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Proceedings of the U.S. EPA Workshop on Research Needs for Community-Based Risk Assessment

OCTOBER 18-19, 2007
RESEARCH TRIANGLE PARK, NC



National Center for Environmental Research
Office of Research and Development

U.S. EPA Workshop on Research Needs for Community-Based Risk Assessment

October 18–19, 2007
Research Triangle Park, NC

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***Abstract to be provided**

Appendices

Session I: Data Needs and Measurement Methods for Community-Based Risk Assessment

Development of Nanoscaled Sensor Systems for Detecting and Monitoring of Environmental Chemical Agents

Desmond Stubbs
Oak Ridge Center for Advanced Studies, Oak Ridge, TN

Project Objectives: The specific objectives are to design, model, and fabricate highly sensitive, highly selective, universal sensing arrays for detecting and monitoring personal exposure to a wide range of chemical agents.

Approach: On October 16, 2006, the Oak Ridge Center for Advanced Studies (ORCAS) hosted a 1-day meeting that brought together scientists from the U.S. Environmental Protection Agency (EPA), the National Institute for Environmental Health Sciences (NIEHS), and nanotechnologists to discuss their shared interest in developing novel nanoscaled analytical instrumentation for a variety of applications, including the development of personal environmental exposure sensors. The meeting served as a followup to a larger one held in April 2006 at the EPA campus in Research Triangle Park, NC (see http://orcas.orau.org/epa/default.htm). EPA and NIEHS investigators were asked to articulate the challenges they encounter as they relate to identifying, characterizing, and monitoring regulated chemical species *in vivo* and *in situ*. A technology needs assessment analysis was conducted, and the results indicated an urgent need for a rugged, light-weight, low-cost, wearable, real-time sensor capable of multi-analyte detection with minimal burden to the individual. The "gold standard" was defined as the ability to simultaneously detect acute as well as subacute chemical agents with the same sensing system in the field and link this data to a specific biological event. This type of device would be capable of remote data acquisition, location recording, and control of the levels and frequency of environmental exposure.

Microfabricated cantilever array platforms pave the way for the development of light-weight, wearable multi-analyte sensors. Cantilever arrays are capable of the simultaneous detection of multiple analytes, with extremely high sensitivity, in real- and near-real time. Selectivity, which has been a longstanding problem for small molecule detection due to the use of unspecific, low-energy receptors, could be achieved by using high-affinity, high-binding-energy, self assembled monolayers (SAMs)—making the sensor more like a dosimeter. Unlike other sensors, the low thermal mass of the cantilever allows periodic regeneration by thermal cycling, achieved by passthrough of electrical current. Selectivity will be enhanced further by integrating three orthogonal modes into the cantilever platform, namely adsorption-induced cantilever bending, resonance frequency variation due to mass loading, and differential mechanical calorimetric response. Because inhaled air should be monitored close to the breathing zone, the sensor will have two units: a passive sensing unit the size of a pea, including telemetry; and a receiver unit the size of a small PDA, designed to be carried in a pocket. The PDA unit will have analysis and display capability, and will support global positioning and biomonitoring device interfaces.

Preliminary Findings and Significance of Findings: Using microelectronic-based arrays, we were able to detect a number of chemicals of interest in the vapor phase. These include: alcohols[1], mercury[2], cocaine[3], and a number of explosives.[4] We also were able to conduct proof-of-concept experiments in liquid media where we successfully detected low levels of bacterial spores in complex media.[5]

Preliminary results suggest that these devices are capable of real-time detection (sub-second scale) of low vapor pressure chemical compounds in the parts per trillion range.

References:

1. Thundat T, Chen GY, Warmack RJ, Allison DP, and Wachter EA. Vapor detection using resonating microcantilevers. *Analytical Chemistry* 1995;67(3):519-21.

2. Thundat T, Wachter EA, Sharp SL, and Warmack RJ. Detection of mercury vapor using resonating cantilevers. *Applied Physics Letters* 1995;66;1695-7.

3. Stubbs DD, Lee SH, and Hunt, WD. Investigation of cocaine plumes using surface acoustic wave immunoassay sensors. *Analytical Chemistry* 2003;75:6231-5.

4. Stubbs DD, Lee S-H, Hunt WD. Clues from digital radio regarding biomolecular recognition. *IEEE Transactions on Biomedical Circuits and Systems* 2007;1(1):50-55.

5. Lee S-H, Stubbs DD, Hunt WD. Rapid detection of bacterial spores using a quartz crystal microbalance (QCM) immunoassay. *IEEE Sensors Journal* 2005;5(4):737-43.

Data Collection Platforms for Integrated Longitudinal Surveys of Human Exposure-Related Behavior

Paul N. Kizakevich and Roy W. Whitmore
RTI International, Research Triangle Park, NC

Project Goal and Objectives: The goal of this research project is to develop a field platform for accurately collecting exposure factor data in longitudinal surveys with low enough participant burden that most people will be willing to participate in week-long studies across each quarter of the year. The objectives are to develop, validate, and evaluate innovative methods for time/activity/location/exertion-level (TALE) data, dietary consumption data, and data on use of consumer products, including pesticide products, household cleaning products, and personal care products.

Approach: A system has been developed that integrates multiple real-time data collection streams and survey modes on a hand-held pocket PC platform. The system integrates diaries and questionnaires with a collection of wireless peripheral devices for monitoring physical and physiological data. Three pocket PC diary modes were studied: interactive menus, voice questionnaires, and passive periodic photos. We also are investigating innovations such as passive microenvironment identification (i.e., beacons), passive exertion assessment, wireless product use event markers, wireless interfaces, intelligent prompting, GPS tracking, and automated daily review to collect the data both accurately and with low participant burden. The system design emphasizes easy reconfiguration to support varied study requirements, investigator needs, and participant preferences. A pilot test was conducted in 40 homes to compare participant burden, participant compliance, data quality, and data collection costs for the pocket PC diaries and paper diary instruments.

Preliminary Findings: To assess burden, the time to use pocket PC menus was monitored and a debriefing questionnaire was executed. For activity and location, participants averaged 16 and 12 seconds per entry. Perceived burden for such data were 60 seconds for paper and voice, and 45 seconds for menus. For cleaning and pesticide questionnaires, participants averaged 52 and 150 seconds per product use. Perceived burden for cleaning/pesticide data was 60/120 seconds for paper and 60/60 seconds for menu entries. For dietary data, participants averaged 64 seconds per entry. To assess compliance, the median number of activities/hour and locations/hour were computed. For activity, these were 1.6/hr (paper), 1.3/hr (menu), 1.2/hr (voice), and 2.8/hr (photo). For location, these were 1.1/hr (paper), 0.9/hr (menu), 0.7/hr (voice), and 7.2/hr (photo). Automated room beacons, heart rate monitoring, and GPS data worked fairly well.

Significance of Findings: The burden for menu-based activity and location data entry is good; however, several participants expressed difficulty with the current TALE menu scheme. Furthermore, some participants reported avoiding activities and limiting diet to reduce entries for paper, voice, and menu diaries. Participants liked using the voice diary, although technical issues affected recording quality. Although most liked the photo diary, some participants expressed privacy issues in their workplace.

Next Steps: We are developing the next generation of the platform, advancing the technology and focusing on lessons learned during the pilot test. After completing these revisions, we will conduct another field test in 40-50 homes, and publish the results regarding its performance.

Session II: The Biological Impact of Non-Chemical Stressors and Interaction With Other Environmental Exposures

Intersections of Social Ecology, Neurobehavioral Development, and Environmental Contamination

Bernard Weiss
Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY

Toxic outcomes for neurobehavioral endpoints in risk assessment typically take the form of subtle functional disturbances, such as lowered scores on neuropsychological tests, rather than blatant pathology. In addition to the risk assessment difficulties posed by finding sufficiently sensitive and specific measures for such endpoints, they almost invariably represent a product not just of chemical exposure alone but also of the social environment in which exposure occurs—the prevailing social ecology. Recognizing that the risks of adverse effects depend on many factors besides exposure level, investigators have adopted the tactic of compensating statistically for the influence of the social environment by treating its features as confounders or covariates external to the primary question of exposure. Socioeconomic status (SES), for example, is typically assigned the status of a covariate, with the aim of using it to broadly characterize and summarize aspects of the social environment such as its potential for inducing stress. Treating it as a covariate is designed in essence to isolate the main effect—toxic exposure. Another different perspective on how the social environment influences toxic outcomes views its properties not simply as a collection of confounding factors but as biologically embedded mediators or effect modfiers that have to be treated as elements in a complex causal nexus. The social ecological setting, through its influence on the vulnerability of the organism to toxic responses, to some degree determines the biologically effective dose. Examples of this principle can be drawn from both laboratory experiments and epidemiological investigations. The literature on lead neurotoxicity, particularly that portion addressing early development, provides a rich source of such examples. Animal studies have demonstrated how developmental lead exposure can combine with environmental conditions to either exacerbate or counteract its adverse neurobehavioral consequences. Environmental enrichment, in the form of group housing and play objects, may attenuate or even eliminate lead's adverse effects while prenatal or postnatal stress interacts with lead exposure to elicit functional outcomes that depend on combinations of exposure level, age, and sex. Similarly, epidemiological studies of lead exposure point to SES as a potent effect modifier, but so far only at a gross level whose critical properties generally fall short of specifics such as maternal attitudes and behavior. Some of these specifics are traceable, moreover, not only to the individual's immediate or near environment but also to the wider social setting, which includes factors such as access to educational opportunities and the incidence of poverty in the surrounding area. Both animal models and epidemiological investigations must take account of how such socioecological characteristics combine with toxic exposures to create patterns of human health risks.

Preparation supported by NIEHS grants ES013247 and ES015509.

Social Environment as a Modifier of Chemical Exposures

Robert Wright
Harvard School of Public Health, Boston, MA

Objective: Psychosocial stressors that correlate with socioeconomic gradients are frequently cited as potential confounders of the effects of chemical toxicants. New evidence suggests that these factors may instead synergistically increase chemical toxicity. In this session, the existing evidence for interactions between psychosocial stress and chemical exposure on neurodevelopment will be presented.

Approach and Preliminary Findings: Data from animal studies demonstrating interactions between social stressors and neurotoxic chemicals will be reviewed, followed by a review of the research conducted in human populations. Finally, preliminary results from research on this topic will be presented.

Significance: Because toxic waste sites are associated with poverty, and other social factors that contribute to psychosocial stress at the individual and community level, the toxicity of chemicals found in these waste sites may be greater per dose than in other communities.

Next Steps: Further research is needed to confirm these results and to potentially incorporate the findings into risk analysis models for toxic waste sites.

Session III: Statistical and Mathematical Modeling for Community-Based Risk Assessment

A Multi-Site Time Series Study of Hospital Admissions and Fine Particles: A Case-Study for National Public Health Surveillance

Francesca Dominici
Department of Biostatistics, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

At a time when technology enables scientists to conduct research at the cellular and molecular levels of life and to make extraordinary therapeutic advancements, we remain challenged to translate these new discoveries into tools to improve the health of populations. Multiple databases are available containing massive amounts of relevant information on the determinants of health. Research on population health can be advanced more rapidly by integrating these databases and by designing new mathematical models to identify and prioritize major threats and their causes. The combination of integrated databases and new analysis tools comprise a national system for population health research.

We have created a national system for population health research to routinely quantify health risks associated with short and long-term exposure to particulate matter and ozone. Specifically, a national database has been assembled comprising time-series data for the period 1999-2005 on daily hospital admission rates for several cardiovascular and respiratory outcomes, accidents, daily levels of fine particles, temperature and dew point temperature for the 203 largest U.S. counties. Daily hospital admission rates are constructed from the National Claims History Files (NCHF) in Medicare. Our study population includes 21 million people, approximately 60 percent of the total U.S. population older than age 65. Using analytical methodology developed for multi-site time series studies of air pollution and health, we estimated county-specific, regional, and national average relative rates of hospital admissions for respiratory and cardiovascular diseases associated with short-term exposure to fine particles. We also have created Web-based tools for data acquisition, integration, and dissemination and make these tools accessible to the scientific community to promote a movement toward reproducible population research.

The pioneering aspect of this work is in the development of a new approach to population health research: moving from individual epidemiological studies toward an integrative framework that (1) combines heterogeneous data sources; (2) provides mathematical tools to analyze the assembled information efficiently; and (3) displays key results to communicate effectively to the public about its health status.

Risk Assessment/Risk Communication: Understanding the Community

Thomas Schlenker
Public-Health Madison-Dane County, Madison, WI

The conceptual model for human health risk assessment based on sources, pathways, routes, populations, internal disposition, endpoints, and risk metrics (*EPA Lead Human Exposure and Health Risk*, Volume 1, July 2007) requires, for accurate risk assessment and effective risk communication, a solid understanding of the communities impacted. Experiences with lead, a well-known toxin, lesser known manganese and previously, unknown *Cryptosporidium* illustrate how unique community characteristics inform risk assessment. Likewise, risk communication must take into account the general community as well as its various segments to be effective.

The long history, voluminous research, national strategies, and substantial funding associated with lead poisoning does not obviate the need to establish the sources and pathways of exposure in specific communities and even households. Prioritizing risk requires engaging the populations most at risk and addressing their concerns. Internal disposition and physiological endpoints must be understood and explained in human terms. Risk metrics, when they exist, are of great utility, but often need to be translated to express their practical value.

Manganese in drinking water only recently has been recognized as a potential toxin (EPA Drinking Water Health Advisory for Manganese, 2004). Infrastructure to support manganese risk assessment and risk communication is meager. Local, community-based research may be required to verify sources and pathways. Special attention must be paid to differentiating the at-risk from the worried well. Indistinct endpoints and absence of risk metrics place greater responsibility on federal agency/local public health interaction.

Until 400,000 people became ill in Milwaukee in 1993, *Cryptosporidium* was considered to be a pathogen only for turkeys (MacKenzie, et al. A massive outbreak in Milwaukee of *Cryptosporidium* infection transmitted through the public water supply. *New England Journal of Medicine* 1994;331(3):161-7). This sudden, unprecedented, and widely publicized intoxication of an urban population revealed gaps and synergies among agencies responsible for public health. The community political process affected both risk assessment and risk communication. The highly politicized HIV-infected community, being also the highest risk group, was especially challenged and challenging.

Perspectives, Issues, and Needs in Community-Based Risk Assessment

George Bollweg
Air and Radiation Division, Region 5, U.S. Environmental Protection Agency, Chicago, IL

The term "community-based risk assessment" can broadly apply to human health risk evaluation of environmental pollutants in specific communities, often with local resident involvement. As community participants become more involved in scoping, analysis, and characterization of risk, community (host) characteristics and nonpollutant stressors have received more interest for analytic evaluation. Different participant roles (e.g., community member, researcher, industry representative, U.S. EPA manager and/or risk assessor) result in different perspectives on priorities, relevant issues for analysis, what's feasible, and other issues. Recent experience with specific assessments illustrates several risk assessment and scientific needs.

