $[exponentiated\ beta\ estimate - 1] * 100$). A p -value < 0.05 was defined as statistically significant for all tests. All statistical analyses were performed using SAS version 9.3 for Windows (SAS Institute, Cary, NC, USA).

3. Results

The children included in this study were 53% female, with a median age of 10.0 years, and a median BMI z-score of 1.0 (interquartile range [IQR]: -0.1, 1.8). The children's mothers had a median educational attainment and SES score of 12 years (IQR: 9, 12) and 6 (IQR: 5, 8), respectively.

Individual metals were detected in 80-100% of maternal and childhood urine samples (Table 1). Apart from Ni, SG-corrected urinary childhood concentrations of Al, Ba, Cd, Co, and Pb were significantly lower, and As, Mn, Mo, and Zn significantly higher, than SG-corrected urinary maternal concentrations. Weak to moderate Spearman correlations were noted between SG-corrected urinary metal concentrations within maternal and child samples, ranging from -0.12 to 0.61, and -0.01 to 0.50, respectively (Tables S1, S2). Intercorrelations between SG-corrected maternal and childhood urinary metal concentrations were weak, ranging from -0.14 to 0.20 (Table 2).

In fully adjusted regression models, most demographic characteristics and BMI z-score were not significantly associated with childhood urinary metal concentrations, though effect estimates (Table 3) were comparable to those from crude models that were only adjusted for SG (Table S3). We noted a one-year increase in age was significantly associated with a 6% increase in urinary Co (95% CI: 2, 10), and a one-unit increase in BMI z-score was associated with a 6% decrease in Mo (95% CI: -11, -1).

Self-reported use of bar soap, laundry products, liquid soap, and shampoo within the past 24 hours was highly prevalent among children (81-98%), unlike the use of all other personal care products (9-53%) (Table S4). Relative to sex, boys were more likely to use hair spray/hair gel and lotion, whereas girls were more common users of cologne/perfume, conditioner, and hair cream. Data on aftershave and shaving cream were removed from the analysis due to an insufficient number of children ($n < 3$) reporting the use of these two products.

Use of certain personal care products in the past 24 hours was associated with childhood urinary metal concentrations in regression models that were only adjusted for SG (Table S5) and those that were fully adjusted (Table 4). In fully adjusted models, use of deodorant, hair spray/hair gel, and other toiletries was associated with higher Ba (28% [3, 58]), Mn (22% [3, 45]), and As (50% [9, 108]), respectively. Among girls, use of cosmetics was significantly associated with higher Mo (42% [1, 99]). In addition, the total number of personal care products used was associated with higher As (7% [3, 11]). However, significantly lower concentrations of As (-21% [-36, -2]) and Zn (-20 [-35, -2]) were associated with hair cream use, and lower Pb concentrations were associated with shampoo (-40% [-62, -7]) and other hair product use (-44% [-65, -9]).

4. Discussion

To our knowledge, this is the first study exploring the potential relationship between self-reported personal care product use and urinary metal levels among children. We found that use of cosmetics, deodorant, hair spray or gel, and other toiletries as well as the total number of personal care products used in the 24 hours prior to sample collection were associated with higher urinary levels of certain metals. Together, our results suggest that personal care products may be a source of metal exposure among children living in Mexico City.

Published studies concerning exposure to metals among children and pregnant women in Mexico have mainly focused on those living in comparatively less population-dense areas of the country. For example, average urinary levels of Ba, Cd, Co, Mn, Ni, and Zn among 6-11 year-olds reported by Moreno et al. (2011) were two to 24 times higher than those found in our cohort, whereas levels of As and Mo were similar. Urinary levels of As, Cd, and Mo among 12-15 year-olds (Garcia-Vargas et al., 2014) and 6-7 year-olds (Roy et al., 2011) were two to four times higher than those observed in this study. Maternal urinary levels of Mo across trimesters (Vázquez-Salas et al., 2014) were two times higher than our third trimester urinary measurements. Collectively, these data suggest that exposure to metals among individuals in our cohort residing in the highly urbanized setting of Mexico City are generally lower than those experienced by pregnant women and children living in regions of the country where the metals-related industry is prevalent. Nevertheless, average urinary

levels of these metals measured in the present study are largely higher than the US general population, participants of the U.S. National Health and Nutrition Examination Survey (Centers for Disease Control and Prevention, 2017).

