The Case for Incorporating Emerging Science into Policy on Metal Exposure

Erik de Water[1], Emily C. Moody[1], Gleicy M. Hair[1], Emrin Horgusluoglu-Moloch[2]
[1]Icahn School of Medicine at Mount Sinai, Department of Environmental Medicine and Public Health, New York, NY, USA
[2]Icahn School of Medicine at Mount Sinai, Department of Genetics and Genomic Sciences, New York, NY, USA
Corresponding Author: erikdewater@gmail.com
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I. Introduction

Exposure to lead (Pb) is a major public health concern, particularly for children and other vulnerable populations (Sanders, Claus Henn, and Wright 2015). The toxic effects of Pb exposure have been well-documented, and include a lower intelligence quotient (IQ), cognitive dysfunction, hypertension, renal damage, and liver dysfunction (Mitra et al. 2017). The successful removal of Pb from gasoline and house paint are key examples of successful public health-based policy interventions. Unfortunately, recent incidents involving Pb poisoning in Flint, MI, and Newark, NJ have shown that contamination of drinking water by Pb leaching from old water pipes is still prevalent today.

The U.S. Centers for Disease Control and Prevention (CDC) defines an elevated blood lead level (BLL) as ≥5 μg/dL (based on the 97.5th percentile of the distribution of BLL in one- to five-year-old children in the U.S. by the National Health and Nutrition Examination Survey; NHANES). However, the CDC emphasizes that there is no safe level of Pb exposure (Smith 2008). The American Academy of Pediatrics (AAP) recommends that all children should be screened for possible Pb sources by their pediatricians at one and two years of age (Warniment, Tsang, and Galazka 2010). Children who screen positive for possible exposure sources, as well as those covered by Medicaid insurance, should be tested at those intervals (Warniment, Tsang, and Galazka 2010). Children who test positive for high Pb levels are referred to public health services to identify and mitigate sources of exposure (Warniment, Tsang, and Galazka 2010). Although individual screening and testing help identify children with high BLLs, community-based interventions for primary prevention are the most efficient and cost-effective means of reducing the burden of lead toxicity at the population level (US Preventive Services Task Force et al. 2019). Although the detrimental effects of Pb have been known for years, it is not the only metal toxicant present in our environment.

Researchers have described many of the same harmful health outcomes occurring after exposure to high levels of other heavy metal toxicants, particularly arsenic (As) and mercury (Hg). Since there is widespread environmental contamination from these metals, humans are frequently exposed to at least one of these toxicants (Orr and Bridges 2017). Nevertheless, policies to reduce environmental exposures omit many known contaminants and often fail to include provisions for incorporating new scientific discoveries. In addition, there are no policies that support screening or educating medical professionals and parents about exposure to environmental health hazards. Here, we will suggest policies that may reduce the disease burden from exposure to As and Hg. First, we will describe common sources of exposure for these metals, the mechanisms underlying their toxicity, and the individuals who are at the greatest risk of exposure. Next, we will discuss recent scientific findings regarding the adverse health effects following exposure to these metals. Finally, we will recommend specific policy changes that may reduce exposure to Hg and As and the incidence of adverse effects.

II. Sources of Metal Exposure and Toxicity

Exposure to As and Hg is virtually unavoidable because they are widespread, nondegradable, and originate from both natural and anthropogenic sources (Al-Saleh et al. 2017). People are exposed to Hg through their diet (e.g., fish, shellfish), pharmaceutical products (e.g., dental amalgams), and industrial sources (e.g., the gold mining industry) (Clifton 2007). Hg exerts its toxic effects on the body by generating free radicals, causing immune system dysfunction, and disrupting cell membrane integrity, neurotransmission, and DNA repair (Bernhoft 2012). Additionally, people are exposed to As through groundwater, diet (e.g., seafood, produce), air pollution, pesticides, cosmetics, and industrial sources (e.g., glass industry) (Chung, Yu, and Hong 2014). As is present within the environment, existing as two different forms: organic As (which is relatively nontoxic as it is not well-absorbed into cells) and inorganic As (which is more toxic, since it affects intracellular processes). Exposure to inorganic As occurs mainly via contaminated drinking water and food sources, particularly rice and produce (including fruit juices), while seafood contains high levels of organic As (Schoof et al. 1999). Although organic As has generally been considered nontoxic, high exposures to organic As from seafood may lead to complications and should not be overlooked (Taylor et al. 2017). Mechanisms of As toxicity include increasing oxidative stress, disrupting biochemical reactions by replacing phosphate, causing chromosomal aberrations, and inhibiting DNA repair (Hughes 2002).

III. Individuals at Risk

Developing fetuses and young children are more vulnerable to metal exposure than adults. Children breathe more air, drink more water, and eat more food per pound of bodyweight than adults (Au 2002). Increased hand-to-mouth activity and more time spent on the floor further increase children's' risk of exposure to metal toxicants (Au 2002). Paired with increased exposure, children have a decreased ability to respond to environmental toxicants compared to adults. Compared to adults, children have relatively immature organs, pathways, neurological connections, and bodily protections (e.g., immune system, liver function, blood-brain barrier) against toxic chemicals (Au 2002). Furthermore, heavy metal exposure has well-documented negative effects on the immune system, which leaves them more vulnerable to pathogens (Bernhoft 2012; Fenga et al. 2017).