Appendices

U.S. EPA Workshop on Research Needs for Community-Based Risk Assessment
October 18–19, 2007

U.S. Environmental Protection Agency
Main Campus, Building C, Auditorium A
Research Triangle Park, NC

AGENDA

Thursday, October 18, 2007

8:45–8:55 a.m.	**Welcoming Remarks** Hugh Tilson, U.S. Environmental Protection Agency (EPA), National Program Director for Health
8:55–9:25 a.m.	**Keynote Address: A Perspective on Community-Based Risk Assessments** Linda Sheldon, U.S. EPA
9:25–9:45 a.m.	**Summary of Session: "Exposure Assessment Methods in Community-Based Risk Assessment" From the International Society of Exposure Analysis (ISEA) 17th Annual Conference** Brad Schultz, Exposure Modeling Research Branch, EPA
9:45–10:00 a.m.	**Break**

Session I: Data Needs and Measurement Methods for Community-Based Risk Assessment

10:00–10:25 a.m.	**Development of Nanoscaled Sensor Systems for Detecting and Monitoring of Environmental Chemical Agents** Desmond Stubbs, Oak Ridge Center for Advanced Studies
10:25–10:50 a.m.	**Data Collection Platforms for Integrated Longitudinal Surveys of Human Exposure-Related Behavior** Paul Kizakevich, RTI International
10:50–11:15 a.m.	**Assessment Methods for Community-Based Risk Assessment** Elaine Faustman, University of Washington
11:15–11:45 a.m.	Panel Discussion
11:45–1:00 p.m.	**Lunch**

Thursday, October 18, 2007 (continued)

Session II: The Biological Impact of Non-Chemical Stressors and Interaction With Other Environmental Exposures

1:00–1:25 p.m. **Social Stress, Stress Hormones, and Neurotoxins**
James Herman, University of Cincinnati

1:25–1:50 p.m. **Intersections of Social Ecology, Neurobehavioral Development, and Environmental Contamination**
Bernard Weiss, University of Rochester School of Medicine and Dentistry

1:50–2:15 p.m. **Social Environment as a Modifier of Chemical Exposures**
Robert Wright, Harvard School of Public Health

2:15–2:45 p.m. Panel Discussion

2:45–3:00 p.m. **Break**

Session III: Statistical and Mathematical Modeling for Community-Based Risk Assessment

3:00–3:25 p.m. **Community-Based Risk Assessment—A Statistician's Perspective**
Louise Ryan, Harvard School of Public Health

3:25–3:50 p.m. **A Multi-Site Time Series Study of Hospital Admissions and Fine Particles: A Case-Study for National Public Health Surveillance**
Francesca Dominici, Johns Hopkins University Bloomberg School of Public Health

3:50–4:15 p.m. **Risk Assessment/Risk Communication: Understanding the Community**
Thomas Schlenker, Public Health Madison-Dane County

4:15–4:45 p.m. Panel Discussion

Friday, October 19, 2007

8:30–9:00 a.m.	**Perspectives, Issues, and Needs in Community-Based Risk Assessment** George Bollweg, EPA Region 5
9:00–9:15 a.m.	**Overview of Breakout Groups** Yolanda Sanchez, ASPH Fellow, EPA
9:15–10:45 a.m.	**Breakout Sessions**
10:45–11:15 a.m.	**Break**
11:15–12:15 p.m.	**Breakout Reports to Group**
12:15–12:45 p.m.	**Closing Remarks** Michael Callahan, EPA Region 6
12:45 p.m.	Adjourn

U.S. EPA Workshop on Research Needs for Community-Based Risk Assessment

October 18–19, 2007

U.S. Environmental Protection Agency
Main Campus, Building C, Auditorium A
Research Triangle Park, NC

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HUMAN HEALTH RESEARCH PROGRAM

BUILDING A SCIENTIFIC FOUNDATION FOR SOUND ENVIRONMENTAL DECISIONS

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Workshop on Research Needs for Community-Based Risk Assessment

October 18-19, 2007

HUGH A. TILSON
National Program Director

Human Health Research Program
Office of Research and Development

U.S. Environmental Protection Agency
Office of Research and Development

EPA HUMAN HEALTH RESEARCH PROGRAM

ORD PROGRAMS INVOLVING HUMAN HEALTH

- *Human Health Research Program*
- Human Health Risk Assessment
- Particulate Matter
- Air Toxics
- Drinking Water
- Endocrine Disruptors
- Safe Pesticides/Safe Products
- Homeland Security

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EPA HUMAN HEALTH RESEARCH PROGRAM

HUMAN HEALTH RESEARCH PROGRAM

The main objective of the Human Health Research Program is to reduce uncertainties associated with the risk assessment process by providing a greater understanding of exposures to environmental stressors and the basic biological changes that follow

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EPA HUMAN HEALTH RESEARCH PROGRAM

Four Long-Term Goals of the Human Health Research Program

- **Long-Term Goal 1**:
  - Risk assessors/managers use ORD's methods, models and data to reduce uncertainty in risk assessment using mechanistic (or mode of action) information
- **Long-Term Goal 2**:
  - Risk assessors/managers use ORD's methods, models and data to characterize aggregate and cumulative risk assessment
- **Long-Term Goal 3**:
  - Risk assessors/managers use ORD's methods, models and data to characterize and provide adequate protection for susceptible subpopulations
- **Long-Term Goal 4:**
  - Risk Assessors/managers use ORD's methods and models to evaluate risk management decisions

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EPA HUMAN HEALTH RESEARCH PROGRAM

Scientific Questions Driving Research on Cumulative Risk

- What biomarkers are available to improve cumulative risk assessments?
- What exposure models are available that can estimate aggregate exposures and cumulative risk?
- How can mode of action and exposure information be used to conduct cumulative risk assessments?
- How can cumulative risk be assessed at the community level?

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EPA HUMAN HEALTH RESEARCH PROGRAM

Research on Community Risk

- Develop tools and framework to assess interaction of environmental chemical and non-chemical stressors at the community level
- Research on assessing exposure and health risk of tribes due to cultural practices
- Evaluate tools for use in assessing community risk
  - Regional demonstration studies
  - Community action for a renewed environment
  - National Children's Study

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A Perspective on Community-Based Risk Assessments

Linda Sheldon
Associate Director for Human Health
National Exposure Research Laboratory

Fundamental Concepts

- Not all communities are the same
- Different communities can have differential risks due to exposure to environmental contaminants and other stressors
- The same community can have differential risks over time

Fundamental Concepts

- Many of EPA's regulations do not consider these differences
  - NAAQS
  - FQPA
- However there are many communities that may be at higher risks because they are not adequately protected through
  - Environmental regulations
  - The distribution of social benefits
- Not a new concept

Fundamental Concept

- **Cumulative Risk:** The combined risks from aggregate exposures to multiple agents or stressors.
- **Cumulative risk assessment:** An analysis, characterization, and possible quantification of the combined risks to health or the environment from multiple agents or stressors.

…Source: *Framework for Cumulative Risk Assessment*, 2003

Questions

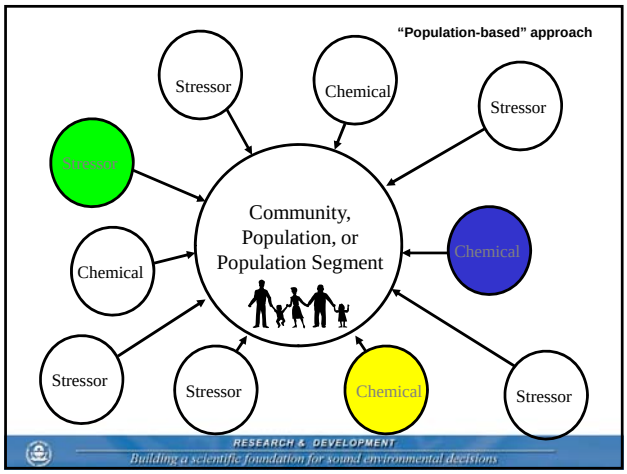
- How do we identify the most important risks in these communities?
- How do we assess the cumulative risk in these communities?
- How do we develop appropriate risk mitigation procedures?

My Perspectives on this Issue

- Developed during the past
  - 3 to 4 years
  - 3 to 4 months
  - 3 to 4 days

Past 3 to 4 years

- NERL research program in Aggregate Risk
- How to extend to cumulative risk
  - Not just going from one to mixtures of chemicals, ***but***
  - Needed to consider multiple stressors
  - Must consider the community to do this



RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

Past 3 to 4 Months

- Introduced to Ecological Research
- Ecologists are always considering
  - Communities – i.e., ecosystems
  - The entire range of stressors and cascading effects
- They have developed models and GIS tools that should be applicable here
- We should learn from the ecologist

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

Past 3 to 4 Days

- ISEA meeting –
  - Application of advanced statistical, GIS, and modeling tools to understand exposure and risk
    - Marie Lynn Miranda – lead and air toxics
    - Marc Serre – water contamination, CAFO
  - Must consider concerns of the community and work with the community
  - Need for tools to use at the community level
  - Need to Develop Partnerships for community work – CARE Program

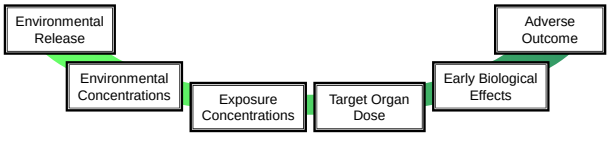
RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

So, what is needed

- Science
- Tools
- Communication
- Partnerships
- Trust

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

Building the Science



This is the "core" research that we are conducting to determine exposure and health risks

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

Building the Tools

- This should be the emphasis
  - Simple easy low cost monitoring methods
  - GIS tools
  - Models for exposure
  - Comparative data bases
  - Tools for interpretation
  - Primers for conducting assessments and using the tools

Communication

- As scientists, we need to keep it simple
  "Working toward Duh"
- Listen to the community
  - Hear their concerns
  - Know that they are different and how this impacts their risk
- Describe the science
  - The issues
  - What we know
  - What we can do to change it
  - What else we know that can help the community

All researchers must be involved with the community at some level

Paradigm shifts

- For Agency: From decision-maker to providing technical assistance to help communities make decisions
- For Exposure and risk analysis: From analysis done for community to partnering in a deliberative process

Summary

- This is important – we have an opportunity to make a difference
- This is hard work
  - Multidisciplinary
  - Communities must be involved
  - Impact is important
- We have the technology to do it and that will keep improving
- We just need learn how to put it together

That's what this workshop is about
THANK YOU!

Report from Yesterday's ISEA Symposium "Exposure Science for Community-based Cumulative Risk Assessment"

B. Schultz
V. G. Zartarian, session co-chair
U.S. EPA Office of Research and Development
National Exposure Research Laboratory

ORD/NCER, ORD/NCCT Planning Meeting
October 18, 2007

Brief Overview

- CARE overview by CARE co-chair
  - Coordinates EPA Program & Regional offices
  - Supplements EPA regulations
  - Coordinated with CDC; MoU, joint efforts
  - To support community-driven risk assessment & risk management
- CARE Level 1: risk ranking/prioritization & selection of risk reduction activities
- CARE L2: risk reduction (& quantifying effects)

Overview (cont'd)

- CARE technical issues overview by environmental health assessment co-chair
- Region 1 (New England) case studies
- Region 6 cases & status of EPA cumulative assessment guidance
- EPA lead on NCS gave NCS overview
  - Basic science info. on the environmental exposures related to health effects
  - Both individually & in combination with other chemical exposures & non-chemical stressors

Overview (cont'd)

- NERL PI on research program
  - Exposure tools research
  - Collaborate with health scientists, risk assessors, CARE program (L1 & L2)
  - Many exposures – **focus on exposures leading to highest risk** and most in demand by communities
  - NCS exposure assessment research
  - Chemical stressor primary expertise
- Summary of some NERL activities
  - Survey of CARE POs for needs
  - Measurement methods research
  - Modeling research

Community Needs & Research Needs for Community-based Cumulative Risk Assessment

- **Community monitoring/low cost techniques** (NERL & NCER)
- **Is the action having an impact on health?** (NCER)
- What does monitoring mean, once we do it?
- What do modeling results mean?
- How to get community involved: relationship between exposure and health? Local partnerships.
- Communities need someone who understands
  - Need to include local conditions, often only visible in person
  - Need to include local values
- **Non-chemical stressors and vulnerability** (NCER)
- Guidance for choosing appropriate methods for measurement collection

Research needs (cont'd)

- Better ways to **quantify** local non-chemical information: lifestyle; access to health care; exposure to violence
- **Inventories/protocols for assessing non-chemical stressors as well as chemical stressors**
- Tools to characterize dietary exposures at community level (diet, sources of food, food preparation, storage) for unique cultural groups
- Simple, user-friendly tools to characterize/translate/use sources/emissions to assess risk and risk reduction scenarios (e.g., simplified version of RAIMI)
  - Documentation on how to select models
  - Documentation on how to use models

Research needs (cont'd)

- Models that start at local/neighborhood level
- Better local source identification/emissions inventories in the community; tools to facilitate that (e.g., GPS; checklists)
- **Quantify benefits so that other communities can apply findings**
- **Note: 1000s of communities & community-driven assessments**
- **Research should be directly usable by community or their local health or environmental department**
  - EPA cannot serve every community individually
  - States may not be able to serve every community individually

Summary

- Community-driven assessment of importance
- Research needs to be usable by communities/local health depts.
- Cumulative risk important
  - Including non-chemical stressors, vulnerability
- Focus on main contributors to risk/health impact to address cumulative risk
- Also, focus on recurring community Qs
- Non-chemical stressors: less in-house expertise
- Protocols for non-chemical stressors needed
- Low-cost measurements important
- Dose-response for risk prioritization important
  - Comparison with other chemical risks
  - Comparison with non-chemical stressors
- Quantifying benefits important for future applications by communities

Objectives

1) To develop tools for estimating human exposures to multiple chemical stressors that are most likely to impact cumulative risks.

2) To apply, evaluate, and demonstrate these exposure tools through selected community case studies.

3) To communicate research findings and provide the tools to stakeholders.

Approach

- Identify partners, stakeholders, research needs
- Collaborate with partners who are focusing on other components of human health source-to-outcomes paradigm
  source->concentration->exposure->dose->risk->outcomes
- Develop exposure tools to address science questions
- Identify initial case studies for collaboration
- Evaluate, apply, demonstrate tools through case studies
- Communicate research and provide tools

Potential Partners/Stakeholders

- EPA Community Action for a Renewed Environment (CARE) program partners (e.g., EPA regional offices, state and city agencies, community groups)
- EPA Cross Program Project Teams (e.g., CARE, accountability, environmental justice, urban environments, tribal)
- Regional risk assessors
- National Children's Study, Vanguard Centers, future Centers
- Researchers in ORD labs/centers
- EPA program office risk assessors/managers
- Other EPA Groups (e.g., OEI, OEJ; RAF; OCHP)
- Academia
- Other federal agencies (e.g., CDC, NIEHS)

Science Questions

1) How to systematically identify and prioritize key chemical stressors within a given community?

2) How to develop individual estimates of exposure to multiple stressors for epi studies?

3) How to use exposure tools to assess community level distributions of exposures:

   a. to develop and evaluate the effectiveness of risk management/mitigation strategies?

   b. to provide better links between reduction actions, exposures, risks, and outcomes?