Many of the observed associations between personal care product use and higher urinary metal levels among the children in our study are supported by information on the formulation and measured content of relevant products. For example, molybdenum trioxide is used as a pigment in cosmetics, and manganese violet and manganese PCA are used as a pigment and humectant, respectively, in hair styling products (Agency for Toxic Substances and Disease Registry, 2012b; Environmental Working Group, 2017; Personal Care Product Council, 2017; Titenko-Holland et al., 1998). This could explain the associations found in this study between colored cosmetics use and higher urinary Mo, and between hair spray/hair gel use and higher urinary Mn. Similarly, barium sulfate is used as an opacifying agent mostly in “leave on” products (Cosmetic Ingredient Review, 2014; Personal Care Product Council, 2017), which could explain our observed association between deodorant use and higher urinary Ba. The positive association observed between both other toiletries and total number of personal care products and urinary As could be due to the use of various products with As present as an impurity (Environmental Defence, 2011; Salama, 2015). However, it is unclear why inverse relationships were observed between use of shampoo or other hair products and urinary Pb, and between the use of hair cream and urinary As and Zn. It is plausible that use of shampoo is an indicator for hygiene practices, such as recent showering and bathing, which remove metal contamination from the body, lowering children’s exposure. All children reporting the use of hair cream or other hair products were also users of shampoo, reflecting a similar hygiene pattern that potentially reduces exposures as well.

A distinctive feature of our study was the collection of maternal urine samples during pregnancy as a surrogate measure of exposure during in utero development of their child, as well as urine samples from these same children at 8-14 years of age. We found that correlations between maternal and childhood metal levels were weak, which may be due to differences in the sources of metal exposure over time, lifestyle choices and other behaviors that drive exposure-source interactions, or toxicokinetics (Ginsberg et al., 2004; Mattison et al., 1991). In addition, strong correlations were not observed between urinary metal levels within mothers or within children, potentially due to differences in exposure sources among various metals. Overall, our correlation results are consistent with those that have been reported in other studies concerning children and pregnant women (Garcia-Vargas et al., 2014; Gardner et al., 2013; Gunier et al., 2014; Molina-Villalba et al., 2015; Moreno et al., 2010).

Our study had limited statistical power due to somewhat modest sample size, and we did not correct for multiple comparisons. As a result, some observations may have been due to statistical chance, but the findings, especially those related to product use, can be reasonably explained. It should be noted that urinary levels of metals reflect total exposure, and consequently, it is not possible to differentiate between routes of exposure. We did not ask the children to report the brand and source of personal care products used or to quantify the amount and frequency of product use, and certain products were pooled together into broad groupings (e.g., colored cosmetics), all of which limited the breadth of our analyses and the

ability to identify more specific sources of metals exposure. Although our product use questionnaire has not been officially validated, many of the questions have been previously administered in other studies and the use of the previous 24 hours recall is expected to be quite accurate. In addition, urinary levels of nearly all metals measured in our study reflect recent exposure (Agency for Toxic Substances and Disease Registry, 2004, 2005a, 2007a, 2007b, 2007c, 2008, 2012b; IARC, 2012; Novotny and Turnlund, 2007) and, consequently, they are considered appropriate biomarkers to examine their potential relationship to child consumer product use over the past 24 hours. The only exception to this is urinary Cd, which is somewhat responsive to recent exposure, but largely indicative of total body burden (i.e., short- and long-term exposure) (Agency for Toxic Substances and Disease Registry, 2012a). Caution is needed if attempting to generalize our results to populations in other countries because geographic variability in behaviors, non-modifiable factors, and/or content of sources may lead to different exposure profiles.

5. Conclusions

We found that recent use of personal care products among children is associated with exposure to multiple metals. Despite growing interest in this topic, the state-of-the-science is limited and, consequently, additional research is recommended, as it will improve risk assessment and exposure management efforts. Specifically, longitudinal studies that collect detailed information on personal care product specifics (e.g., brand, product line, and metal content) and use patterns (e.g., amount and frequency) and repeated urine samples would allow for more thorough analyses, including the investigation of temporal relationships, which was not possible in our study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by grants R01ES021446, P01 ES02284401, and P30ES017885 from the National Institute of Environmental Health Sciences (NIEHS), and RD 83543601 from the US Environmental Protection Agency (US EPA). Its contents are solely the responsibility of the grantee and do not necessarily represent the official views of the NIEHS or the US EPA. Further, the US EPA does not endorse the purchase of any commercial products or services mentioned in the publication. This work was also supported and partially funded by the National Institute of Public Health, Ministry of Health of Mexico. We would like to thank American British Cowdray (ABC) Hospital for providing facilities for this research.