Other high-risk groups include immigrant and refugee families (Korfmacher and George 2012), older children, adults with pica behavior (eating non-food substances including dirt and clay) (Baldwin and Marshall 1999), and workers with occupational exposure to metal toxicants, which include gold miners and pharmaceutical industry workers (Clifton 2007). Families of exposed workers may also be at increased risk if workers do not have access to showering facilities or change their uniforms before arriving home.

IV. Adverse Health Effects of Metal Exposure

i. Neurodevelopment

High levels of prenatal and childhood exposure to As and Hg have been linked to a wide variety of poor neurodevelopmental outcomes. Children who have higher exposures to these metals exhibit the following symptoms compared to children with low exposures:reduced IQ (Solan and Lindow 2014; Rodríguez-Barranco et al. 2013), poor working memory (Boucher et al. 2014; Tsai et al. 2003) and attention span (Rodríguez-Barranco et al. 2016; Boucher et al. 2012), and impaired motor function (Ohlander et al. 2016; Parvez et al. 2011). Higher exposure to metal toxicants has been observed in children with neurodevelopmental disorders, such as Attention-Deficit/Hyperactivity Disorder (ADHD) (Sagiv et al. 2012) and Autism Spectrum Disorder (ASD) (Kern et al. 2016; Li et al. 2018).

ii. Neurodegenerative Disorders

In addition to the risks associated with toxic metal exposure during early life, these metal toxicants may also cause significant neurological effects among adults and the elderly. Many studies have identified associations between toxic metal accumulation and neurodegenerative disorders (Cicero et al. 2017; Hock et al. 1998). Neurodegenerative disorders, which includes Alzheimer's Disease (AD) and Parkinson's Disease (PD), are caused by interactions between genes, lifestyle choices, and environmental factors. Recent studies have shown that toxic metal exposure increases the risk of AD (Ashok et al. 2015; Chin-Chan, Navarro-Yepes, and Quintanilla-Vega 2015) and PD (Singh, Goel, and Kaur 2011).

iv.iii. Renal Dysfunction

Hg and As are paradigmatic renal toxicants. There is increasing evidence that chronic exposure to lower levels of toxic metals may impair renal function and increase the risk for developing chronic kidney disease (CKD) (Moody, Coca, and Sanders 2018; Orr and Bridges 2017). Chronic early-life exposure to As has been linked to renal injury, which potentially increases during childhood and adulthood (Orr and Bridges 2017).

V. Current Role of Healthcare Providers

Screening children for Pb is recommended for all children between one and two years of age. This is followed by testing in children who screened positive for risk factors, and children who are covered by Medicaid health insurance. The American College of Obstetrics and Gynecology (ACOG) recommends that all pregnant women undergo screening for risk factors for Pb exposure through a comprehensive health risk assessment during the first prenatal visit and blood testing for Pb in women if a single risk factor is identified ("Lead Screening During Pregnancy and Lactation - ACOG" n.d.). However, it is not clear whether most practitioners adhere to this recommendation. In fact, many children and adults potentially at risk for exposure to Pb and other heavy metals may be overlooked and may not undergo screening nor receive information on how to reduce exposure and protect their health.

All primary care providers should be aware of risk factors associated with toxic metal exposure and provide the appropriate screening tools, blood tests, and educational materials on reducing exposure sources and mitigating biological risk. Furthermore, they should be able to provide affected individuals with strategies for reducing the adverse effects of exposure. Unfortunately, most medical providers report little to no training in environmental health and low self-competence ratings in environmental health topics (Gehle, Crawford, and Hatcher 2011; Massaquoi and Edwards 2015; Tinney et al. 2015). Therefore, many physicians are not equipped to provide appropriate care regarding exposure to the array of environmental toxicants.

VI. Policy Recommendations

Based on the growing body of research showing associations between exposure to As and Hg and impaired neurodevelopment, neurodegenerative disorders, and renal dysfunction, we propose the following measures to prevent and reduce exposure to these metals:

i. Public Health

- An expert panel should convene to review the current state of scientific research regarding exposure to heavy metal toxicants at the national level, among at-risk populations, and strategies for reducing exposure risk. One topic to address includes developing reference levels for As and Hg among pregnant women and children. In the absence of reliable data, references could be based on the 97.5th percentile of the NHANES blood distribution for each metal in children and pregnant women (as has been done with Pb).
- Nationally available educational materials should be regularly updated by incorporating new research findings on the health effects of heavy metal exposure. These educational factsheets (topics listed in Figure 1) should be distributed to at-risk populations to increase awareness of the health effects of exposure to metals and provide strategies for reducing exposure.

ii. Legislative Actions

- We propose a move toward precautionary policies at the federal, state, and local government levels. Primary prevention via source control is the most effective strategy for reducing exposure at the population level. Examples of successful legislative actions to reduce Pb exposure include removing Pb from gasoline, removing Pb paint from houses built before the 1960s, and reducing Pb in drinking water (https://nchh.org/information-and-evidence/healthy-housing-policy/10-policies/). Existing regulations should be health-based and regularly evaluated and updated based upon current scientific findings.

iii. Health Professionals

- Governing bodies for medical education programs - i.e., the Association of American Medical Colleges (AAMC) and the American Nurses Credentialing Center (AANC) -

should include requirements for providing environmental health education.