Science Question #1 - Overview

- Rationale
  - research planning
  - systematic approach for community assessments
  - guidance for collecting community information
- Stakeholders
  - ORD/NERL, EPA CARE program and Level I projects for tools review tables
  - EPA CARE, Region 4 and OEI for CARE questionnaire data
  - EPA Region 5/CARE for Detroit exposure modeling

Science Question #1- Planned Tools

- Summary of relevant programs, guidance, research needs
- Summary tables for models, data, and methods, to enhance CARE Community Screening Workbook
  - Models: fate/transport, exposure, dose, risk
  - Methods: community level, individual level, under development
  - Data: biomarkers, outdoor air, indoor air, UV, drinking water, house dust/residues, food
- Quantitative community level 4-model comparison with Detroit case study
- EPA CARE program survey results

Detroit CARE Level I Case Study

- Identify and prioritize cumulative air toxic sources in the community and seek ways to reduce exposure and risks
- Initial meetings between NERL leads and Region 5 CARE Project Officers
- Gathering available information
- Exposure model comparison with Detroit case study
- Planned GIS mapping of emissions, concentrations, and exposures

Science Question #2 - Overview

- Rationale
  - Need exposure tools to support the National Children's Study (NCS)
  - Need refined tools for individual-level exposures to multiple "agents" over time in epidemiological studies
- Stakeholders
  - NCS, specific Study Centers and communities, academia
- Status
  - Review of NCS Research Plan –identified role for models; needs for methods and approaches
  - Initial efforts to identify potential case studies

Science Question #2 – Potential Case Studies

- Air pollution
  - Community-level air measurements
  - Relate to ambient measurements and models
- Diet
  - Community dietary measurements
  - Questionnaire and checklist to identify unique dietary patterns and food consumption
- Multimedia exposure and dose assessment
  - Relate to biological measurements and models (e.g., for Arsenic)

Science Question #2 – Planned Tools

- Methodology, strategies & guidelines for epidemiological study-related measurement collection, e.g.,
  - Biomonitoring and interpretation
  - Environmental methods
  - Model inputs and evaluation
  - Exposure field study designs
- Dietary exposure model for individuals
- Cumulative inhalation model(s) for epi studies
- Cumulative multimedia model(s) for epi studies

Science Question #3 - Overview

- Rationale
  - Exposure tools needed to refine risk assessments
- Planned Tools
  - Linkage of refined tools for emissions, concentrations, and exposures for community risk assessments
  - New methods for continuous monitoring of multiple pollutants in communities
  - Cumulative community inhalation exposure model(s)
  - GIS tools for illustrating reduction scenarios
  - Approaches for area source risk assessments
- Stakeholders
  - CARE program, Regions, ORD labs/centers, Program Offices (e.g., OAQPS, OPPT), CDC

2006 Boston CARE (Level II) Case Study

- 2-year risk-reduction project (BPHC Safe Shops)
- Regulatory and community focus on auto shops; EPA/CDC pilot study
- 600 shops clustered in diverse, low-income neighborhoods
- Goal: measurably reduce negative environmental and public health impacts by auto shops on workers and residents by reducing emissions
- Current tools to measure results are surveys for changes in best practices and pollution prevention
- CARE lead has requested ORD assistance to help quantify impacts of program; enhance science

Boston CARE: Progress

- 7/07 Meeting to discuss EPA auto shop efforts
  - NESHAP auto body area source rule
  - OAQPS Collision Repair Campaign
  - OPPT DfE Auto Body Program
  - CARE Program (Boston Safe Shops, others)
  - Lawrence, MA RARE auto body project
- 8/07: cross-ORD meeting to discuss project support
- Meetings between ORD/NERL and stakeholders
- Research on available studies and tools to assess cumulative risk from auto shops
- Drafting ORD research plan to be finalized and shared with collaborators, stakeholders

EPA/ORD/NERL Communities Project Timeline

Develop tools to assess community risk	**2009**
Project Research Plan	2008
Review of available tools (models, methods, data, approaches) for community-focused cumulative risk assessments	2008
Apply tools to assess community risk	**2011**
Develop and apply exposure tools to help communities and to enhance science related to community cumulative risk assessments	2010
Provide tools to stakeholders and demonstrate tools' utility through selected case study applications	2011

Expected Results/Benefits

Research outputs to

- "Facilitate identification of environmental stressors that pose an unreasonable risk to human populations,
- Reduce exposure of humans to multiple environmental stressors through multiple pathways,
- Reduce exposure of populations at risk to environmental stressors, and
- Improve effectiveness of risk management decisions"
  (EPA/ORD Human Health Multi-Year Plan, p. 14)
  - Exposure assessment tools to address project goals, objectives, science questions
  - Effective transfer and communication of research and tools through published results and presentations

Disclaimer

Although this work was reviewed by EPA and approved for presentation and publication, it may not necessarily reflect official Agency policy.

Nanoscaled, microelectronic sensor systems for detecting and monitoring of environmental chemical agents

By Desmond Stubbs

Presented to:
Community-Based Risk Assessment Workshop

October 18, 2007

Where did ORCAS come from?

UT + Battelle + ORAU = UT-BATTELLE

ORAU = Georgia Tech, Virginia Tech, Duke, NC State, Vanderbilt, and others

The Mission…

- ORCAS is a think and do consortium of research universities, government, industry, and non-governmental organizations.
- It is focused on critical issues with strong science and technology content.
- Problems are framed broadly, taking into account their scientific, technical, economic, social, and policy dimensions to develop research and integrated strategies for addressing those challenges.
- We attempt to ensure that our ideas and research are translated into action.

April 2006 Workshop…

Nanotechnology Applications in Environmental Health: Big Plans for Little Particles

•Introduction of two research communities
  – Nanomaterials/nanosensors
  – Environmental health/ecological health

•Exploration of the "art of the doable" on the nano-side

•Discussion of the possible environmental health effects, exposure assessment and ecological health applications

•Better informed communities with likelihood of beneficial interactions in the future

The Case for Nanotechnology – ***Commentary by Michael Strano (Asst. Professor, University of Illinois- Urbana)***

•It has been pointed out that generally the detection limit of a sensor scale approximates the cube of its characteristic length. So smaller sensor elements mean lower detection limits generally.

•The case varies both with the type of material used in its design and the physical and chemical properties of that material.

•Fluorescence-based techniques are some of the most powerful molecular detection methods available. Single molecule fluorescence analysis is a now routine. For optical fluorescence-based sensors, there are classes of nanoparticles that exhibit extremely enhanced photostability in fluorescent emission. This means that for the first time, new types of sensors can be devised with extremely long operational lifetimes. This is not possible with conventional fluorophores (e.g., single-walled carbon nanotubes are infinitely photostable at moderate light fluxes).

•Some nanosystems emit light at longer wavelengths where few conventional materials operate whereas few conventional materials do so. The human body is particularly transparent to near-infrared light in a narrow region of the electromagnetic spectrum. These systems will form the basis of novel detection technologies that can operate in strongly scattering media where fluorescent spectroscopy is limited.

•Nanoparticles can also possess features that are commensurate with biomolecules and other important macromolecular analytes. Electrodes that are narrow enough to fit or conform to biological structures should be capable of transducing subtle changes in these structures,

The Case for Nanotechnology – **Sensor shelf-life, Real-time detection, Useful life**

•Shelf Life – varies as a function of the sensing layer. For example, bioreceptors (antibodies, enzymes, lipid layers) are limiting factors because of their inherent short life span under non physiological conditions. On the other hand, aptamer- and polymer-based sensing layers have been used in an effort to extend the lifetime of the device.

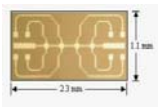
•Real-time Detection - is a common feature of nanosensing technology. The nanosensors described in the meeting all operated on a time scale ranging from seconds to minutes.

•Useful life - The binding mechanisms for the sensor platform can be described as reversible—requiring little or no surface treatment to return the sensor to its steady state—or irreversible where analyte binds with high affinity such that surface treatment is required to remove the bound substrate.

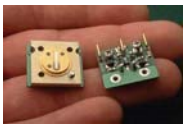
Examples of Technologies Employed in Exposure Assessment

Technology Description	Technology Platforms	Value to EPA	Advantages	Limitations
Location and activity sensors	Global Positioning Systems (GPS), Geographic Information Systems (GIS) and Accelerometers.	Provides information on potential sources of environmental exposure (exposure potential).	Provides location and activity information of study participants. Commercially available.	Unable to receive data inside steel and concrete structures.
Electronic Diary	Personal Data Assistants (PDA) devices.	Provides link between personal exposure, daily activities and dietary consumption.	Real-time information, captured in personal diaries, and questionnaires. Commercially available.	Requires a certain level of technology literacy to operate.
Wearable Sensors	Microelectronic Arrays: Cantilever arrays, acoustic sensors, Radio-frequency Identification (RFID) tags, Microelectromagnetic systems (MEMs) sensors.	Provides a less intrusive method of monitoring personal exposure to a variety of environmental pollutants in real-time.	Real-time PM measurements. Size: micro-nano. Sensitivity: ppb/ppt range. Low cost (~$3/chip). Child-friendly design.	Micro- to nano- scale device poses design issues. Still under R&D and not commercially available. Selectivity issues.
Portable Sensors	Fluorometric biosensors, Optical sensors, Potentiometric sensors, Amperometric sensors.	Links personal exposure to environmental pollutants/stressors to health effects.	Near real-time measurements. Links pollutant to health effects. Sensitivity: ppb/ppt range.	Selectivity issues. Not commercially available.

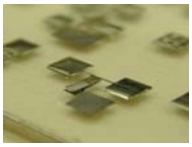
Emerging Technologies in Exposure Assessment



Passive RFID Tag



Electronic nose: "Dog-on-a-chip"

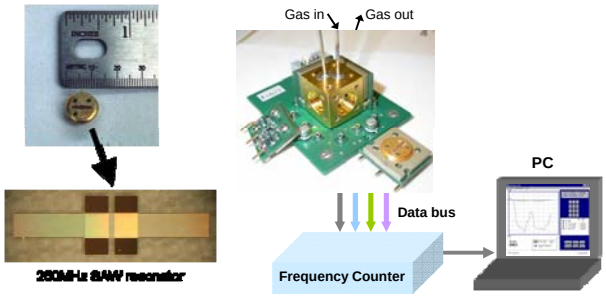


Microelectromagnetic Sensor

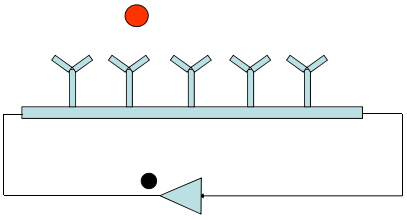
Interferometric Optical Sensor

Vapor phase sensor system

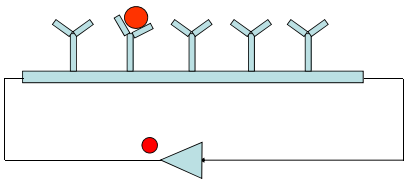
Flow cell and oscillator circuit



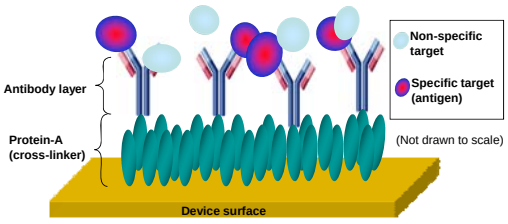
Principle of Operation



Principle of Operation



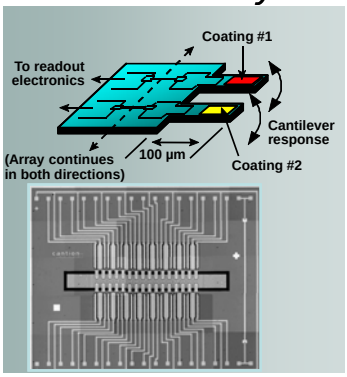
Antibody Immobilization on Au Electrodes



Courtesy Sang Hun Lee

Multi-Analyte Detection - Arrays

- Arrays of sensors on a *single chip* with *selective coatings for* application-specific programmable sensors
- Arrays give more information than separate sensors
- Coupled to *custom* readout electronics
- Telemetry
- Mass production
- Inexpensive

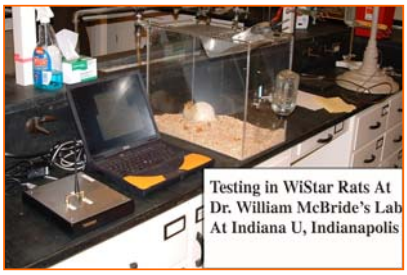


Implanted Behind Neck in WiStar Rats to Measure Ethanol Levels

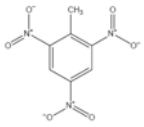
Rats Injected with One g/Kg of Eth

Body Temperature & Eth Monitored For Several Hours

Data from Interstitial Fluid Tracked Blood Lvl



Why TNT?



2,4,6-Trinitrotoluene (TNT)
Low vapor pressure ~ 1.99 x 10^{-4} Torr

Ability to detect trace levels of TNT is key to:

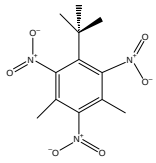
•Reducing fatalities from land mines (TNT constitutes 80% of all land mines -there are over 100 million scattered across the planet)

•Tracking explosives materials (Anti-terrorism)

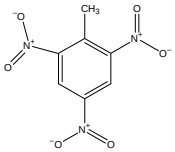
•Environmental concerns (water and soil contamination)

TNT Analogs

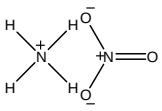
Musk Oil (Musk Xylene) | TNT | Ammonium nitrate



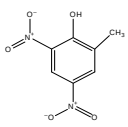
1-*tert.* -Butyl-3,5-dimethyl -2,4,6-trinitrobenzene



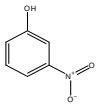
2-Methyl-1,3,5-trinitro-benzene



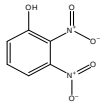
TNT Analogs



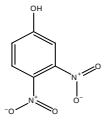
2-Methyl-4,6-dinitro-phenol



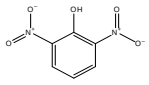
3-Nitro-phenol



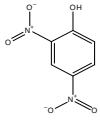
2,3-Dinitro-phenol



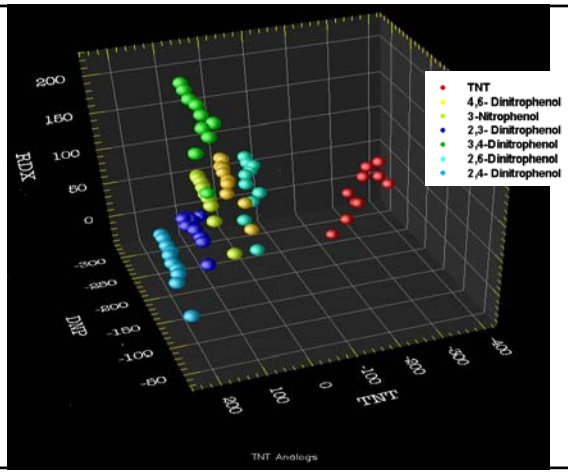
3,4-Dinitro-phenol



2,6-Dinitro-phenol



2,4-Dinitro-phenol



Questions?

turning knowledge into practice

Data Collection Platforms for Integrated Longitudinal Surveys of Human Exposure-Related Behavior