References

- Agency for Toxic Substances and Disease Registry, 2004 (4). Toxicological Profile for Cobalt. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2005a (8). ToxGuide for Zinc. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2005b (8). Toxicological Profile for Zinc. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.

- Agency for Toxic Substances and Disease Registry, 2007a (8). Toxicological Profile for Arsenic. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2007b (8). Toxicological Profile for Barium and Barium Compounds. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2007c (8). Toxicological Profile for Lead. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2008 (9). Toxicological Profile for Aluminum. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2012a (9). Toxicological Profile for Cadmium. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Agency for Toxic Substances and Disease Registry, 2012b (9). Toxicological Profile for Manganese. U.S Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR): Atlanta, GA.
- Andrade VM, Aschner M, Marreilha dos Santos AP 2017 Neurotoxicity of Metal Mixtures In: Aschner M., Costa LG, eds. Neurotoxicity of Metals. Cham: Springer International Publishing: 227–265.
- Basu N, Abare M, Buchanan S, Cryderman D, Nam DH, Sirkin S, Schmitt S, Hu H, 2010 A combined ecological and epidemiologic investigation of metal exposures amongst indigenous peoples near the Marlin mine in Western Guatemala. *Sci. Total Environ.* 409, 70–77. [PubMed: 20952048]
- Bocca B, Forte G, 2009 The epidemiology of contact allergy to metals in the general population: prevalence and new evidences. *The Open Chemical and Biomedical Methods Journal* 2, 26–34.
- Breast Cancer Fund, 2016 (10). *Pretty Scary 2: Unmasking Toxic Chemicals in Kids' Makeup*. Breast Cancer Fund, Campaign for Safe Cosmetics: San Francisco, CA.
- Callan AC, Hinwood AL, Ramalingam M, Boyce M, Heyworth J, McCafferty P, Odland JØ 2014 Maternal exposure to metals--concentrations and predictors of exposure. *Environ. Res.* 126, 111–117.
- Chen Z, Myers R, Wei T, Bind E, Kassim P, Wang G, Ji Y, Hong X, Caruso D, Bartell T, Gong Y, Strickland P, Navas-Acien A, Guallar E, Wang X, 2014 Placental transfer and concentrations of cadmium, mercury, lead, and selenium in mothers, newborns, and young children. *J. Expo. Sci. Environ. Epidemiol.* 24, 537–544. [PubMed: 24756102]
- Centers for Disease Control and Prevention, 2009 (2). *Fourth National Report on Human Exposure to Environmental Chemicals*. U.S Department of Health and Human Services, Centers for Disease Control and Prevention (CDC): Atlanta, GA.
- Centers for Disease Control and Prevention, 2017 (1). *Fourth National Report on Human Exposure to Environmental Chemicals: Updated Tables, January 2017, Volume One*. U.S Department of Health and Human Services, Centers for Disease Control and Prevention (CDC): Atlanta, GA.
- Cosmetic Ingredient Review, 2014 (6). *Safety Assessment of Barium Sulfate as Used in Cosmetics*. Cosmetic Ingredient Review: Washington, DC.
- Environmental Protection Agency, 2008 (9). *Child-Specific Exposure Factors Handbook*. U.S Environmental Protection Agency (EPA), National Center for Environmental Assessment, Office of Research and Development: Washington, DC.
- Environmental Defence, 2011 (5). *Heavy Metal Hazard: The Health Risks of Hidden Heavy Metals in Face Makeup*. Environmental Defence: Toronto, ON.
- Environmental Working Group, 2017 EWG's Skin Deep[®] Cosmetics Database. Environmental Working Group (EWG): Washington, DC <https://www.ewg.org/skindEEP/> (accessed 17.06.20).
- Food and Drug Administration, 2016 Kohl, Kajal, Al-Kahal, Surma, Tiro, Tozali, or Kwalli: By Any Name, Beware of Lead Poisoning. Food and Drug Administration (FDA): Washington, DC <https://www.fda.gov/cosmetics/productsingredients/products/ucm137250.htm#15> (accessed 17.08.13).
- Fortenberry GZ, Meeker JD, Sánchez BN, Barr DB, Panuwet P, Bellinger D, Schnaas L, Solano-González M, Ettinger AS, Hernandez-Avila M, Hu H, Tellez-Rojo MM, 2014 Urinary 3,5,6-

