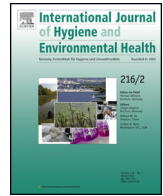




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Review

Human biomonitoring in Israel: Recent results and lessons learned

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ABSTRACT

The use of human biomonitoring (HBM) as a tool for environmental health policy and research is developing rapidly in Israel. Despite challenges in securing political and financial support for HBM, the Ministry of Health has initiated national HBM studies and has utilized HBM data in environmental health policy decision making. Currently, the Ministry of Health is collecting urine samples from children and adults in the framework of the National Health and Nutrition Study (MABAT), with the goal of ongoing surveillance of population exposure to pesticides and environmental tobacco smoke, and of combining HBM data with data on diet and health behavior. In academic research studies in Israel, biomarkers are used increasingly in environmental epidemiology, including in three active birth cohort studies on adverse health effects of phthalates, brominated flame retardants, and organophosphate pesticides. Future Ministry of Health goals include establishing HBM analytical capabilities, developing a long term national HBM plan for Israel and participating in the proposed HBM4EU project in order to improve data harmonization. One of the lessons learned in Israel is that even in the absence of a formal HBM program, it is possible to collect meaningful HBM data and use it in an *ad hoc* fashion to support environmental health policy.

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1. Introduction

Israel is a small, densely populated country (population of 8.5 million; 387.3 persons per square km of land) with significant environmental pressures resulting from rapid economic and population growth (Organization for Economic Co-operation and Development, 2011; World DataBank, 2016). Responsibility for environmental health issues, and specifically for chemical management policy, is shared among several ministries, making coherent policy-making regarding chemicals in air, food, personal care products, and water a challenge. Policy making in environmental health in Israel is frequently crisis driven, with other national priorities more pressing, such that resources are not always available for an integrated and systematic evaluation of environmental health problems (Preuss et al., 2006).

Human biomonitoring (HBM) has emerged as a tool for assessing cumulative exposure to complex mixtures of chemicals and for monitoring chemical exposures in the general population (Sexton et al., 2004). Many countries, including the US, Canada, Germany, France, and Belgium, have developed National Biomonitoring Programs (Choi et al., 2015).

As in many developing countries, adverse reproductive health trends and increasing rates of diseases such as asthma, obesity, diabetes, and certain types of cancer have raised concerns about health impacts of environmental chemicals in Israel (Berman et al., 2012; Environment and Health Fund and Ministry of Health, 2014). Although to date there is no formal National Human Biomonitoring Program or network in Israel, and no legal foundation in Israel for HBM, in 2009 the Israel Ministry of Health initiated a national HBM study in an attempt to gather data on integrated chemical exposure of the population from various exposure sources and in order to promote surveillance and prevention of potentially harmful exposures to chemicals in the population.

In addition, academic researchers in Israel are increasingly using HBM tools in environmental epidemiology, and have conducted studies to develop novel biomarkers for environmental exposures. The purpose of this article is to review recent HBM studies in Israel, to highlight regulatory uses of this data in environmental health policy, and to describe challenges and lessons learned in developing a national HBM framework in a small country.

2. Recent HBM studies in Israel

We searched for information on HBM studies conducted in the Israeli population in the last five years (since 2011), excluding studies in occupational settings. Relevant sources were a literature review by PubMed search using key words: human; biomonitoring; Israel; as well as communication with researchers and funding agencies. We briefly present methods and results of these studies. We elaborate on the 2011 Ministry of Health HBM study as it is the most relevant to a national HBM framework.