EPA STAR Grant RD-831541-01

Principal Investigators:

Roy Whitmore, Ph.D., Statistician

Paul Kizakevich, M.S., Biomedical Engineer

Paul Kizakevich, presenting

RTI International is a trade name of Research Triangle Institute

3040 Cornwallis Road ▪ P.O. Box 12194 ▪ Research Triangle Park, North Carolina, USA 27709
Phone 919-541-5809 Fax 919-541-5966 e-mail kiz@rti.org

Need for Integrated Data Collection

- **Routes of exposure**
  - Inhalation
  - Ingestion
  - Dermal contact
- **Modifiers of exposure**
  - Breathing rate, exertion, specific activities
  - Food and beverage consumption
  - Use of consumer products
  - Carpet, gloves, open doors/windows, microenvironment)
  - Season, geographical location, temperature, humidity

Overall Objectives

Develop a personal data collection system that:

- integrates data input streams for collection of human exposure-related behaviors
- supports EPA human exposure assessment models
- is easily adapted for other human exposure assessment studies
- has sufficiently low burden that most members of the general household population of the U.S. will be willing to participate in the study for at least 1 week per season for 1 year

Approach

- **Develop diary methodologies for data collection**
- **Develop sensors & automation to reduce burden**
- **Evaluate methods in the general population**
- **Assess, improve, and enhance developments**
- **Re-evaluate methods and technologies**
- **Facilitate system use for other research studies**

Methods
Activity/Location/Exertion/Environment Data Collection

- **Paper diary** – traditional forms and booklets
- **Menu diary** – menus and forms on Pocket PC (PPC)
- **Voice diary** – questions/answers on PPC
- **Photo diary** – periodic photos on PPC
- **Automation**
  - GPS for outdoor location and movement
  - Wireless beacons for indoor residential locations
  - Wireless Polar chest belt for heart rate monitoring
  - Accelerometers for movement and compliance monitoring

Methods
Dietary Data Collection

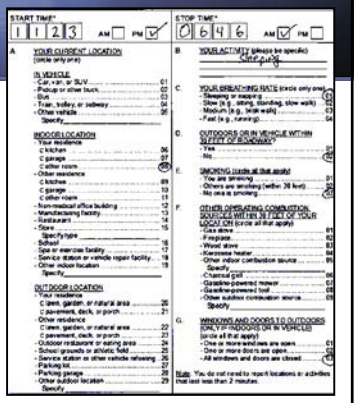
- **Paper diary** – forms and booklets (24-hour recall)
- **Menu diary** – menus and forms on PPC (real-time)
- **Voice diary** – questions/answers on PPC (real-time)
- **Automation** – none

Methods

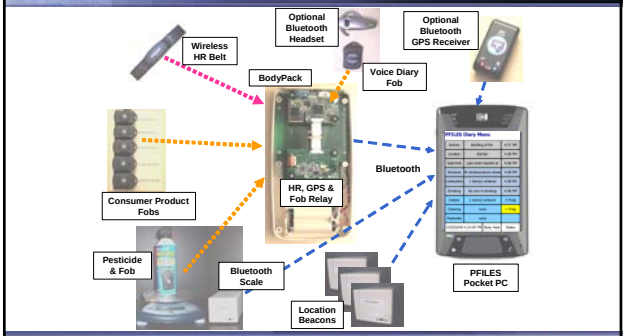
Consumer Product Data Collection

- **Paper diary** – forms and booklets (24-hour recall)
- **Menu diary** – menus and forms on PPC (real-time)
- **Automation** – wireless buttons record each product use event
  - **Personal care products**
    - Soaps and shampoos
    - Fob-initiated time stamp
  - **Household cleaning products**
    - Kitchen and bathroom cleaners and sanitizers
    - Fob-initiated time stamp; then Pocket PC forms/questionnaire
  - **Pesticide products**
    - Fob-initiated time stamp; Pocket PC-based forms/questionnaire
    - Aerosols weighed before and after use; weights sent wirelessly to PPC

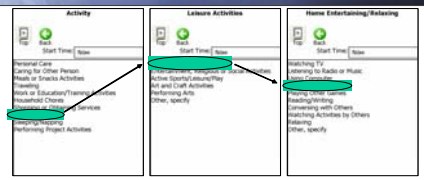
Paper Form Diary



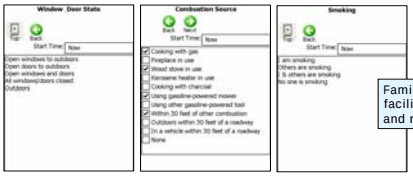
Personal Data Collection Platform



Pocket PC Menu Diaries



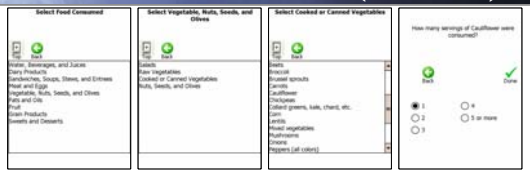
Multilevel menus are used to capture activity and location data.



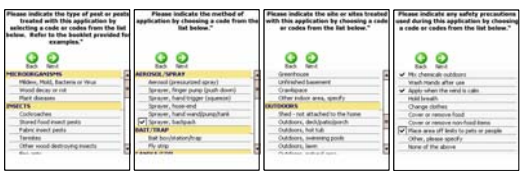
Familiar navigation style to facilitate user interaction and reduce error.

Single and multi-selection menus are used for environmental data.

Pocket PC Menu Diaries (continued)



Multilevel menus are used to capture dietary data, with radio-buttons for serving size.



A sequence of questionnaire forms are presented in response to a pesticide fob event.

Photo Diary

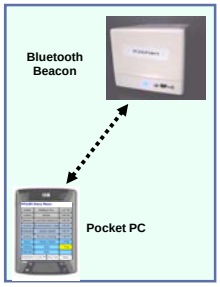
120º lens | Pocket PC | Image Censoring & Analysis

Voice Diary

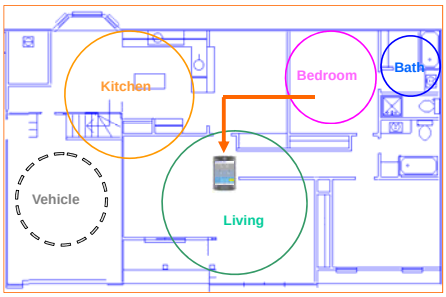
Headset/Fob **Pocket PC** **Activity / Location / Diet Coding**

Locator Beacons …

- **Beacons are placed throughout the residence in study-designated rooms**
- **Each beacon is configured for:**
  - Maximum detection range for designated room
  - Study detection interval (e.g., 60 seconds)
  - Beacon ID code for room identification
  - Designated Pocket PC Bluetooth address
- **Location tracking:**
  - At each interval, the beacon microcomputer powers up the internal Bluetooth module
  - The beacon attempts to establish a Bluetooth connection with the designated Pocket PC
  - If a connection is established, the beacon sends a time/date stamped Beacon ID code to the Pocket PC
  - The internal Bluetooth module is powered down until the next interval



Example Residential Beacon Use



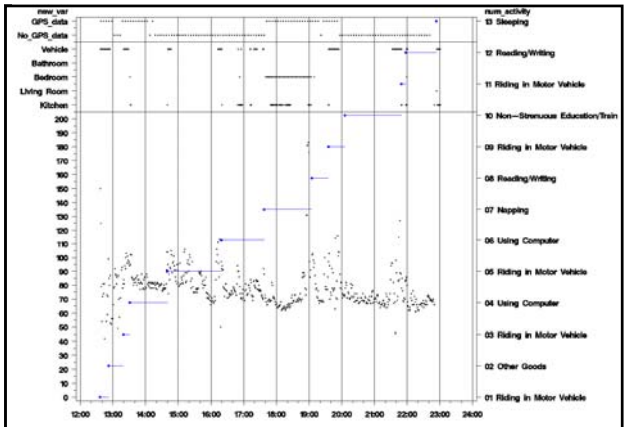
Pilot Evaluation of Technologies

- **Purpose:**
  - Evaluate technical performance of technologies & systems
  - Evaluate participant & analyst burden for various diary modes
- **Participants** (N=48)
  - Gender: Female (N=35); Male (N=13)
  - Age: 18-34 (N=14); 35-65 (N=25); >64 (N=9)
  - Ed: HS/GED (N=14); some college (N=16); college grad. (N=18)
- **Field study design**
  - Four data collection modes: Paper, PPC menu, PPC voice, PPC photo
  - All had heart rate and residential location beacon monitoring
  - All use wireless fobs to record product use events
  - Each participants used the data collection system for 7 days

Example activity and dietary data

Time	Activity
12:00:44	Grooming/Dressing
15:24:06	Wash/Dry/Sort/Iron Clothes
15:25:40	Riding in Motor Vehicle
15:26:40	Clothes
16:42:33	Eating/Drinking
16:44:44	Picking up/Putting Away Items
18:23:56	Household Paperwork
18:24:57	Relaxing or Resting
19:38:21	Picking up/Putting Away Items
19:39:52	Preparing Food
19:40:33	Watching TV
23:14:07	Other Washing
23:14:38	Sleeping

Time	Food / Beverage
17:01:43	Tea
18:05:59	Cheese (plain or as part of dish)
18:05:59	Crackers, any kind
18:03:02	Beef or veal
18:03:02	Potatoes, any other
18:03:02	Other salad
13:06:20	Nuts (peanuts, etc.)
13:06:20	Coffee
21:59:52	Tea
13:15:03	Banana
13:15:03	Chicken, turkey or other poultry
17:51:26	Beans, green
17:51:26	Potatoes, any other



Participant reporting compliance

Diary Mode	Activities per hour	Locations per hour
Paper	1.42	0.95
PPC	1.12	0.75
Voice	1.29	1.34
Photo	2.69	2.59

Top 15 activities reported by mode

Activity	PPC (%)	Paper (%)	Voice (%)	Photo (%)
Riding in Motor Vehicle	23.0	22.4	21.9	16.2
Eating/Drinking	11.7	8.4	5.9	3.2
Non-strenuous Work	8.1	8.2	7.8	4.4
Sleeping	6.2	4.2	2.9	0.0
Watching TV	5.6	4.5	4.9	9.2
Walking	3.8	6.5	8.0	17.6
Grooming/Dressing	3.6	5.0	2.4	4.1
Visiting with Others	2.7	1.0	1.0	5.8
Picking up/Putting Away Items	2.5	1.3	0.9	2.4
Preparing Food	2.5	3.9	4.9	5.8
Tub Bath	2.5	0.1	0.0	0.0
Relaxing or Resting	2.2	2.0	3.4	2.8
Reading/Writing	2.1	2.1	1.2	1.8
Using Computer	2.0	1.6	1.2	3.2
Moderately Strenuous Work	1.6	0.1	1.4	0.00

Data Entry Burden (median)

Time to complete entry in seconds

	Measured Menu	Perceived Menu	Perceived Voice	Perceived Paper
Act/Loc/Environ	28	45	60	60
▪ Activity	11			
▪ Location	9			
▪ Combustion	1			
▪ Smoking	3			
▪ Windows/doors	4			
Cleaning products	36	60	n/a	60
Pesticides	131	60	n/a	120

*Burden for each entry of an **activity/location** and for each product use questionnaire*

Data Coding Burden (median)

	Analyst hours	Study hours	Analyst hours per 24-hr day
Menu[1]	00.0	630.1	0.00
Photo[2]	58.5	282.4	4.97
Voice[2]	87.4	427.0	4.91
Paper[3]	69.7	979.7	1.71

1. Pocket PC menu diary is self-coded by the participant
2. Time for coding by a single analyst.
3. Included time for 100% re-key verification.

Top 10 food items reported by mode

Order	Paper food item	Paper (%)	PPC food item	PPC (%)	Voice food item	Voice (%)
1	Tap water	6.5	Tea	8.2	Bottled water	10.5
2	Bottled water	6.3	Tap water	8.0	Tap water	7.9
3	Soft drink	5.1	Bottled water	6.2	Soft drink	4.7
4	Coffee	3.1	Soft drink (soda, cola, etc.)	5.6	Chicken, turkey or other poultry	4.2
5	Other grain product	2.9	Chicken, turkey or other poultry	3.8	Other grain product	3.9
6	Chicken, turkey or other poultry	2.6	Chocolate / candy	3.1	Rice and rice mixtures	3.7
7	Cheese	2.4	Beef or veal	2.5	Coffee	2.9
8	Tea	2.3	Juice mixtures	2.5	Cheese	2.6
9	Potatoes, any other	2.2	Lettuce salad with assorted vegs.	2.2	Other non-alcoholic drink	2.4
10	Butter	2.0	Other sweets or dessert	2.2	Pork or ham	2.4

Comments / Conclusions

- The burden for menu-based activity and location data entry is low; however several expressed difficulty with the menus.
- Activity and location reporting was lower than in previous studies.
- Participants liked using the voice diary, although technical issues affected recording quality.
- While most liked the photo diary, some participants expressed privacy issues in their workplace.
- Some participants reported avoiding activities and limiting diet to reduce entries for paper, voice, and menu diaries
- Further improvement in menu structures, prompting, and automation may help to improve compliance and avoid behavior modifications

Assessment Methods for Community Based Risk Assessment

Elaine M. Faustman, Ph.D.
INSTITUTE OF RISK ANALYSIS AND RISK COMMUNICATIONS
UNIVERSITY OF WASHINGTON

Three types of studies were examined in order to understand what pesticide exposures were occurring in children

1. Community Based Participatory Research project (CBPR)
2. Longitudinal multiple sampling project aimed at understanding between and within family variability
3. Longitudinal Cohort Study

Estimated Organophosphate and Carbamate Usage on Apples and Potatoes in Washington State, 2001

Study Counties for the Center for Child Environmental Health Risks Research

Examples of Chemicals Applied to Washington State Crops, 2001

Chemical class	crop	Chemical	Pounds applied
Organophosphates	Apples	Azinphos-methyl	241,000
		Chlorpyrifos	234,000
		Phosmet	138,000
	Potatoes	Ethoprop	119,000
		Metamidophos	143,000
N-Me Carbamates	Apples	carbaryl	202,000
	Potatoes	Aldicarb	153,000
Dithiocarbamate	Apples	Mancozeb	82,000
	Potatoes	Mancozeb	343,000

Source: "Agricultural Chemical Usage (PCU-BB)" National Agricultural Statistics Service, Agricultural Statistics Board, U.S. Department of Agriculture (http://jan.mannlib.cornell.edu/reports/nassr/other/pcubb Accessed 05/03)

The Take-home Pathway for Agricultural Pesticides: Contributions of Occupational Factors to Home Contamination

G.C. Coronado, I. Islas, S.A. Snipes, J. Grossman, and B. Thompson

Communities in the CBPR Project

- Community was defined as either a town or a labor camp
- Pairing of an intervention community with a control community was performed separately for towns and labor camps
- All Communities are in the Yakima Valley of Eastern Washington

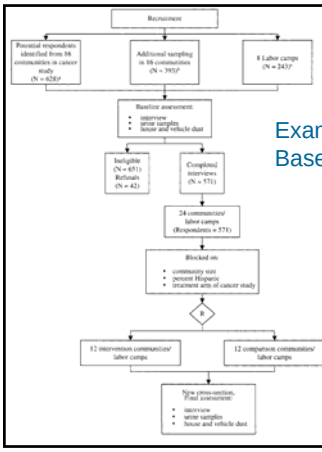
Towns

Intervention	Control
Sawyer	Harrah
Donald	Tieton
Buena	Outlook
Moxee	Zillah
Cowiche	Wapato
Mabton	Whitstran
Granger	Prosser
Toppenish	Grandview

Labor Camps

Intervention	Control
Bond Varner Camp	Golding Farms Camp
Green Giant Camp	Crewport
Willow Park	Rainbow court
Yakima Golding Farms	Horse Heaven Mobile Park

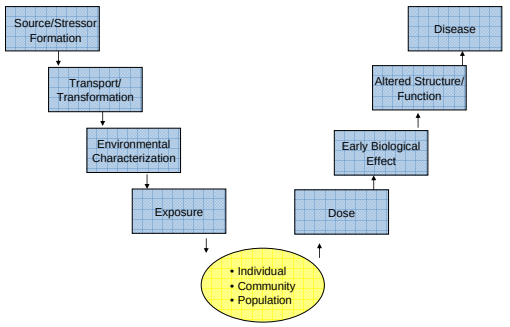
Thompson et al 2003



Example from Community Based Participation Project

Thompson et al 2003

Environmental Public Health Continuum



Adapted from Hal Zenick

Over 250 community-wide events occurred.