- trichloro-2-pyridinol (TCPY) in pregnant women from Mexico City: distribution, temporal variability, and relationship with child attention and hyperactivity. *Int. J. Hyg. Environ. Health* 217, 405–412. [PubMed: 24001412]
- Garcia-Vargas GG, Rothenberg SJ, Silbergeld EK, Weaver V, Zamoiski R, Resnick C, Rubio-Andrade M, Parsons PJ, Steuerwald AJ, Navas-Acién A, Guallar E, 2014 Spatial clustering of toxic trace elements in adolescents around the Torreón, Mexico lead-zinc smelter. *J. Expo. Sci. Environ. Epidemiol.* 24, 634–642. [PubMed: 24549228]
- Gardner RM, Kippler M, Tofail F, Bottai M, Hamadani J, Grandér M, Nermell B, Palm B, Rasmussen KM, Vahter M, 2013 Environmental exposure to metals and children's growth to age 5 years: a prospective cohort study. *Am. J. Epidemiol.* 177, 1356–1367. [PubMed: 23676282]
- Ginsberg G, Slikker W, Jr, Bruckner J, Sonawane B, 2004 Incorporating children's toxicokinetics into a risk framework. *Environ. Health Perspect.* 112, 272–283. [PubMed: 14754583]
- Gunier RB, Mora AM, Smith D, Arora M, Austin C, Eskenazi B, Bradman A, 2014 Biomarkers of manganese exposure in pregnant women and children living in an agricultural community in California. *Environ. Sci. Technol.* 48, 14695–14702. [PubMed: 25390650]
- Hanna LA, Peters JM, Wiley LM, Clegg MS, Keen CL, 1997 Comparative effects of essential and nonessential metals on preimplantation mouse embryo development in vitro. *Toxicology* 116, 123–131. [PubMed: 9020513]
- Hornung RW, Reed L, 1990 Estimation of average concentration in the presence of nondetectable values. *Appl. Occup. Environ. Hyg.* 5, 46–51.
- Iavicoli I, Fontana L, Bergamaschi A 2009 The effects of metals as endocrine disruptors. *J. Toxicol Environ Health B Crit Rev.* 12(3):206–223. [PubMed: 19466673]
- International Agency for Research on Cancer, 2012 IARC Monographs – 100C, Nickel and Nickel Compounds. International Agency for Research on Cancer: Lyons, France.
- Kessler R, 2015 More than cosmetic changes: taking stock of personal care product safety. *Environ. Health Perspect.* 123, A120–A127. [PubMed: 25933009]
- Kleinbaum DG, Kupper LL, Muller KE, Nizam A, 1998 Selecting the best regression equation, in: *Applied Regression Analysis and Other Multivariate Methods*. Brooks/Cole Publishing Company, Pacific Grove, CA, pp. 386–492.
- Lewis RC, Meeker JD, Peterson KE, Lee JM, Pace GG, Cantoral A, Téllez-Rojo MM, 2013 Predictors of urinary bisphenol A and phthalate metabolite concentrations in Mexican children. *Chemosphere* 93, 2390–2398. [PubMed: 24041567]
- Lohman TG, Roche AF, Martorell R, 1988 *Anthropometric Standardization Reference Manual*. Human Kinetics Books: Champaign, IL.
- Manová E, von Goetz N, Keller C, Siegrist M, Hungerbühler K, 2013 Use patterns of leave-on personal care products among Swiss-German children, adolescents, and adults. *Int. J. Environ. Res. Public Health* 10, 2778–2798. [PubMed: 23823714]
- Marinovich M, Boraso MS, Testai E, Galli CL, 2014 Metals in cosmetics: an a posteriori safety evaluation. *Regul. Toxicol. Pharmacol.* 69, 416–424. [PubMed: 24852494]
- Mattison DR, Blann E, Malek A, 1991 Physiological alterations during pregnancy: impact on toxicokinetics. *Fundam. Appl. Toxicol.* 16, 215–218. [PubMed: 2055350]
- Molina-Villalba I, Lacasaña M, Rodríguez-Barranco M, Hernández AF, Gonzalez-Alzaga B, Aguilar-Garduño C, Gil F, 2015 Biomonitoring of arsenic, cadmium, lead, manganese and mercury in urine and hair of children living near mining and industrial areas. *Chemosphere* 124, 83–91. [PubMed: 25434277]
- Moreno ME, Acosta-Saavedra LC, Meza-Figueroa D, Vera E, Cebrian ME, Ostrosky-Wegman P, Calderon-Aranda ES, 2011 Biomonitoring of metal in children living in a mine tailings zone in Southern Mexico: A pilot study. *Int. J. Hyg. Environ. Health* 213, 252–258.
- Novotny JA, Turnlund JR, 2007 Molybdenum intake influences molybdenum kinetics in men. *J. Nutr.* 137, 37–42. [PubMed: 17182798]
- de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J, 2007 Development of a WHO growth reference for school-aged children and adolescents. *Bull. World Health Organ.* 85, 660–667.