2.1. Ministry of health surveillance studies

2.1.1. 2011 Israel biomonitoring study: methods, results, and policy implications

The Israel Biomonitoring Study was conducted by the Ministry of Health in 2011 with the goals of measuring urinary levels of several environmental contaminants (organophosphate (OP) pesticides, phthalates, bisphenol A (BPA), cotinine, and polycyclic aromatic hydrocarbons (PAHs)) in the Israeli population, comparing levels with other international populations, and identifying demographic, behavioral, and dietary predictors of exposure to these contaminants (Berman et al., 2013a). Participants from the adult general population (ages 20–73) were recruited from 5 regions in Israel. As

the population of Israel is comprised of both Jewish (~75% of the population) and Arab (~21%) citizens, the sample included Jewish (74.1%), Arab (24.3%), and other (1.6%) participants. It is unclear to what extent the study population is representative of the general adult population in Israel, as a convenience non-random sampling technique was employed to recruit individuals to the study. However, the recruitment strategy was designed to include individuals from different ethnic and geographical subpopulations in Israel.

Participants provided a spot urine sample and completed an in depth interview including questions on health, lifestyle, and diet (24 h recall and food frequency questionnaire). Urine samples were analyzed at the University of Erlangen-Nuremberg in Germany.

Higher socioeconomic status (education and income) emerged as an important predictor of increased exposure to both OP pesticides and BPA, likely due to increased consumption of fruits and vegetables and more eating outside the home in higher socioeconomic groups (Berman et al., 2013b, 2014). On the other hand, higher socioeconomic status was associated with lower exposure to environmental tobacco smoke (ETS) (based on cotinine) in non-smokers (Levine et al., 2013). We identified dietary predictors for BPA, OP pesticides and PAH metabolites (Levine et al., 2015) but also identified the need for more targeted questions on dietary patterns in order to improve our methodology for identifying dietary predictors of exposure to environmental contaminants in future HBM studies.

In order to identify contaminants as a potential public health cause for concern and priority for public health policy intervention, we compared urinary levels in our population to other international populations and/or to health based threshold values (HBM1 and biomonitoring equivalent values). We note that for the contaminants measured in our study health based threshold values were available only for BPA and phthalates.

Median creatinine adjusted concentrations of several OP metabolites (dimethyl phosphate, dimethyl thiophosphate) were high in our study population compared to the general US and Canadian populations (Fig. 1). Adjusted concentrations of total dimethyls were almost 10 times higher than in NHANES adults and almost 3 times higher than in Canadian adults. For the chlorpyrifos specific metabolite 3,5,6-trichloro-2-pyridinol (TCPy), median urinary levels in our population were high compared to the US general population (2.34 $\mu\text{g/g}$ compared to 0.88 $\mu\text{g/g}$), as were 95th percentile values (8.52 $\mu\text{g/g}$ compared to 3.2 $\mu\text{g/g}$) (unpublished data).

The percent of non-smokers with quantifiable urinary cotinine (63%) was relatively high in our study population, reflecting widespread exposure to ETS. Since cotinine is measured in serum in the US National Health and Nutrition Examination Survey (NHANES) and was not measured in the French study “Exposure of the French population to environmental pollutants” in 2006–2007, we limited our comparison to the Canadian general population in 2009–2011. Compared to 14.6% of non-smokers aged 20–39 and 11.2% aged 40–59 with urinary cotinine levels above the level of detection (1 $\mu\text{g/L}$) in Canadian adults, in our population rates were higher, 67% and 45% respectively.

Phthalate metabolite concentrations were higher in our study population compared to the general US population but values were below health-based threshold values. For example, for the phthalate metabolite mono(2-ethyl-5-hydroxyhexyl)phthalate (5OH-MEHP), both median (30.4 $\mu\text{g/L}$) and 90th percentile values (91.1 $\mu\text{g/L}$) in our study population were very low compared to the HBM-1 value (300 $\mu\text{g/L}$ for women of reproductive age and 750 $\mu\text{g/L}$ for males 14 years and older) determined by the Human Biomonitoring Commission (2015).

Median creatinine adjusted urinary BPA concentrations in the study population (3.0 $\mu\text{g/L}$) were comparable to those in Belgium and Korea; higher than those reported for the general US, German,

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