Exposure Assessment FACILITY CORE

Analytical chemistry
Interpreting exposure data
Mechanistic modeling of exposure and dose

PROJECT OVERVIEW

The Exposure Assessment Research Core focuses on analytical chemistry needs and physiologically based toxicokinetic (PBTK) modeling. The Core provides analytical support for the Community Based Participatory Research (CBPR) and Pesticide Exposure Pathways Projects. For the Pesticide Exposure Pathways Project, this assistance consists of technical advice and consultation on analytical chemistry approaches for exposure assessment methods required for the wide range of studies proposed by the CBPR Project, which include air, dust, soil, urine, blood, and skin wash. For the CBPR Project, support is provided in training for urine, blood, and house and car dust collection. Sampling for the CBPR Project will include around 200 households. The Core will also analyze samples collected in the field by the CBPR Project. The focus of the project will be organophosphates (OP) for the farmworkers and non-farmworkers groups. In the warehouse worker group, urine and house and vehicle dust will analyzed for OPs and perhaps some non-OP pesticides.

The Exposure Assessment Research Core assists other Research Projects and Facility Cores by providing advice on how to interpret analytic results in the proposed studies. The Core also utilizes a rich archive of previous studies conducted by Center scientists on pesticide exposures of adults and children in the Yakima Valley and for Western Washington urban populations. During the first period of funding, kinetic modeling performed by the Core also proved invaluable for understanding and translating information on molecular mechanisms and genetic susceptibility.

WHY CHILDREN?

Young children can differ greatly from adults in their ability to metabolize compounds (Ginsberg et al. 2002) and special care must be taken when considering children's exposure to pesticides. Some of the special susceptibilities of children to pesticide exposure and health effects that are important considerations for the Exposure Assessment Facility Core are:

1) Many xenobiotics are metabolized more rapidly in children. For toxicants such as chlorpyrifos, whose metabolite chlorpyrifos-oxon is more effective than the parent compound in inactivating acetylcholinesterase (AChE), exposure to children may result in increased acute effects.

2) Studies in rats have suggested more rapid absorption of a number of compounds through the gastrointestinal tract of young versus mature animals.

3) Children have lower concentrations of plasma proteins (notably albumin, gamma globulins, and lipoproteins) which bind many pesticides. This may result in higher unbound pesticide concentrations in the blood, leading to more acute effects following exposure.

4) Because infants have a lower fraction of body fat compared to adults, lipophilic pesticides, such as azinphos methyl and chlorpyrifos, will distribute into a smaller volume, with resulting higher concentrations in blood.

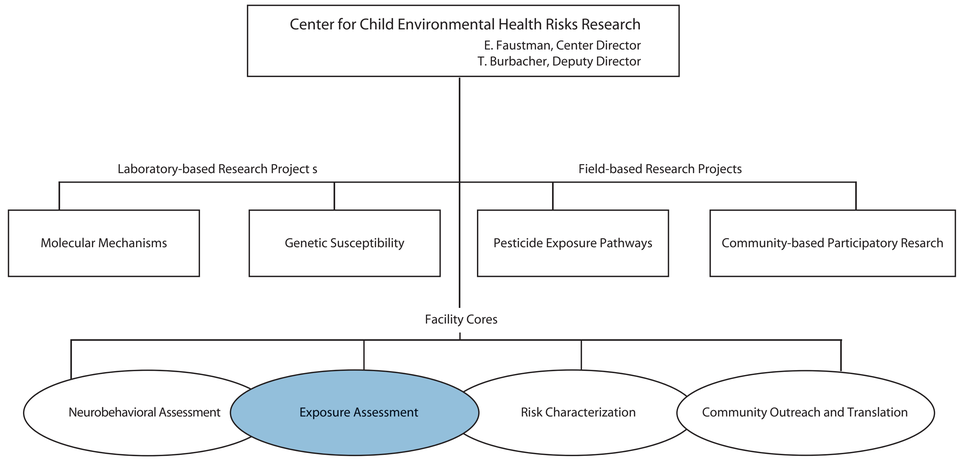
5) The developing blood-brain barrier in infants may be less effective at screening pesticide and metal toxicants compared to adults. This has been documented for lead exposure in animal studies.

7) While there is a smaller alveolar surface area available for toxicant absorption, infants have a respiratory volume per body weight that is about twice that of adults.

8) The skin area per body weight value in infants is about twice that of adults, increasing the importance of dermal absorption of pesticides.

9) Younger children have increased pesticide exposure through pica soil ingestion and increased dermal contact with house dust.