- Pearson MA, Lu C, Schmotzer BJ, Waller LA, Riederer AM, 2009 Evaluation of physiological measures for correcting variation in urinary output: implications for assessing environmental chemical exposure in children. *J. Expo. Sci. Environ. Epidemiol.* 19, 336–342. [PubMed: 18841168]
- Personal Care Product Council, 2017 Cosmetics Info. Personal Care Product Council: Washington, DC <http://www.cosmeticsinfo.org/> (accessed 17.06.20).
- Punshon T, Li Z, Marsit CJ, Jackson BP, Baker ER, Karagas MR, 2016 Placental metal concentrations in relation to maternal and infant toenails in a U.S. cohort. *Environ. Sci. Technol.* 50, 1587–1594. [PubMed: 26727403]
- Rana SV. Perspectives in endocrine toxicity of heavy metals--a review. *Biol Trace Elem Res.* 2014; 160(1):1–14. [PubMed: 24898714]
- Roy A, Kordas K, Lopez P, Rosado JL, Cebrian ME, Vargas GG, Ronquillo D, Stoltzfus RJ, 2011 Association between arsenic exposure and behavior among first-graders from Torreón, Mexico. *Environ. Res.* 111, 670–676. [PubMed: 21439564]
- Sainio EL, Jolanki R, Hakala E, Kanerva L, 2000 Metals and arsenic in eye shadows. *Contact Dermatitis* 42, 5–10. [PubMed: 10644018]
- Salama AK, 2015 Assessment of metals in cosmetics commonly used in Saudi Arabia. *Environ. Monit. Assess.* 188, 553. [PubMed: 27613289]
- Strigboh RK, Basu N, Stephens J, Asampong E, Perkins M, Neitzel RL, Fobil J, 2016 Multiple elemental exposures amongst workers at the Agbogbloshie electronic waste (e-waste) site in Ghana. *Chemosphere* 164, 68–74. [PubMed: 27580259]
- Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ 2012 Heavy Metal Toxicity and the Environment In: Luch A (eds) *Molecular, Clinical and Environmental Toxicology. Experientia Supplementum*, 101:133–164.
- Titenko-Holland N, Shao J, Zhang L, Xi L, Ngo H, Shang N, Smith MT, 1998 Studies on the genotoxicity of molybdenum salts in human cells in vitro and in mice in vivo *Environ. Mol. Mutagen.* 32, 251–259. [PubMed: 9814440]
- Valko M, Jomova K, Rhodes CJ, Kuca K, Musilek K 2016 Redox- and non-redox-metal-induced formation of free radicals and their role in human disease. *Arch Toxicol.* 90(1):1–37. [PubMed: 26343967]
- Vázquez-Salas RA, López-Carrillo L, Menezes-Filho JA, Rothenberg SJ, Cebrián ME, Schnaas L, Viana GF, Torres-Sánchez L, 2014 Prenatal molybdenum exposure and infant neurodevelopment in Mexican children. *Nutr. Neurosci.* 17, 72–80. [PubMed: 24479423]
- Villarreal V., Castro MJ 2016 Exposure to Lead and Other Heavy Metals: Child Development Outcomes In: Riccio CA, Sullivan JR, eds. *Pediatric Neurotoxicology: Academic and Psychosocial Outcomes.* Cham: Springer International Publishing; 143–165.
- Watkins DJ, Fortenberry GZ, Sánchez BN, Barr DB, Panuwet P, Schnaas L, Osorio-Valencia E, Solano-González M, Ettinger AS, Hernández-Ávila M, Hu H, Téllez-Rojo MM, Meeker JD, 2016 Urinary 3-phenoxybenzoic acid (3-PBA) levels among pregnant women in Mexico City: Distribution and relationships with child neurodevelopment. *Environ Res.* 147, 307–313. [PubMed: 26922411]
- World Health Organization, 1996 Trace Elements in Human Nutrition and Health. World Health Organization (WHO): Geneva, Switzerland.
- Wu XM, Bennett DH, Ritz B, Cassady DL, Lee K, Hertz-Picciotto I, 2010 Usage pattern of personal care products in California households. *Food Chem. Toxicol.* 48, 3109–3119. [PubMed: 20696198]