- National recommendations should be implemented for primary care physicians, obstetricians, and pediatricians to include targeted screening questions about risk factors for high exposure to Hg and As among high-risk populations (COUNCIL ON ENVIRONMENTAL HEALTH 2016). These recommendations would target pregnant women at the first prenatal visit, immigrant or refugee children establishing care, adults with occupational exposures, and patients of any age with cognitive deficits. Levels of metal toxicants should be measured among patients who are at risk for exposure based on these screening questions.

VII. Future Directions and Addressing Research Needs

- Expert panels should convene regularly (i.e., bi-annually) to evaluate and identify emerging metal toxicants. These panels may include toxicologists, government officials, and health practitioners.
- More research is needed to identify optimal biomarkers for each metal (e.g., blood, urine, or a combination of biomarkers).
- Point-of-care lab testing must be developed to test multiple metal concentrations within adequate limits of detection and minimize measurement error.
- Reference levels above which medical intervention (e.g., chelation therapy) is required, need to be established by the CDC.
- Experts must determine which interventions should be implemented to reduce concentrations in individuals who were exposed to high levels of As and Hg.
- Researchers should continue to evaluate whether policy changes produce the desired changes using exposure levels and health outcomes as metrics.

- Health effects of metal exposures
- Sources of exposure
- High-risk groups of exposure
- Prevention strategies to prevent exposure
- Strategies to reduce health effects in already exposed populations
- Information should be easy to understand by people with different educational backgrounds

Figure 1. Key elements that should be included in an educational factsheet on metal exposures.

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Erik de Water, PhD, MS is a postdoctoral associate in the Department of Psychiatry & Behavioral Sciences at the University of Minnesota. He obtained a BS in Psychology, MS in Clinical Neuropsychology and MS in Developmental Psychology from Leiden University, the Netherlands, followed by a PhD in Developmental Psychology from Radboud University, the Netherlands. He recently completed a postdoctoral fellowship in Environmental Medicine and Public Health at the Icahn School of Medicine at Mount Sinai in New York City. His research focuses on early-life exposures and self-control and its neural circuitry in children and adolescents. Currently, he is studying cognitive interventions to improve self-control in children with fetal

alcohol spectrum disorders, and he is working as a neuropsychologist with children with neurodevelopmental, psychiatric and fetal alcohol spectrum disorders.

Emily C. Moody, **MD, MHS, MS** is a primary care physician and a pediatric environmental health research fellow at the Icahn School of Medicine at Mount Sinai in New York City. She is board-certified in Internal Medicine and Pediatrics and her research focus is on understanding long term health consequences of in-utero and early childhood exposures. She is also active in community engagement in East Harlem and is an advocate for poorer communities which often bear a greater health burden from environmental pollution.

Gleicy Hair, PhD joined the Department of Environmental Medicine and Public Health at the Icahn School of Medicine at Mount Sinai in New York City as a postdoctoral fellow in May 2018. She earned her PhD in Biomedical Engineering from the Federal of Rio de Janeiro University in Rio de Janeiro, Brazil and her work focused on the development of a computational system to support clinical diagnosis of dengue cases using machine learning. Prior to joining Mount Sinai, she worked as a research assistant at the National Infectiology Institute - Oswaldo Cruz Foundation also in Rio de Janeiro, Brazil. Dr. Hair has a strong interest in epidemiology, high dimensional data analysis, data mining, machine learning, biostatistics, and bioinformatics. Since joining Mount Sinai, Dr. Hair's research has examined children's metal exposure, exosomal microRNAs in urine and associations with children's blood pressure and renal function biomarkers in the laboratory of Dr. Alison Sanders.

Emrin Horgusluoglu-Moloch, PhD is an NIH F32-funded postdoctoral fellow in the Department of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai. During her PhD training at Indiana University, she has gained extensive experience in two major sub-disciplines of imaging genetics by working with Dr. Andrew J Saykin and Dr. Kwangsik Nho in the School of Medicine. Her research focused on genome-wide association studies (GWAS) and integration of medical imaging with genome-wide array data (e.g. imaging genetics) to identify common/rare susceptibility variants associated with various complex traits and understand neuro-genetic mechanisms of Alzheimer's disease (AD). She has devoted much of her career to biomarker development with an emphasis on advanced informatics strategies for integration of imaging, medical, and bioinformatics data. After graduating from Indiana University, she completed a postdoctoral fellowship under the supervision of Dr. Bin Zhang, identifying biomarkers for AD in order to develop better diagnostic tools that can recognize AD at early symptomatic and especially pre-symptomatic stages.

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