Interpreting Biomarkers of Exposure In Humans

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Science Issues

Biomonitoring is a useful tool for understanding the linkages between external chemical exposures and possible health outcomes in humans. The importance of this research is to increase our understanding of how to properly interpret and use biomarkers to assess human exposures and internal doses. Chemicals or their metabolites are commonly measured in fluids such as urine, blood, or saliva. In recent years, there has been an explosion of available human biomonitoring data from researchers in academia, private industry, and government. Unfortunately, a majority of these studies have collected little or no environmental measurement data. Environmental measurement data are vital in understanding the important sources (i.e., dust, air, food), pathways, and routes (i.e., ingestion, inhalation, and dermal) of human exposures to chemicals. Biomarker data by themselves only show that humans were exposed to a chemical at some point in time. The Office of Research and Development (ORD) has conducted and/or funded numerous human exposure studies in the past several years that have simultaneously collected environmental measurement and biomarker data. Statistical analyses are ongoing to understand the relationship between external exposure, internal dose, and biomarkers of exposure, and EPA has already learned a great deal from these analyses. This knowledge and tools for its application will benefit risk assessors and decision-makers, thus improving EPA's ability to identify agents of concern, select effective risk mitigation strategies, and demonstrate accountability for reducing adverse health effects of environmental chemicals.

Science Questions

- How can previous personal exposures be assessed or reconstructed through biological measurements?
- What is the range of typical personal exposures, and how does this relate to observed measures of internal dose through multiple routes?
- What tools are needed to design future exposure and epidemiological studies that will include the collection of biomarker of exposure samples and associated metadata?
- How can biomarkers of exposure be used to improve current exposure and risk assessment methodologies and to support accountability?

EPA and CDC Exposure and Biomarker Studies

The Agency is currently performing statistical analyses on human exposure and/or biomonitoring data collected from several studies to understand the relationship between external exposure, internal dose, and biomarkers of exposure. These include such studies as the Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) Study, Children's Pesticide Post-application Exposure Study (CPPAES), Biological and Environmental Monitoring for Organophosphate and Pyrethroid Pesticide Exposures in Children Living in Jacksonville, FL (JAX), Minnesota Children's Pesticide Exposure Study (MNCPES), and National Health and Nutrition Examination Surveys (NHANES).

Research to Address Science Questions

- Develop a framework and modeling tools to guide future biomarker of exposure applications.
- Develop better measurement methods and procedures for collecting biomarkers of exposure in human research studies.
- Develop statistical methods and models to assess human exposures to chemicals.
- Identify and provide valuable data inputs for modelers in their toxicokinetic and exposure models.
- Develop tools and approaches for interpreting biomarkers to assess human exposures.
- Use biomarkers to assess culmulative exposures and risk.
- Use PBPK models and available exposure data to reconstruct human exposures to chemicals.

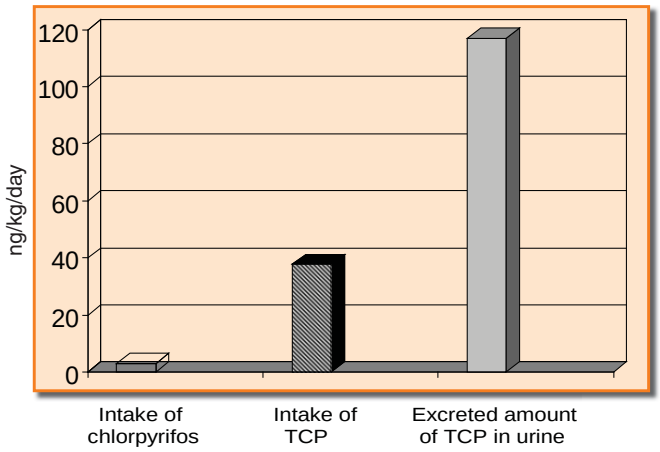

Figure 1. The median potential aggregate absorbed doses of chlorpyrifos and TCP compared with the excreted median amounts of TCP in the preschool children's urine in North Carolina.

Research Application – Interpreting Biomarkers to Assess Human Exposures

For example in the CTEPP study, the urinary biomarker of exposure for the pesticide chlorpyrifos, 3,5,6-trichloro-2-pyridinol (TCP), was also measurable in several media such as food, air, and dust. Dietary ingestion was the dominant route of the children's exposure to both chlorpyrifos and TCP; however, the children's median dietary intake was more than 10 times higher for TCP than for chlorpyrifos.

Figure 1 shows that the children's total intake of TCP was substantially greater than their total intake of chlorpyrifos by all routes of exposure. This is an important scientific finding since the scientific community had considered TCP as a reliable urinary biomarker of exposure to chlorpyrifos in humans for some time.

Examples of Research Partnerships

- An interagency agreement (IAG) was developed with CDC to examine the urinary biomarker concentrations of chemicals (bisphenol-A, phthalate metabolites, atrazine/metabolites, diakyl phosphates, and pyrethroids metabolites) from children in the CTEPP study. These cutting-edge methods were recently developed by CDC.
- EPA is collaborating with the University of Washington through an EPA's 2004 Science to Achieve Results (STAR) research grant to use CTEPP data to help predict aggregate pesticide exposures of children using second order probabilistic methods and comparison of those predictions to observed levels of urinary biomarkers.

Impact

This research will identify the strengths and limitations of using existing biomarker data as quantitative estimates of human exposures to chemicals. Future studies will be greatly improved by understanding how to properly collect and interpret biomarkers of exposure in humans. Important data inputs will be provided to modelers for their toxicokinetic and exposure models to reduce the uncertainties of human exposures to these chemicals. Cutting-edge methods will be developed for the collection and analysis of biomarkers of exposure (i.e., urine, blood, hair, saliva) in humans. The data generated from this research will provide valuable scientific data/ information to risk assessors and decision-makers.

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