Highlights

- Urinary concentrations of 10 metals were measured in a Mexican birth cohort
- Metals were detected with high frequency at third trimester and 8-14 years of age
- Metals were not strongly correlated at or between both time points
- Children's personal care product use was associated with urinary metal levels

Table 1.

Urinary concentrations of metals^a measured among ELEMENT mothers at third trimester and children at 8-14 years of age (ng/mL)

	LOQ	Subject	%>LOQ	n	GM	AM	Median (IQR)	Max	p-value
Al	8.6	Mothers	88	188	25.3	37.6	24.6 (14.6, 43.9)	333	<0.0001
		Children	81	242	17.7	25.8	17.6 (10.6, 26.8)	343	
As	0.23	Mothers	100	205	13.8	18.7	12.6 (9.40, 18.0)	296	0.0 03
		Children	100	242	15.5	19.5	14.5 (10.6, 20.4)	386	
Ba	1.10	Mothers	95	205	4.0	5.75	4.16 (2.50, 6.70)	51.8	<0.0001
		Children	91	242	3.09	5.02	2.92 (1.91, 4.65)	85.0	
Cd	0.04	Mothers	99	205	0.18	0.34	0.17 (0.12, 0.26)	17.0	0.0002
		Children	98	242	0.14	0.17	0.14 (0.11, 0.18)	1.16	
Co	0.06	Mothers	100	205	1.24	1.63	1.23 (0.81, 1.76)	17.2	<0.0001
		Children	100	242	0.80	0.91	0.78 (0.64, 0.92)	12.6	
Mn	0.40	Mothers	93	205	0.82	1.15	0.73 (0.57, 1.11)	16.8	<0.0001
		Children	96	242	1.26	1.56	1.26 (0.84, 1.79)	10.4	
Mo	2.90	Mothers	80	205	17.3	29.5	24.0 (12.2, 36.2)	286	<0.0001
		Children	100	242	50.9	59.0	52.0 (37.5, 67.1)	293	
Ni	2.96	Mothers	99	205	9.53	20.5	8.44 (5.94, 12.4)	1,030	0.51
		Children	99	242	9.27	11.4	8.73 (6.30, 12.2)	106	
Pb	1.20	Mothers	82	205	2.9	4.33	3.06 (1.78, 5.51)	77.5	<0.0001
		Children	82	242	2.3	3.33	2.10 (1.41, 3.24)	113	
Zn	53.9	Mothers	97	188	288	375	288 (187, 459)	2,704	<0.0001
		Children	99	222	408	469	403 (306, 547)	2,313	

AM, arithmetic mean; GM, geometric mean; IQR, interquartile range; LOQ, limit of quantitation.

^aUrinary concentrations were corrected for specific gravity.

Table 2.

Spearman correlations^a between urinary metal concentrations^b measured among ELEMENT mothers at third trimester and children at 8-14 years of age

Mothers	Children										
	Al	As	Ba	Cd	Co	Mn	Mo	Ni	Pb	Se	Zn
Al	0.13	0.06	0.07	0.05	-0.01	0.13	-0.01	-0.14	0.05	0.07	0.06
As	0.18*	0.14	-0.01	0.02	-0.06	0.01	0.09	-0.01	0.09	0.16*	0.09
Ba	-0.07	0.07	0.04	0.06	-0.01	0.05	0.03	0.06	0.08	-0.04	0.06
Cd	-0.03	0.02	0.02	0.01	0.01	-0.04	-0.03	-0.03	-0.03	0.01	0.09
Co	0.08	0.17*	0.01	0.06	-0.01	0.03	0.14*	0.01	0.01	0.11	0.09
Mn	0.15*	0.15*	0.06	0.12	-0.01	0.07	0.05	-0.05	0.04	0.05	0.07
Mo	-0.01	0.06	0.02	-0.11	0.06	-0.05	0.01	0.12	-0.02	-0.06	-0.05
Ni	0.07	0.06	0.18*	0.11	0.01	0.12	0.06	0.03	0.01	0.07	0.09
Pb	0.04	0.15*	-0.07	0.09	0.04	-0.06	0.05	-0.01	0.14	-0.03	0.09
Se	0.12	-0.03	0.08	0.02	-0.14	-0.03	-0.07	-0.01	-0.11	0.01	0.01
Zn	0.20*	0.09	0.08	0.03	-0.03	0.01	-0.04	0.01	-0.04	0.08	0.13

