Using Biomonitoring Data to Inform Exposure Assessment in Children

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Key Words:
Biomonitoring
Children
Exposure

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Introduction

The United States Environmental Protection Agency (US EPA) conducts human exposure research to improve the scientific basis of risk assessment. Exposure research is required to: (1) screen and prioritize compounds and potential exposures; (2) identify important stressors, sources, and pathways; (3) identify determinants of exposure; and (4) characterize potential exposure. Exposure research is also required to predict and classify exposure and dose for human health studies (toxicological, clinical, epidemiological) and public health tracking, as well as to predict and assess exposure and dose to design and test intervention and regulation. Currently, the US EPA is being called on to assess cumulative risk resulting from exposures to multiple stressors. The Agency is also being required to identify vulnerable populations, characterize life-stage risks, and evaluate gene-environment interactions. The use of biomonitoring data holds a great deal of promise for characterizing exposure and informing cumulative risk assessment.

There have been important applications of biomonitoring for environmental health assessment. Results of biomonitoring for lead and mercury have shaped prevention strategies, identified susceptible subpopulations, and improved the scientific basis for health risk estimates. In the case of dioxin and PCBs, biomonitoring has also enabled scientists and public health professionals to track population trends and to evaluate progress in reducing exposures. More recently, biomonitoring for perchlorate, brominated flame retardants, and persistent fluorinated compounds has provided important indications of emerging environmental health issues.

Despite these successes, there are significant challenges associated with estimating and interpreting toxicant exposures and health risks from biomonitoring data. The science of detecting contaminants has outpaced the science of interpreting public health implications of measured internal exposure. Though low levels of environmental contaminants can be measured in tissues of children and fetuses, it is not always known whether the measured exposure leads to an adverse health outcome. In addition, information on exposure pathways is often required to link biomonitoring results to contaminant sources and to reduce exposures and risks.

Use of biomonitoring to inform our understanding of the complex relationships between environmental exposures, individual vulnerability, and health outcomes requires sound scientific understanding of the systems that are being assessed and appropriate tools for characterizing these systems. The US EPA is actively conducting research to better understand the health implications of children's biomonitoring data and how to mitigate exposures. Research activities include the following:

- International Biomonitoring Workshop,
- Preliminary demonstration of application of advanced statistical techniques to interpret children's exposure and biomonitoring data,
- Development of conceptual framework for interpreting biomonitoring data for cumulative risk characterization.

International Biomonitoring Workshop

In September 2004, the US EPA and the ILSI Health and Environmental Sciences Institute, together with the Centers for Disease Control and Prevention, the Agency for Toxic Substances and Disease Registry, and the International Council of Chemical Associations, co-sponsored an International Biomonitoring Workshop (Doerrer and Holsapple, 2004; Albertini et al., 2006). Workshop participants discussed key issues related to the use of biomonitoring data for environmental public health protection. These issues included appropriate uses for biomonitoring data, information needed to use biomonitoring data in risk assessment, and citeria for using biomonitoring data in exposure and health research. Processes and information needed to link biomarker measurements to exposure, internal dose, or health outcome were also discussed.

Six case studies, considering biomarkers for different classes of chemicals were used to explore workshop questions: inorganic arsenic, methyl eugenol, organophosphorus pesticides, perfluorooctanesulfonate, phthalates, and polybrominated diphenyl ethers. Several themes emerged from the workshop discussions. Biomonitoring was identified as a public health victory. It was acknowledged that biomarkers integrate all routes of exposure, and this can be an advantage or a disadvantage to understanding exposure. Workshop participants emphasized the requirements for interpreting biomarkers depends on the question. The need for careful study design for future emphasis on short-lived compounds was also identified. Finally, participants noted that single biomarkers cannot be used alone unless the question is very simple

Analysis of NERL Children's Exposure Data

The US EPA recently conducted an exposure study called Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) (Wilson et al, 2004; Morgan et al, 2005). The CTEPP study measured the total exposure of 257 preschool children (ages 3-5 years) to more than 50 different chemicals commonly found in their everyday environments. The participants were from homes and day care centers in North Carolina and Ohio. Monitoring of each participant was performed over a 48-hour period. Samples of food, drinking water, air, urine, dust, soil, transferable residues on floors, and surface wipes were collected and analyzed. The most frequently detected pollutants in environmental media included

- Chlorpyrifos, diazinon, *cis*- and *trans*-permethrin, *alpha*- and *gamma*-chlordane, and pentachlorophenol
- Benzybutylphthalate, di-*n*-butylphthalate, and bisphenol-A
- PAHs

Metabolites of chlorpyrifos and diazinon were also detected at a high rate in environmental samples. Pollutants or metabolites that were frequently detected and measurable in the children's urine samples included 3,5,6-TCP; 2,4-D; and pentachlorophenol.

An exploratory effort to apply advanced statistical techniques to identify exposure determinants and links to biomarker data as been initiated using the CTEPP data. This work investigates the benefits, limitations, and impact on biomarker interpretation of two

statistical modeling techniques: structural equation modeling and hierarchical Bayesian modeling. Results demonstrate the power of these techniques for characterizing links between biomarker data and exposure. Preliminary results also demonstrate the significant impact available data can have on model results.

Interpreting Biomonitoring Data for Cumulative Risk Characterization

At the US EPA we are beginning to address some of the significant questions associated with using biomonitoring data to characterize cumulative risks resulting from exposures to multiple stressors. For children, we are interested in understanding the relationships between multiple exposures and multiple outcomes, as children grow and develop over time. In this preliminary conceptual effort, we considered several issues. First, because there is unlikely to be a single "ideal" biomarker (a single measure with all the important characteristics for relating health outcomes with a particular exposure), an array of biomarkers will be needed (e.g, one biomarker might give information about short-term exposures, another about long-term exposures). Second, we are interested in understanding what biomarkers and biomonitoring data tell us about disease in the community and risk to the population. Third, we are interested in assessing the utility of biomarkers for understanding risk to multi-factorial diseases (e.g., asthma, neurodegenerative diseases, etc.).

A framework was developed (Ryan, et al, 2006) to provide the conceptual basis for considering biomonitoring data and other health metrics in assessment of cumulative

exposure and risk. In this framework, biomonitoring and other health data are used to characterize the receptor (individual, community or population), potential exposures, and health outcomes. By considering an array of metrics across the exposure-outcome continuum, this framework begins to address the multi-factorial nature of environmental disease and cumulative risk.

More Information

US EPA National Center for Computational Toxicology

http://www.epa.gov/comptox/

International Biomonitoring Workshop (ILSI)

http://www.hesiglobal.org/Events/biomonitoringworkshop.htm

US EPA National Exposure Research Laboratory (Children's Exposure)

http://www.epa.gov/heasd/

US EPA Framework for Cumulative Risk Assessment

http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=54944

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