This Community Health Fair is an example.

Photo: Gloria Coronado

Total number of participants at community-wide events is greater than 6,000!

Over 1,800 total events took place in the communities.

Approx. 1,000 Home Health Parties such as this occurred.

Photo: Gloria Coronado

Total number of participants in all levels of community activities was over 18,000!

Community Intervention

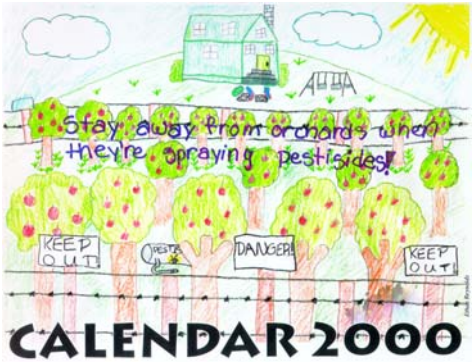
Handing out toys such as frisbees and basketballs draws kids to the Community Intervention project's table where they learn simple things to help reduce their exposure to pesticides.

Photo: Gloria Coronado

Community Intervention

After a series of presentations made in second and third grade classrooms, students were invited to enter a coloring contest. Winning entries were included in a calendar. In this drawing the woman tells the man to wash his own clothes, because she's going to a dance…and she reminds him to leave his boots outside.

Photo: Gloria Coronado



Handwashing Song

Wash, wash, wash your hands
Every time you eat.
Soapy, sudsy, soapy, sudsy
Washing hands is neat!

Handwashing Puzzle

Images courtesty of JE Grossman

Sample Evaluation Question

Pablo is hungry.
He's going to eat an apple.
What should he do before he eats the apple?

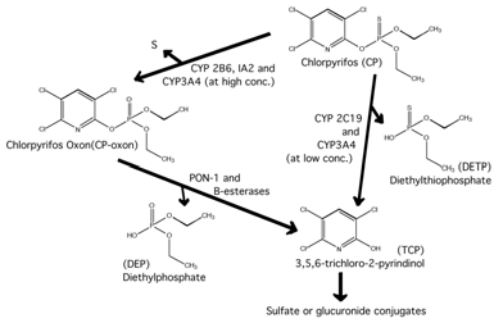
Which picture should come next?



Images courtesty of JE Grossman

Agricultural Pesticides: Contributions of Occupational Factors to Home Contamination

Metabolic Scheme for CP



Faustman et al. (2006)

Metabolites of Organophosphate Pesticides

- Biomarkers of exposure
- Nonspecific Diakyl Phosphate (DAP) metabolites
  - Six DAP Metabolites
  - Each metabolite can be produced by multiple OPs
  - Divided into two groups
    - Dimethyl metabolites
      - DMP, DMTP, DMDTP
    - Diethyl metabolites
      - DEP, DETP, DEDTP
- Specific metabolites
  - Chlorpyrifos metabolites
    - TCP, DEP, DETP
  - Chlorpyrifos-methyl metabolites
    - TCP, DMP, DMTP

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Metabolites of Organophosphate Pesticides

Selected OPs and DAP metabolites

Diethyl OPs			
chlorpyrifos		DEP	DETP
diazinon		DEP	DETP
disulfoton	DEDTP	DEP	DETP
ethion	DEDTP	DEP	DETP
parathion		DEP	DETP
Dimethyl OPs			
azinophos methyl	DMDTP	DMP	DMTP
chlorpyrifos methyl		DMP	DMTP
dichlorvos (DDVP)		DMP	
malathion	DMDTP	DMP	DMTP
methyl parathion		DMP	DMTP
naled		DMP	
phosmet	DMDTP	DMP	DMTP
trichlorfon		DMP	

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Metabolites of Organophosphate Pesticides

Selected OPs and DAP metabolites

Diethyl OPs			
chlorpyrifos		DEP	DETP
diazinon		DEP	DETP
parathion		DEP	DETP
disulfoton	DEDTP	DEP	DETP
ethion	DEDTP	DEP	DETP
Dimethyl OPs			
dichlorvos (DDVP)		DMP	
trichlorfon		DMP	
naled		DMP	
chlorpyrifos methyl		DMP	DMTP
methyl parathion		DMP	DMTP
azinophos methyl	DMDTP	DMP	DMTP
malathion	DMDTP	DMP	DMTP
phosmet	DMDTP	DMP	DMTP

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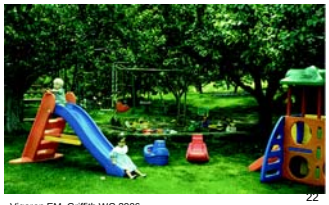
Monitoring Results

Evidence of pesticides in environment

- 36% of homes and 42% of cars had quantifiable levels of 2 or more OPs in dust.
- 60% of households (home and vehicles together) had evidence of 2 or more OPs in collected dust.



Vigoren EM, Griffith WC 2006

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Monitoring Results

Most children are exposed

- 86% of children had quantifiable levels of at least one dialkyl metabolite.
- 95% of adults had quantifiable levels of at least one dialkyl metabolite.

Evidence of **multiple** exposures

- 36% of children had quantifiable levels of both dimethyl and diethyl metabolites.
- 45% of adults had quantifiable levels of both dimethyl and diethyl metabolites.

Vigoren EM, Griffith WC 2006

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Evidence of Take-home Pathway

- **Workers** who thinned were more likely than those who did not thin to have detectable levels of azinophos-methyl in their house dust and vehicles.
- **Children** of thinners were more likely to have detectable levels.
- **Contrary to expectations,** workers who reported mixing, loading or applying pesticides had lower incidence of detectable pesticide residues in their homes, vehicle dust, and in their children's urine.

Vigoren EM, Griffith WC 2006

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What do these values mean for my Children?

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Samples Collected in Studies of Farmworker Families

- Types of samples collected from individuals and their children in 3 seasons
  - Urine analyzed for metabolites of OPs—collected 3 times in 1 week
  - Blood analyzed for parent OPs, metabolites of OPs, AChE in RBCs and plasma, genotypes and phenotypes of metabolizing enzymes—collected once
  - Buccal Cells analyzed for gene expression—collected 2 times in 1 week
- Dust is collected from homes and autos in thinning and non-spray seasons season and analyzed for parent OPs

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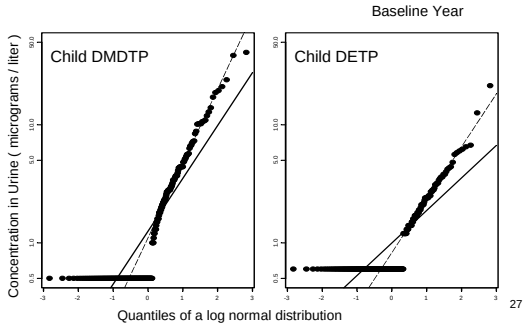
Many Values Are Below Limits of Detection



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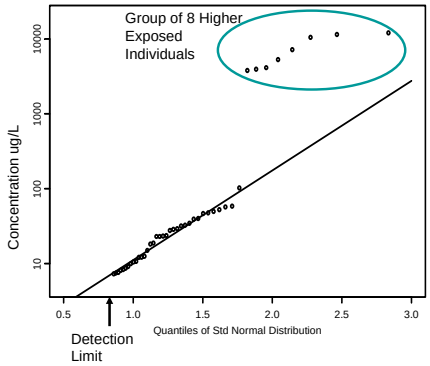
NHANES Compared to Farmworker Family Data for DMTP in Urine

28

DMP in Adult Urine: QQ Plots to Estimate Population Distribution



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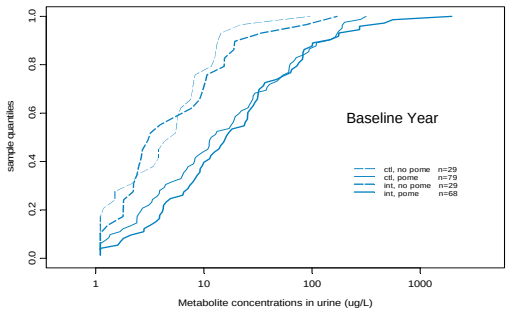
Distribution of Adult DMTP from year 1: Impact of Crop



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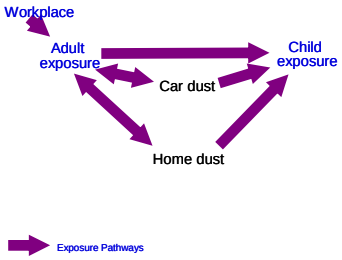
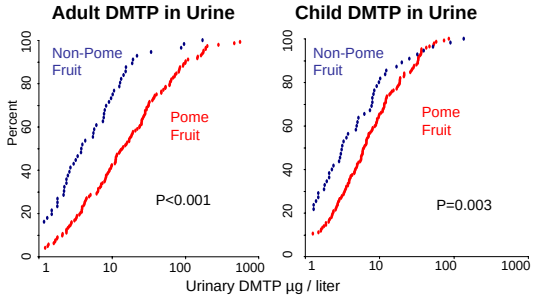
Assessing Children's Pesticide Exposure via the Take-home Pathway



Vigoren et al 2007

Urinary metabolites higher in adults who worked in pome fruit and their children



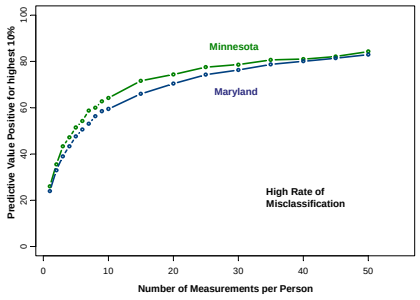
Coronado et al., Env. Hlth. Persp., 2004, 2006

Two longitudinal studies of OP metabolites used to estimate within and between variability

- Multiple measurements in the same person across time permit estimation of both within and between person variability
  - Within and between person variability treated as a random effect and other variables such as age, gender ,residence, season treated as fixed effects
- TCP had a low percentage below limits of detection
- Measurements below limit of detection (LOD) were treated as being left censored in statistical analyses

Predictive Value Positive for Identifying Persons in the Upper 10% of the Population

The predictive value positive is the percent of the population assigned to a group that are correctly classified.



Based upon large within person variances it will require a large number of samples of urinary metabolites to correctly identify persons in a population who are more highly exposed to CP and CPM.

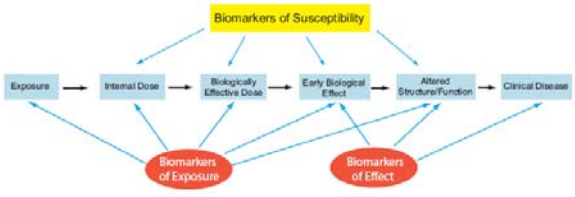
Sources of Uncertainty

Stochasticity
- Characterization of Within and Between Person Variability

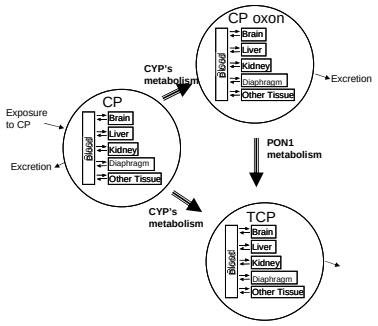
Parameter Uncertainty
- Year-to-Year Variability
- Observations below Limits of Detection (LOD)

Model Uncertainty
- Crop vs. Agricultural Job Task
- Identification of Highly Exposed Individuals

Biomarkers for Monitoring Exposure and Effect in Populations



Physiologic Based Toxicokinetic Models of CP Metabolism



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Methodology Underlying Integrated Framework Tool

- Bayesian Based Mixed Effects Model
  - Correlational structure of a multivariate distribution used to estimate correlations between pesticide concentrations, metabolites, gene expression levels, and other variables
  - Markov chain Monte Carlo methods used for parameter estimation

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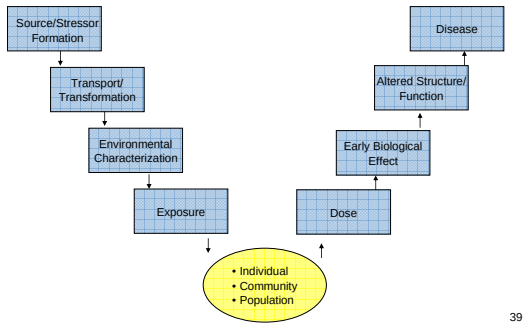
Environmental Public Health Continuum



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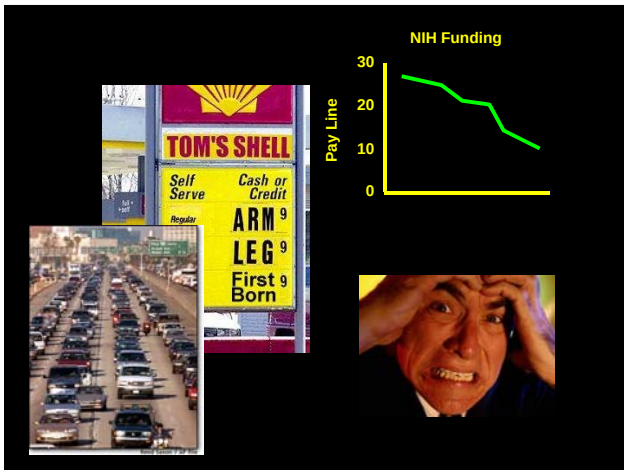
Adapted from Hal Zenick

Social Stress, Stress Hormones and Neurotoxins

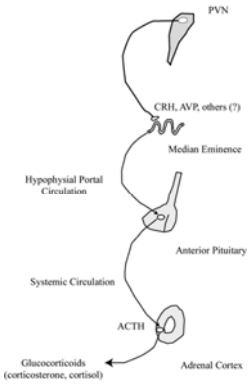
James P. Herman, PhD
Stress Neurobiology Laboratory
Department of Psychiatry
University of Cincinnati



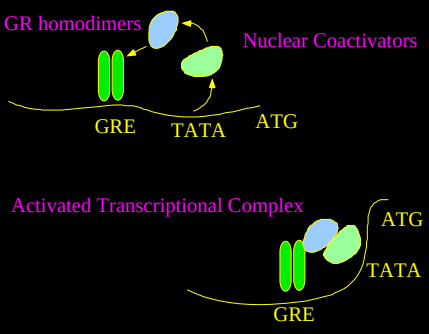
Stress Responses

✓ **Anticipatory in nature:**
- *Caused by possible threat to homeostasis
- *Generated by stimulus comparison
  - innate programs
  - learning

Reactive in nature:
- *Caused by direct threat to homeostasis
- *Generated by reflexive pathways



Herman and Seroogy, Neurol. Clin. 24:641 (2006)



The HPA Stress Axis and Organismic Homeostasis: Redistribution of Resources

Short-term benefit:
- *Energy mobilization
- *Energy diversion
- *Limits immune responses
- *CNS Arousal

Long-term consequences:
- *Metabolic Disease, obesity
- *Musculoskeletal atrophy, HPG problems
- *Immune dysfunction
- *Depression, PTSD(?)