RESEARCHERS



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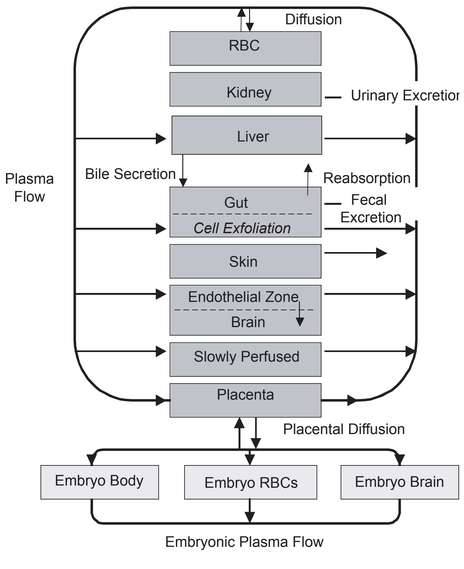

Fig. 1 Conceptual diagram of the physiologically based toxicokinetic (PBTK) model for pesticide disposition. Key maternal and embryonic compartments are shown connected by plasma flow. Transport between compartments is flow driven with the exception of transport into the maternal brain, red blood cells and placenta, which are modeled as diffusion limited processes (adapted from Lewandowski et al).

SPECIFIC AIMS

1. Provide analytical chemical support to the Community-Based Participatory Research (CBPR) Project and the Pesticide Exposure Pathways Project by conducting analyses for OP pesticides and metabolites in house dust, vehicle dust and adult and child urine samples.

2. Provide assistance with the interpretation of exposure data to the CBPR Project and the Pesticide Exposure Pathways Project. Interpretation of the results from the house dust, vehicle dust and urinary analyses is not a straightforward process due to the complex relationship between environmental samples and urinary metabolites.

3. Coordinate mechanistic modeling of exposure and dose among all Center projects to be linked with dynamic modeling performed by the Risk Characterization Core. Stochastic models will be generated to explore links between measured environmental pesticide levels and biomonitoring results and ultimately to biological effects. This will require mathematical representation of human behaviors, chemical transfer and absorption processes, and the pharmacokinetics of metabolism and excretion. Exposure and pharmacokinetic models will then be linked with biologically-based dose response models to better explore exposure response relationships.

ANTICIPATED OUTCOMES

During the next year the Core will assist in the design of the Community-Based Research Project and identify appropriate chemical analytical methods for analysis. In the future, we will look at additional urinary biomarkers of exposure other than diakyl phosphate metabolites of organophosphate pesticides. In addition to identifying appropriate analytical techniques, other study design issues will include the number of samples to be collected from each person and whether these samples should be composited before analysis. This will involve working closely with the Risk Characterization Facility Core.

The Exposure Assessment Core will also maintain a database of results from the analytic laboratory and other data about samples. The results include all details from the analytic laboratory regarding the preparation of the individual samples. These data will be merged with field information on the collection of individual samples and data from questionnaires and surveys collected from the CBPR Project. The database is open to all researchers in the Center and assists Center researchers in the interpretation of analytic data. In particular this database will also be linked to the Research Mapping Project within the Community Outreach and Translation Core to assist in explaining the results to the communities.

REFERENCES

Curl, C.L., R. A. Fenske, K. Elgethun. (2003). "Organophosphorus pesticide exposure of urban and suburban preschool children with organic and conventional diets", Environ Health Perspect 111(3): 377-382.

Curl, C. L., R. A. Fenske, J. C. Kissel, J. H. Shirai, T. F. Moate, W. Griffith, G. Coronado and B. Thompson (2002). "Evaluation of take-home organophosphorus pesticide exposure among agricultural workers and their children." Environ Health Perspect 110(12): A787-92.

Fenske, R. A., J. C. Kissel, C. Lu, D. A. Kalman, N. J. Simcox, E. H. Allen and M. C. Keifer (2000). "Biologically based pesticide dose estimates for children in an agricultural community." Environ Health Perspect 108(6): 515-20.

Fenske, R. A., C. Lu, N. J. Simcox, C. Loewenherz, J. Touchstone, T. F. Moate, E. H. Allen and J. C. Kissel (2000). "Strategies for assessing children's organophosphorus pesticide exposures in agricultural communities." J Expo Anal Environ Epidemiol 10(6 Pt 2): 662-71.

Kissel JC, Curl CL, Kedan G, Lu C, Griffith W, Barr DB, Needham LL, Fenske RA. 2004. Comparison of organophosphorus pesticide metabolite levels in single and multiple daily urine samples collected from preschool children in Washington State. J Expo Anal Environ Epidemiol.

Thompson, B., G. D. Coronado, J. E. Grossman, K. Puschel, C. C. Solomon, I. Islas, C. L. Curl, J. H. Shirai, J. C. Kissel and R. A. Fenske (2003). "Pesticide take-home pathway among children of agricultural workers: study design, methods, and baseline findings." J Occup Environ Med 45(1): 42-53.

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