^aCorrelations were based on data from 167 to 198 metal-metal pairs.

^bUrinary concentrations were corrected for specific gravity.

*p<0.05.

Percent change (95% CI)^a in urinary metal concentrations in relation to demographic characteristics and BMI z-score among ELEMENT children at 8-14 years of age

Table 3.

Variable	Al ^b	As ^b	Ba ^b	Cd ^b	Co ^b	Mn ^b	Mo ^b	Ni ^b	Pb ^b	Zn ^c
Boys (ref: girls)	10 (-8, 32)	-9 (-21, 6)	8 (-11, 31)	8 (-6, 23)	4 (-7, 16)	-12 (-24, 2)	-11 (-22, 3)	-2 (-14, 12)	6 (-11, 26)	-7 (-19, 7)
Age (yr.)	-1 (-6, 5)	1 (-4, 5)	4 (-2, 10)	1 (-4, 4)	6 (2, 10)*	-1 (-5, 5)	-3 (-7, 2)	1 (-3, 5)	3 (-2, 9)	-1 (-5, 4)
BMI (z-score)	1 (-7, 8)	-1 (-6, 6)	4 (-4, 12)	-4 (-9, 1)	3 (-1, 8)	-2 (-8, 4)	-6 (-11, -1)*	-1 (-5, 5)	-5 (-11, 2)	2 (-4, 8)
SES score ^d	-3 (-6, 1)	1 (-2, 4)	-1 (-4, 3)	-1 (-3, 2)	-1 (-3, 1)	1 (-3, 3)	-2 (-5, 1)	1 (-2, 3)	-2 (-6, 1)	1 (-2, 4)
Maternal ed. (yr.)	-1 (-4, 3)	2 (-1, 4)	2 (-1, 6)	1 (-2, 3)	1 (-1, 3)	2 (-1, 5)	1 (-1, 4)	1 (-2, 3)	-1 (-3, 3)	-1 (-3, 2)

^aResults from linear regression models using ln-transformed urinary metal concentrations, adjusted for all other variables in table and specific gravity. Effect estimates are expressed as percent change in urinary metal concentrations relative to the reference group.

^bTotal sample size for Al, As, Ba, Cd, Co, Mn, Mo, Ni, and Pb was 217 for all variables.

^cTotal sample size for Zn was 198 for all variables.

^dHigher score indicates higher household possessions.

* p<0.05.

Table 4. Percent change (95% CI)^a in urinary metal concentrations in relation to personal care product use in the past 24 hours among ELEMENT children at 8-14 years of age