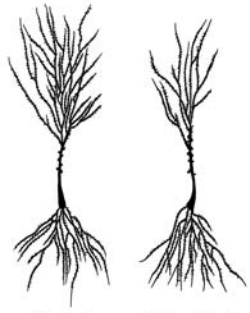
Neurobiological Consequences of Stress

- **Stress-related affective disease states (depression, PTSD) affects 10% of the population in any given year**
- **Stress exacerbates other affective disease states, such as schizophrenia and bipolar disease**
- **Stress exacerbates other organic disease processes**
- **Stress hormone secretion can contribute to cell loss/cognitive decline in aging and dementia**

Stress, Stress Hormones and (Neuro)toxicity

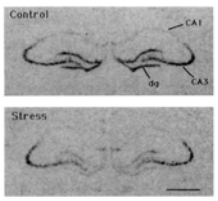
- **Stress and Neuronal Function**
- **Stress as a Predisposing Factor in Neurodegeneration**
- **Stress as a Co-morbid Condition? Implications for Toxicology**

Social Stress Shrinks Dendrites in the Hippocampus



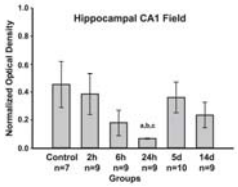
Stress Reduces Neurotrophic Factor Expression in Cortex and Hippocampus

Rats



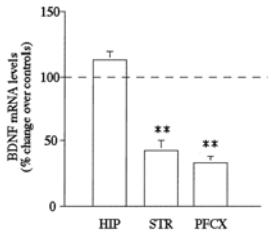
Smith et al, J. Neurosci. 15:1768 (1995)

Mice



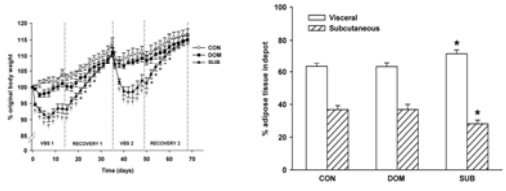
Pizarro et al, Brain Res. 1025:10 (2004)

Prenatal Stress Reduces Neurotrophic Factor Expression in Cortex and Striatum



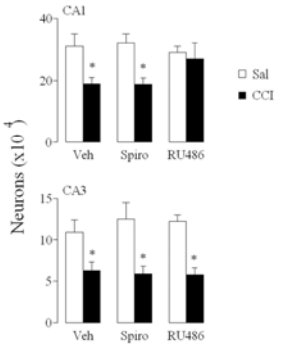
Fumagelli et al, Eur. J. Neurosci 20: 1384 (2004)

Social Stress Increases Abdominal Fat Accumulation (Obesity)



Tamashiro et al., Amer. J. Physiol. 293: R1864 (2007)

Glucocorticoids Mediate Hippocampal Damage Following Head Trauma

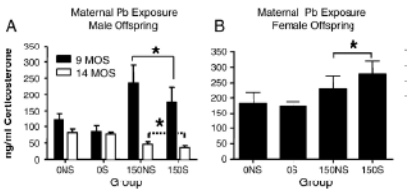


Herman and Seroogy, Neurol. Clin. 24: 461 (2006)

Stress as a Predisposing Factor in Neurodegeneration: Other models

- **Kainate neurotoxicity in hippocampus (epilepsy model)**
- **Infarct size and ischemic cell death (stroke model)**
- **Senescence-related cognitive deficits and neuron loss (aging and Alzheimer's Disease)**

Toxins Alter Stress Axis Function



White et al, Tox. App. Pharm., E-pub

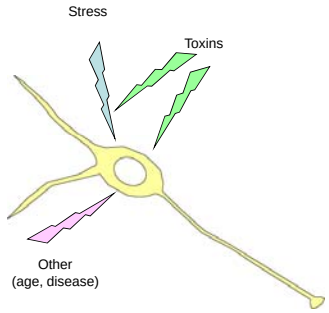
Stress as a Co-morbid Condition? Implications for Toxicology

- **Stress enhances relapse of addictive behaviors (smoking, alcohol, other drugs of abuse)**
- **Social stress promotes abdominal obesity**
- **Prenatal stress interacts with lead exposure to alter brain neurochemistry, behavior and HPA axis drive**
- **Stress: represents one of the 'hits' in the multi-hit hypothesis of toxicity**

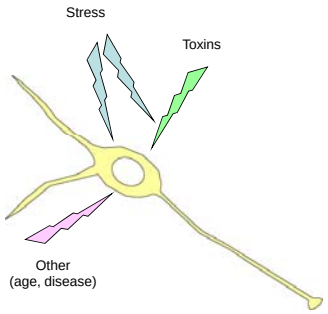
Stress as a Co-morbid Condition? Implications for Risk Assessment

- **Substance abuse and obesity are prevalent in lower SES populations**
- **Lower SES groups have disproportionate exposure to some environmental toxicants (e.g., lead)**
- **Environmental toxicants can modulate glucocorticoid secretion**
- **Glucocorticoids enhance neurotoxic processes**

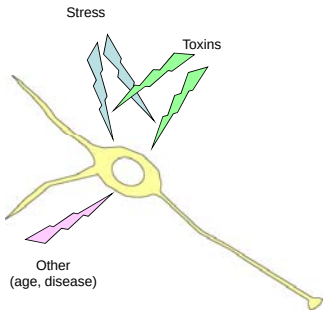
Stress and Cellular Endangerment



Stress and Cellular Endangerment



Stress and Cellular Endangerment



"Social Modifiers in Environmental Neuroepidemiology: The Role of Context in Chemical Exposure"

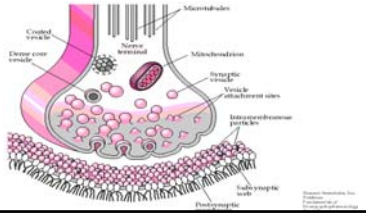
Robert Wright MD MPH
Department of Pediatrics,
Children's Hospital, Boston,
Department of Environmental Health
HSPH

Biological Vulnerability

- Construction of the central nervous system (CNS) begins in utero,
- Continues throughout childhood and involves the production of 100 billion nerve cells and 1 trillion glial cells.
- Cell migrate, differentiate, and form synapses

Synapses

- Transmits signals between neurons
  - Environmental stimuli will cause neurons to fire
  - Neuronal/synaptic firing is a signaling process to mold the synaptic architecture of the brain

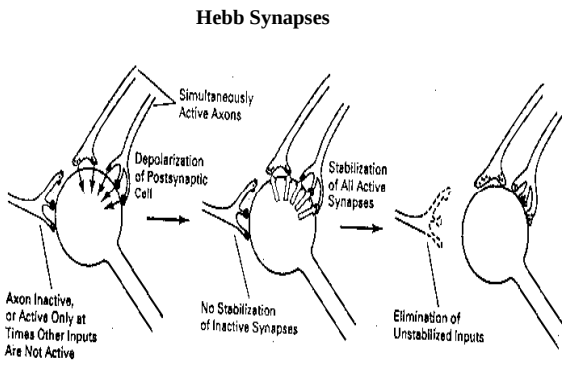


How does the Brain Build this Network?

- Some of it is stochastic
  - Synapses are made by the billions, and in some respects randomly, between neurons.
  - We make a net gain in synapses from fetal life till about age 2 years
  - Then the number of synapses in our brain starts to decrease
    - Why?

Synaptic Networks

- Environmental Stimuli cause nerves to fire:
- When they fire neurotransmitters are released into synaptic junctions
  - This releases growth factors- signals that this is an important neuronal connection (i.e. it gets used)
- In other words there is a "natural selection" process
  - Functional synapses release growth factors
  - Nonfunctional synapses do not release the growth factors



So how do Environmental Chemicals affect Development?

- At "low" doses (blood lead around 5-10 ug/dL)
  - Lead will interact with Protein Kinase C
    - Stimulate neurotransmitter release
    - Neurons fire in the absence of an appropriate environmental stimuli
  - Lead mimics calcium
    - Calcium is critical to nerve signal transmission
    - Calcium enters neurons during depolarization
    - Lead blocks calcium channels

Lead and the Brain

- Net effect
  - Lead stimulates nerves to fire in a more stochastic fashion
  - Lead also inhibits neurotransmission (both appropriate neurotransmission and inappropriate neurotransmission)
- Changes the underlying synaptic architecture, making it less efficient

Plasticity

- The brain's capacity to diminish the effects of toxic insults through structural/functional changes
  - This occurs through the same processes as synaptic selection
  - In other words plasticity allows for new connections to be made which improve function following an insult
- Maladaptive vs adaptive plasticity

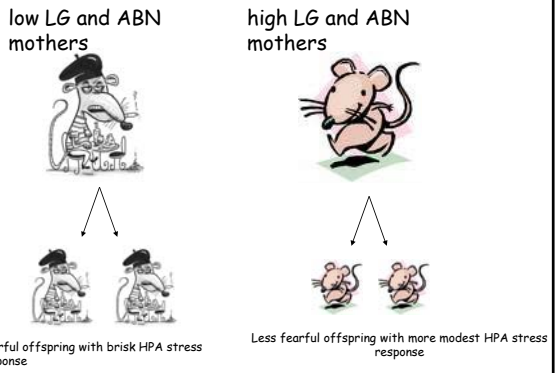
Neurodevelopment and Social Environment

- **Chronic Stress known to impair memory and learning capacity**

Example: Handling Paradigm

- Licking/grooming in mothers is stimulated by human handling of pups.
- Maternal LG and Arch back nursing behaviors program more appropriate long term HPA axis response to stress.
- Maternal LG/ABN clusters in family lines
  - Is it genetic?

Weaver et al. Epigenetic programming by maternal behavior Nature Neuroscience |Volume 7| Number 8|August 2004

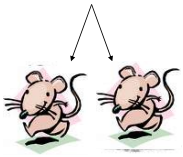


EFFECTS OF CROSS-FOSTERING

low LG and ABN mothers

Fearful offspring with brisk HPA stress response

high LG and ABN mothers



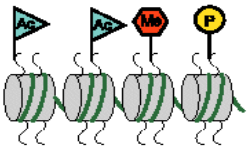
Less fearful offspring with more modest HPA stress response

Programming And Epigenetics

- Fetal origins of Disease
  - Prenatal (and early life exposures), increase risk of late life disease
    - HTN,
    - Obesity
  - Handling paradigm is an example of neuro-programming

•Methylation of histone or of DNA usually turns a gene off.
•Acetylation of histone usually turns a gene on.
•Phosphorylation -- we're not sure what that does.

The Histone Code



Epigenetics and the Brain

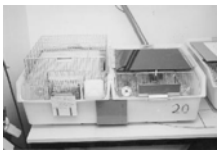
- Epigenetics plays an important role in synaptic pruning via environmental stimuli.
  - Epigenetic marks within neurons change with synaptic activity
- This "epigenetic opening" of synaptogenesis to environment is maximal during childhood
- It is the source of the exceptional cognitive adaptability of humans, and possibly the source of its fragility

Handling Paradigm

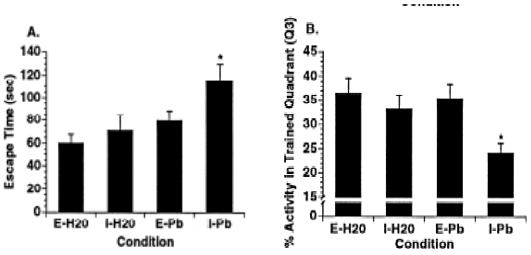
- Weaver et al
  - Glucocorticoid receptor expression is more active in offspring of high-LG mothers compared with low- LG mothers,
  - Effect inversely correlated with methylation across Glucocortoid Receptor promoter sequence in the hippocampus
  - REGARDLESS OF GENETIC BACKGROUND

Social Environment and Pb

- Guilarte et al
- Lead poisoned animals during lactation
- Randomized to 2 groups
  - Animals raised in social isolation
  - Animals raised in groups with social stimulation
    - Tested on memory in Water maze



Acquisition Time **Probe Test**



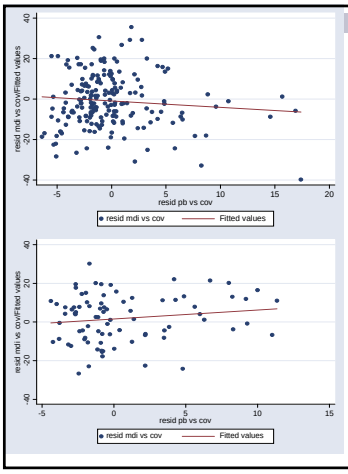
Can Reducing Stress be a Treatment?

- Mexico City
- Coopersmith self-esteem administered to mothers when child 24 months of age
- Cross-sectional analysis
- Covariates
  - Blood Pb, mom's IQ, mom's education, child's sex,

Main Effect of Maternal Self-Esteem

mdi24	Coef.	P>|t|	[95% CI]	
Blood Pb	-.11	0.569	-.50	.276
autoes	***.46***	***0.006***	***.12***	***.78***

Adjusted for Maternal IQ, education, Infant Sex,



Blood Pb and MDI

Self esteem Quartile 1,2,3

Self esteem Quartile 4

Another Pilot Study: Maternal Child Lung Study

- Pregnancy cohort recruited from 1986-1992
- Study of in utero/environmental tobacco smoke exposure and respiratory outcomes
- Women enrolled before 20th EGA week
- Children followed after birth
- Measured ETV (violence) and WCST as pilot

Effect of Cotinine in Predicting Errors on WCST: Stratified by Median Violence Exposure

	Cotinine Beta (Low violence)	Cotinine Beta (High violence)
% Errors	2.9 (p=0.6)	9.8 (p=0.07)
# Perseverative Responses	1.7 (p=0.7)	11.1 (p=0.007)
%Perseverative Responses	2.0(p=0.7)	10.7 (p=0.007)
# Perseverative Errors	0.8 (p=0.9)	10.7 (p=0.01)
% Perseverative Errors	1.4 (p=0.8)	9.9 (p=0.02)

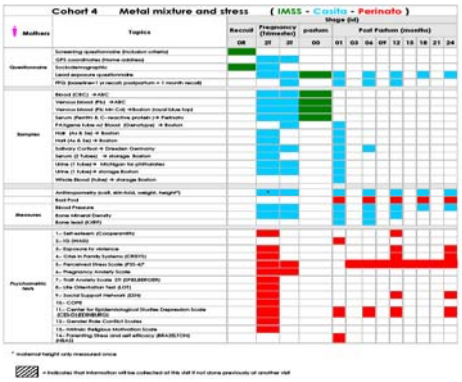
Mexico Birth cohort

- The work just reviewed led to the establishment of a new birth cohort in Mexico City.
- R01 ES013744 Stress, Lead, Iron Deficiency and Neurodevelopment.

ELEMENT
Early Life Exposure in Mexico to Environmental Toxicants Project

Mexico City Cohort

- Long term goals
  - Identify factors that increase/decrease metal toxicity
  - Understand the biology of metal neurotoxicity
  - Prevent toxicity
  - Treat toxicity after it has occurred



Tar Creek Superfund Site

The *MATCH* Study

(Metals **A**ssessment **T**argeting **C**ommunity **H**ealth**)**

"Ga-Du-Gi"- Working Together

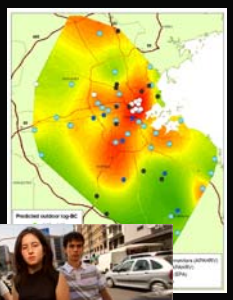
Thanks

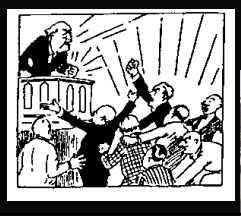
Element
Adrienne Ettinger
Mara Tellez-Rojo
Hector Lamadrid
David Bellinger
Rosalind Wright
Howard Hu
Lourdes Schnaas
Adriana Mercado

Tar Creek
David Bellinger
Adrienne Ettinger
Rosalind Wright
Howard Hu
Mary Happy
Mark Osborn
Rebecca Jim
Earl Hatley

Community-based Risk Assessment – a statistician's perspective

Louise Ryan
Department of Biostatistics
Harvard School of Public Health





Outline

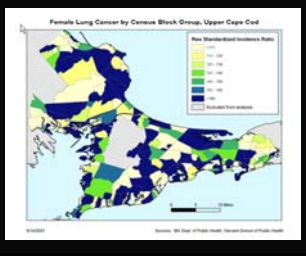
- Use some examples to
  - Illustrate challenges
  - Describe useful statistical tools and areas where more research would be helpful
- My examples
  - Classic cancer cluster investigation
  - Home Allergen Study
  - Exposure assessment for various Boston based studies
  - Mercury and IQ

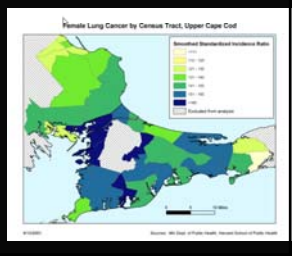
Cancer risks on Cape Cod

- Citizens near air-force base concerned about excess cancer rates reported on upper cape
- Clear evidence of multiple exposures
- Excesses small to moderate (SIRs around 120)
  - Power limited by total pop of ~30K
  - No individual exposure assessment

Cape Cod - continued

- Data very noisy – smoothing no help
- Very frustrating experience for all
- Need guidelines on what's achievable

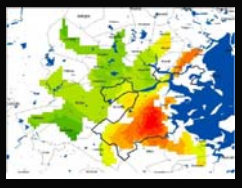




Home Allergen Study

- Mother/child pairs recruited at birth. Followed for asthma, allergy, respiratory disease
- Interest in allergens, molds, adjusting for social factors
- Geocode study subjects and assign areal level characteristics (e.g. based on census)

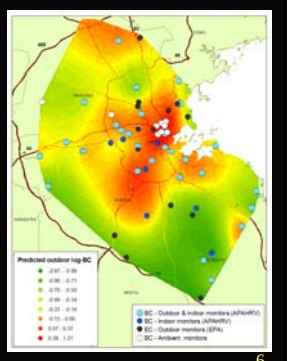
Intriguing geographical variation in maternal serum IGE. But geoadditive modeling (Kammen & Wand) suggests "hotspot" confounded with race, poverty.



$$Y = \beta_0 + \beta X_1 + g(X_2) + h(lat, lon) + \varepsilon$$

Boston and New England studies of cardiovascular response to air pollution

- Estimate exposure from
  - EPA EC monitors
  - Various Indoor & outdoor monitors (different studies)
  - GIS-based measures (traffic density, potentially climate, land use etc)
- Goal – relate predicted exposures to health outcomes (heart rate variability, arythmias, birth weight), accounting for estimation error
- Latent variable formulation very promising

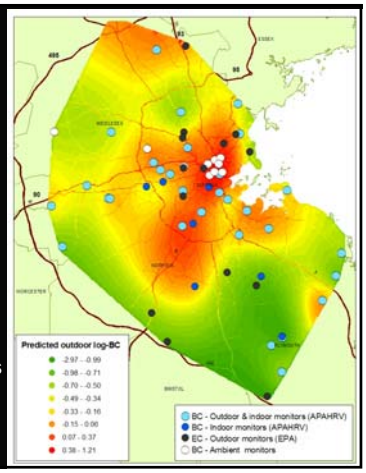


Note

- Higher predictions near main roads
- Smoothness of estimated surface elsewhere

Further directions

- Use "science-based" models to inform the modeling (Fuentes and Raftery, 2005).
- Unusual data sources (e.g. satellites)



Features so far

- Sparse data
- Clever combination of data from multiple sources
- Spatio-temporal modeling

Lets look at another example (methyl mercury) where hierarchical model helps to make sense of limited data. Not a classic community-based risk assessment, but illustrates many of the ideas

8

Mercury

- Released by coal-burning powerplants, bioaccumulates through foodchain to methylmercury, human exposure via fish consumption

- High level exposures clearly toxic, low level chronic effects controversial

9

The controversy

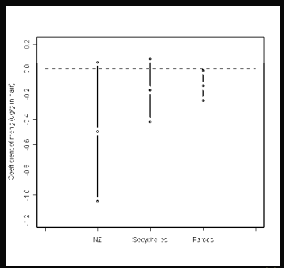
- Conflicting conclusions from two large, well conducted epidemiological studies
  - Seychelles study (n=779) - no effect
  - Faroes study (n=1022) - effects
- Both studies
  - had prenatal enrollment
  - had reliable biomarkers of exposure
  - adjusted for similar important confounders
  - measured similar outcomes
- NAS confirmed quality of both studies, identifed a third. Argued against focus on p-values. Studies less discrepant if focus is on dose response estimation.

10

MEHG and IQ (7-9 years)

- IQ has been "monetized"
- IQ is related to other endpoints
- Study results
  - -.50 (.28) (NZ)
  - -.17 (.13) (Seychelles)
  - -.13 (.061) (Faroes)
- Can we combine data?

Estimated regression coefficients and 95% CIs



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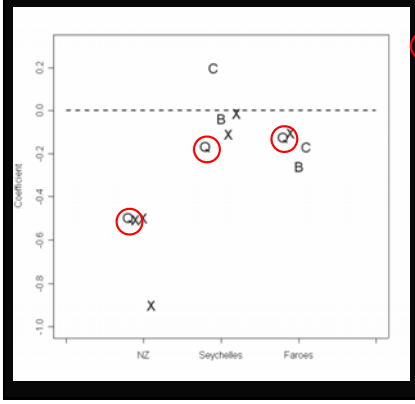
Endpoints Available in the three studies

Study	Age	Endpoint	Cognition/ Achievement	Attention/ Behavior	Motor
Seychelles[1]	9 years	WISC-III	X		
		CVLT (short term)	X		
		BNT (total)	X		
		WRAML	X		
		VMI	X		
		CPT Reaction time		X	
		CBCL		X	
		Finger Tapping			X
Faroes[2]	7 years	Full scale IQ[3]	X		
		Reader Visual (copying)	X		
		BNT (no cues)	X		
		CVLT (short term)	X		
		CPT Reaction Time		X	
		Finger Tapping			X
		Hand-Eye Coordination			X
New Zealand[4]	6-7 yrs	WISC-R	X		
		TOLD-SL	X		
		WISC-RP (Performance IQ)	X		
		MCC-PP	X		

Graphical representation



Q – IQ

B – Boston Naming

C – California Verbal Learning

X – other cognitive endpoints

Dashed line – no effect

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Random effects formulation

- Express data as set of estimated dose response coefficients, standard errors and study and endpoint codes

β	τ^2	Study	Endpoint
-.17	.13	1	1
-.124	.057	2	1
-.50	.28	3	1
.20	.154	1	2
Etc			

$$\hat{\beta}_i = \mu + \eta_{study_i} + \delta_{endpoint_i} + \varepsilon_i, \quad \varepsilon_i \sim N(0, \tau_i^2)$$

$$\eta_{study_i} \sim N(0, \sigma^2_{study}), \ \delta_{endpoint_i} \sim N(0, \sigma^2_{endpoint})$$

14

Hierarchical Modeling Results

- Not enough data to reliably estimate separate study and endpoint variance components
- Assume $\sigma^2_{study} = R\sigma^2_{endpoint}$ and repeat for different R

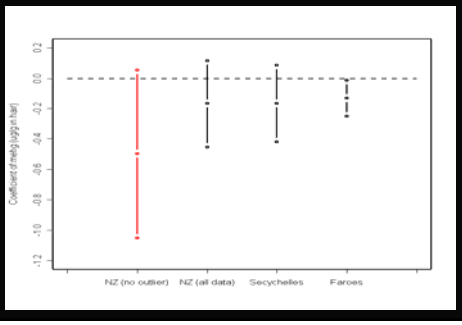
R	$\hat{\sigma}_{study}(se)$	$\hat{\beta}_{IQ}(se)$	95% Conf. Int	DIC*
3.0	.0343 (.0303)	-.125 (.054)	(-0.248, -0.034)	-3.704
2.5	.0379 (.0328)	-.126 (.0559)	(-0.256, -0.033)	-3.873
2	.0429 (.0362)	-0.128 (0.0587)	(-0.265, -0.030)	-4.112
1.5	.0499 (.0408)	-0.131 (.063)	(-0.281, -0.028)	-4.455
1.0	.0612 (.0476)	-0.136 (.0699)	(-0.305, -0.023)	-4.997
.5	.0420 (.0505)	-0.127 (0.0569)	(-0.259,-0.031)	-4.103
.4	.0371 (.0324)	-0.126 (.0541)	(-0.251, -0.033)	-3.846
.25	.0286 (.0262)	-0.123 (.0498)	(-0.236, -0.037)	-3.423

* Smaller values of DIC indicate better fit

15

Effect of the NZ outlier

NZ had one extremely exposed child who was just fine!



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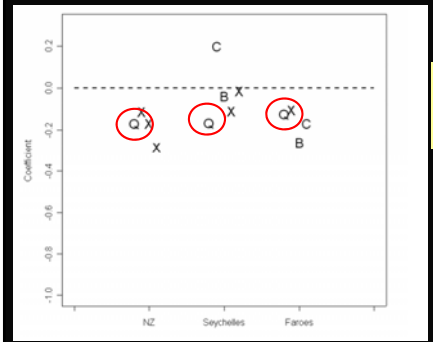
Including the NZ outlier



Results appear more concordant

Q - IQ

17

More sensitivity analyses

- Hair/blood ratio
- Alternative scaling of Faroes IQ – estimated IQ effect strengthens to -.23

Analysis	Hair/blood ratio*	$\hat{\sigma}_{study}$ (se)	$\hat{\beta}_{IQ}$ (se)	95% Conf Int
Exclude NZ outlier	250	.0531 (.0474)	-.115 (.0592)	(-0.266, -0.018)
Exclude NZ outlier	200	.0499 (.0408)	-0.131 (.0632)	(-0.281, -0.028)
Include NZ outlier	250	.0304 (.0250)	-0.096 (.0360)	(-0.173, -0.025)
Include NZ outlier	200	0.0389 (.0292)	-0.108 (.0436)	(-0.204, -0.025)
Alternative Faroes IQ	250	0.1027 (.0669)	-0.196 (.1091)	(-0.451, -0.030)
Alternative Faroes IQ	200	0.1240 (.0708)	-0.233 (.1213)	(-0.512, -0.038)

* ppb mercury in hair to ppb mercury in cord blood

Range -.10 to -.23

All exclude 0

18

What have we learned?

- ✓ Uncertainty tends to be large when dealing with data collected in real world communities
- ✓ Need to measure characteristics of community, as well as individuals
- ✓ Major benefits to statistical techniques (Bayes) to sythesize information from multiple sources
  - Data (similar or unrelated studies)
  - Expert opinion
- ✓ Some good tools around
  - Spatio-temporal models
  - Hierarchical models
- ✓ Don't over-interpret model results, p-values.
- ✓ Do lots of sensitivity analysis

"Bayes was a bad boy" Pasky

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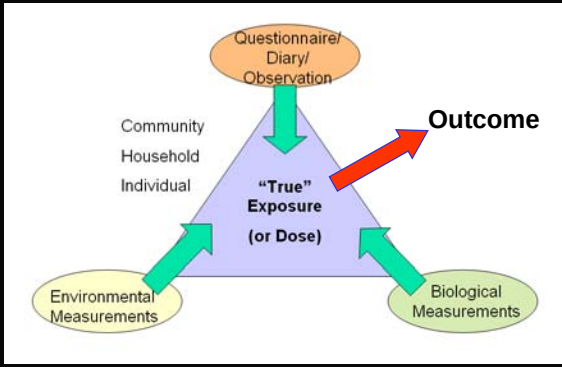
Remaining frontiers?