Product	Al ^b	As ^b	Ba ^b	Cd ^b	Co ^b	Mn ^b	Mo ^b	Ni ^b	Pb ^b	Zn ^c
Bar soap	-10 (-44, 42)	1 (-29, 44)	-8 (-43, 50)	3 (-26, 42)	-8 (-31, 22)	-7 (-36, 36)	-4 (-32, 36)	-15 (-38, 18)	6 (-31, 63)	-7 (-34, 31)
Cologne/perfume	23 (-1, 52)	4 (-12, 22)	9 (-13, 36)	-2 (-15, 15)	-3 (-15, 10)	11 (-7, 32)	7 (-9, 25)	-4 (-17, 11)	15 (-6, 40)	17 (-1, 37)
Conditioner	2 (-21, 31)	-14 (-29, 4)	-5 (-27, 23)	9 (-9, 30)	8 (-7, 26)	-3 (-21, 20)	-5 (-22, 15)	-1 (-16, 19)	-1 (-22, 25)	-9 (-25, 10)
Cosmetics	-8 (-40, 42)	24 (-12, 74)	-16 (-48, 37)	25 (-13, 78)	-6 (-32, 29)	-16 (-43, 23)	42 (1, 99) [*]	-4 (-31, 33)	-14 (-45, 34)	25 (-12, 78)
Deodorant	15 (-6, 41)	-8 (-21, 8)	28 (3, 58) [*]	-7 (-19, 8)	3 (-9, 17)	7 (-9, 27)	-12 (-25, 2)	5 (-9, 21)	-2 (-19, 18)	2 (-12, 20)
Fingernail polish	8 (-17, 42)	4 (-16, 29)	-13 (-36, 18)	-12 (-30, 10)	22 (1, 49)	6 (-17, 34)	14 (-8, 41)	3 (-16, 27)	13 (-14, 49)	-1 (-20, 23)
Hair spray/hair gel	-4 (-22, 18)	2 (-13, 19)	-17 (-33, 3)	-4 (-17, 12)	-4 (-16, 9)	22 (3, 45) [*]	12 (-5, 31)	-4 (-17, 12)	11 (-8, 35)	15 (-2, 35)
Hair cream	-12 (-33, 16)	-21 (-36, -2) [*]	-6 (-30, 26)	7 (-12, 31)	-4 (-19, 14)	3 (-18, 30)	-5 (-23, 17)	-7 (-23, 13)	-2 (-25, 27)	-20 (-35, -2) [*]
Laundry products	9 (-37, 90)	-11 (-42, 36)	23 (-31, 119)	6 (-29, 56)	6 (-24, 49)	11 (-29, 76)	7 (-30, 63)	15 (-22, 69)	58 (-5, 165)	-23 (-49, 15)
Liquid soap	-7 (-27, 17)	1 (-16, 21)	-11 (-30, 14)	-14 (-27, 1)	5 (-17, 10)	-11 (-27, 8)	-5 (-21, 14)	10 (-7, 300)	-2 (-21, 22)	-15 (-28, 2)
Lotion	-2 (-25, 28)	11 (-9, 36)	-2 (-26, 29)	13 (-6, 37)	-7 (-21, 9)	-14 (-31, 6)	-1 (-18, 22)	-1 (-18, 19)	7 (-27, 19)	9 (-11, 33)
Mouthwash	-14 (-30, 7)	-2 (-17, 15)	11 (-11, 39)	7 (-8, 25)	-6 (-18, 7)	-14 (-28, 3)	-14 (-27, 1)	-7 (-20, 8)	1 (-18, 22)	1 (-14, 18)
Shampoo	-31 (-57, 12)	2 (-29, 48)	2 (-38, 69)	-24 (-46, 7)	-9 (-32, 22)	-3 (-35, 43)	-13 (-39, 26)	5 (-25, 46)	-40 (-62, -7) [*]	-16 (-41, 19)
Other hair products	-13 (-48, 47)	41 (-5, 109)	-7 (-46, 61)	11 (-23, 61)	19 (-13, 64)	-2 (-36, 50)	39 (-6, 106)	2 (-29, 46)	-44 (-65, -9) [*]	14 (-22, 66)
Other toiletries	-11 (-42, 37)	50 (9, 108) [*]	-15 (-46, 34)	11 (-18, 50)	-13 (-33, 13)	-28 (-50, 2)	2 (-26, 41)	24 (-8, 67)	-22 (-48, 17)	-8 (-33, 26)
Total # of products	2 (-3, 8)	7 (3, 11)[*]	-1 (-6, 5)	-2 (-5, 2)	1 (-3, 4)	1 (-3, 5)	1 (-2, 5)	-2 (-6, 1)	2 (-2, 7)	4 (-1, 8)

^aResults from linear regression models using ln-transformed urinary metal concentrations. Models concerning individual personal care products were adjusted for total number of personal care products used, age, sex (except for cosmetics (girls only) and fingernail polish (girls only)), and specific gravity. Models concerning total number of personal care products were adjusted for age, sex, and specific gravity. Effect estimates are expressed as percent change in urinary metal concentration relative to the reference group.

^bTotal sample size for Al, As, Ba, Cd, Co, Mn, Mo, Ni, and Pb was 242 for all products, except for cosmetics (girls only) and fingernail polish (girls only), which was 129.

^cTotal sample size for Zn was 222 for all products, except for cosmetics (girls only) and fingernail polish (girls only), which was 121.

^{*} p<0.05.