- ✓ Spatio-temporal models still relatively primitive
- ✓ Good tools around for combining information. Further work needed to finesse them to handle multiple scales, levels of accuracy etc
- ✓ Design a neglected topic! We've worked with Battelle to develop strategies for clever subsampling to maximize information/minimize cost. Working on extensions to spatial setting (with ACC funding)

20



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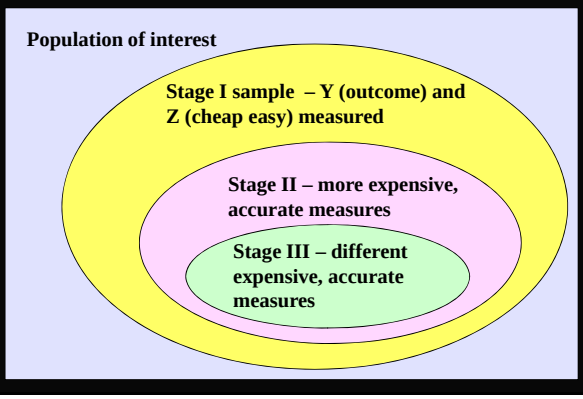
Multi-Stage Sampling Paradigm



Case Example

$Y \sim Bin(P_Y = 0.003)$ Cost associated with measuring Y = \$20

$X \sim N(0,1)$ Cost for exposure assessment = \$1000

$\Psi_{Y,X} = 2.0$ Odds ratio between X and Y

Total Cohort Size = 100,000

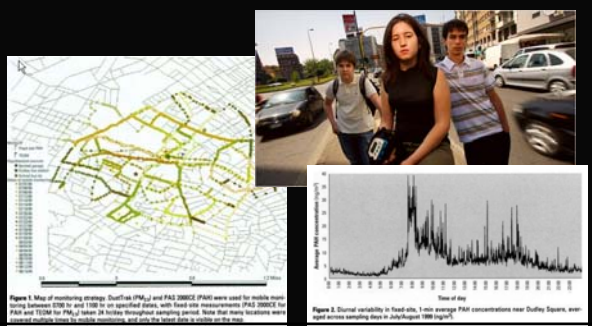
Surrogate Z costs \$50 and has correlation .5 with X

We determined designs with 80% power

Design	Random Sample		Covariate Dependent Sample (for X)		Outcome Dependent Sample (for X)	
	Cost	N	Cost	N	Cost	N
Analyze subset only	Cost = \$5,606,940 n =5,497					
Incorporate surrogate	\$1,813,330 (32%)	n_Y=23,319 n_Z=23,319 n_X=181	\$1,791,020 (32%)	n_Y=23,686 n_Z=23,686 n_X=133	\$404,520 (7.2%)	n_Y=5,536 n_Z=5,536 n_X=17

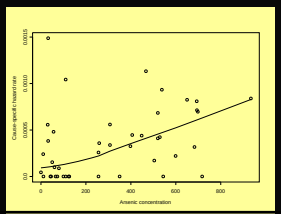
Frontiers - continued

- ✓ Spatial design in general very interesting. What are the properties of "Roving Designs"?



Arsenic in drinking water

Arsenic is a naturally occurring metal. Humans exposed to high levels in Taiwan, Chile & Bangladesh.



Data from Taiwanese farming community very noisy

Adjusting for drinking variation

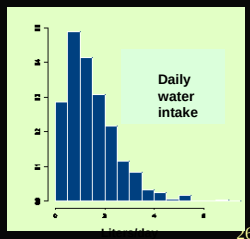
Consider outcome for a single individual and suppose

$$\text{Logit}(\Pr(Y=1)=\beta_0+\beta_1 * D * C$$

D = amount drunk, C = concentration in the water

D is unobserved, but distribution estimable from an EPA survey.

What is impact on estimation of β_1 (compared to assigning everyone their village well concentration)?



Impact on Benchmark Dose
(dose corresponding to 1% risk)

Adjustment?	BMD	BMDL
No	165	145
Yes	195	86

mean of posterior distribution

lower 5% percentile

Thanks!

Come to Duke tomorrow for more details on the sub-sampling project

A Multi-Site Time Series Study of Hospital Admissions and Fine Particles: A Case-Study for National Public Health Surveillance

Francesca Dominici
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Department of Biostatistics
Johns Hopkins Bloomberg School of Public Health

EPA Workshop October 17 2007

Sponsored by the EPA, CDC Center of Excellence, and NIEHS

A NATIONAL SYSTEM FOR TRACKING POPULATION HEALTH

- Multiple government databases contain massive amounts of information on the environmental, social, and economic factors that determine health
- Research on population health could be rapidly advanced by:
  - integrating these existing databases
  - bringing to bear new statistical models that would describe major threats and their causes
- These integrated databases and new analysis tools would create a national system for population health research

Air pollution and health: Fundamental questions

- Is there a risk at current levels?
- How can we estimate it?
- How big is the risk?
- What causes it?

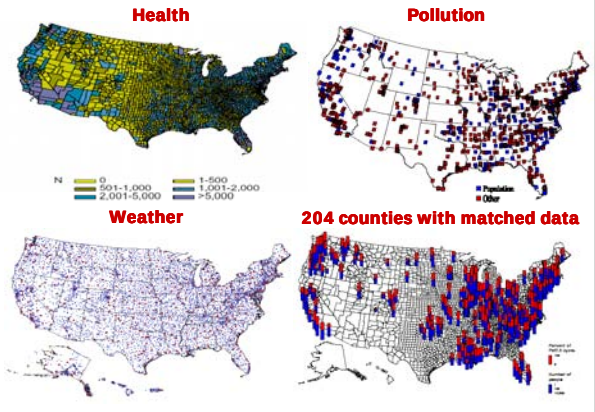
Health Effects Fine Particles: Objectives

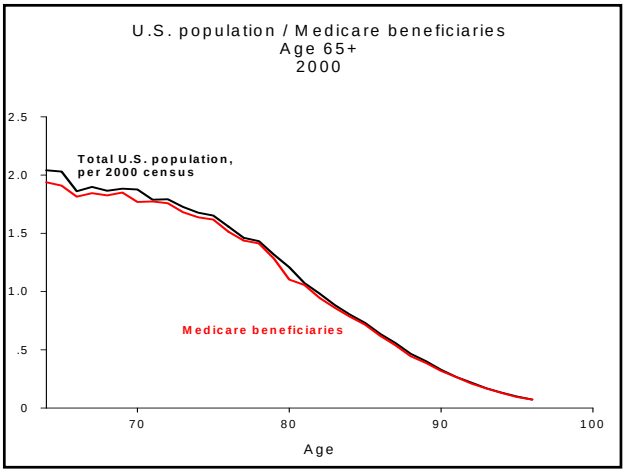
1. assemble a national database of time series data for the period 1999-2005 on hospital admissions rates for cardiovascular and respiratory diseases, fine particulates, and weather for 204 US counties
2. develop state-of-the-art statistical methods
3. estimate maps of relative risks of hospital admissions associated with short-term changes in fine particles
4. illustrate how integration and analysis of national databases can lead to a national health monitoring system

Integrating National Data Sources

- NCHF: 48 million identification numbers
- MCBS: subset of 15,000 Medicare participants with additional information on risk factors
- AIRS: air pollution monitoring network
- NOAA: weather monitoring network
- US Census: location characteristics

Integrating national data bases

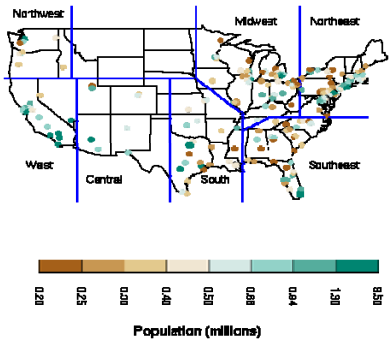




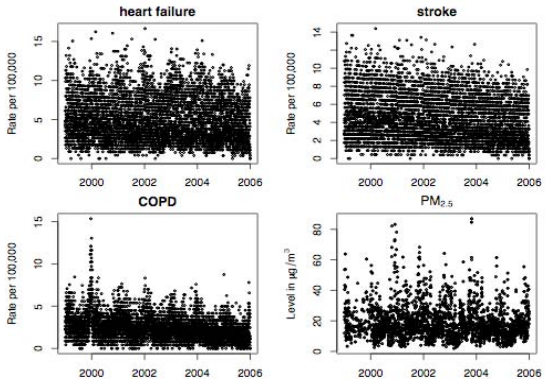
National Medicare Cohort (1999—2005)

- National study of fine particles ($PM_{2.5}$) and hospital admissions in Medicare
- Data include:
  - Billing claims (NCHF) for everyone over 65 enrolled in Medicare (~48 million people),
    - date of service
    - treatment, disease (ICD 9), costs
    - age, gender, and race
    - place of residence (ZIP code/county)
  - Approximately 204 counties linked to the air pollution monitoring

MCAPS study population: 204 counties with populations larger than 200,000 (11.5 million people)



Daily time series of hospitalization rates and $PM_{2.5}$ levels in Los Angeles county (1999-2005)



Multi-site time series studies

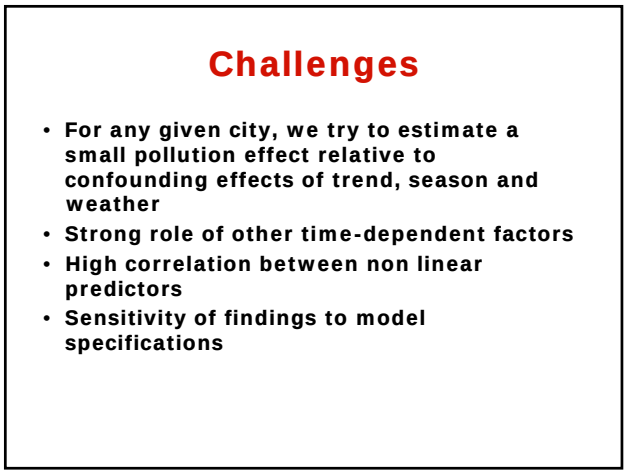
- Compare day-to-day variations in hospital admission rates with day-to-day variations in pollution levels within the same community
- Avoid problem of unmeasured differences among populations
- Key confounders
  - ➢Seasonal effects of infectious diseases and weather

Statistical Methods

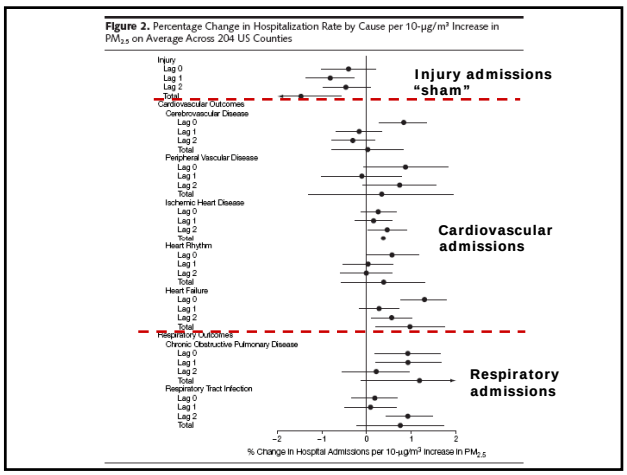
- **Within city**. Semi-parametric regressions for estimating associations between day-to-day variations in air pollution and mortality controlling for confounding factors
- **Across cities**. Hierarchical Models for estimating:
  - national-average relative rate
  - Regional-average relative rate
  - exploring heterogeneity of air pollution effects across the country

Challenges

- For any given city, we try to estimate a small pollution effect relative to confounding effects of trend, season and weather
- Strong role of other time-dependent factors
- High correlation between non linear predictors
- Sensitivity of findings to model specifications



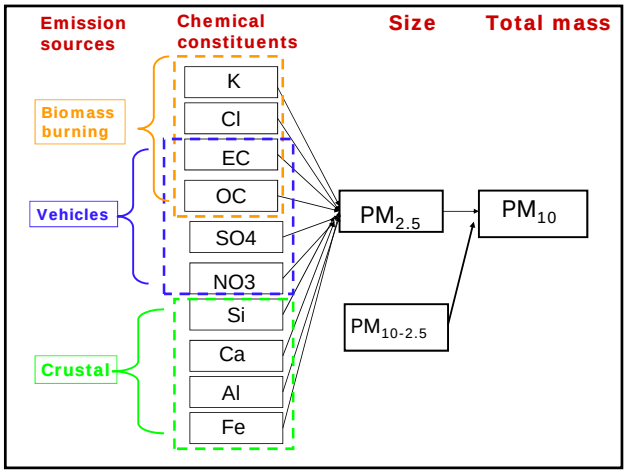
March 8 2005



New Scientific Questions

What are the mechanisms of PM toxicity?

- Size?
- Chemical components?
- Sources?

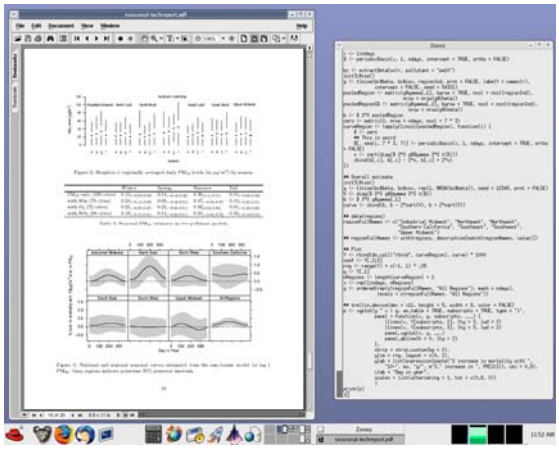


Air pollution and health: Questions and (some) answers

- **Is there a risk?**
  - Multi-site time series studies such as NMMAPS (1987—2000) provide strong evidence of short-term association between air pollution and mortality
  - Preliminary results from Medicare data (1999—2002) indicate that current air pollution levels still affect health
- **How can we estimate it?**
  - National datasets are powerful resources for assessing the health effects of air pollution
  - Statistical models that can integrate information across space and time
  - National average estimates for the effect of PM are robust to various model formulations and statistical methods

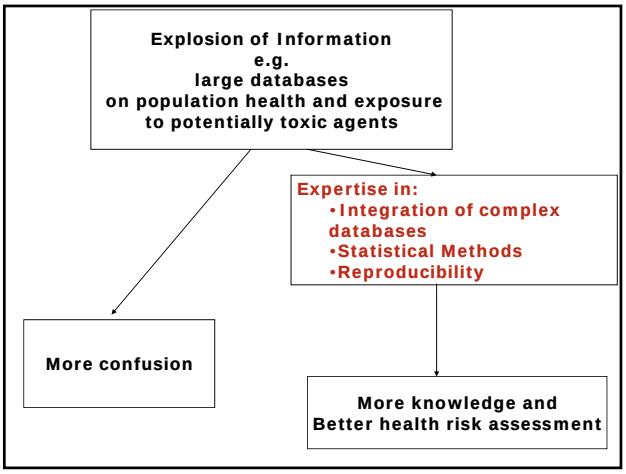
Reproducible research

- We want to reproduce previous findings
  - "Did you do what you said you did?"
- Test assumptions, robustness of findings; check methodology
  - "Is what you did any good?"
- Implement and test new methodology
  - "I can do it better!"



Discussion

- Linking national databases and developing statistical methods that can properly analyze these them, are essential steps for a successful national public health tracking system
- Because of the small risks to be detected and the large number of potential confounders, single-site studies are generally swamped by statistical error
- A national system, that routinely analyze data from multiple locations in a systematic fashion, is a very promising approach for tracking population health

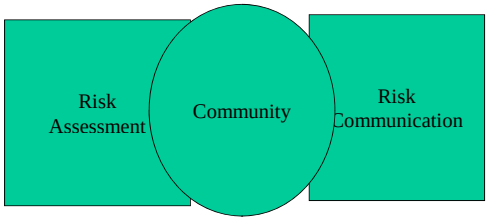


Acknowledgments

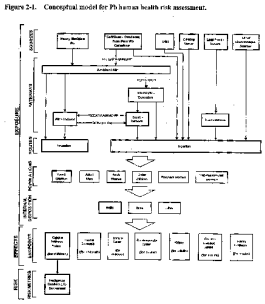
- Our team:
  - R. Peng
  - S. Zeger
  - J. Samet
  - A. McDermott
  - M. Bell
  - L. Pham
- Our sponsors:
  - EPA
  - JHU CDC Center of Excellence
  - NIEHS

Risk Assessment/Risk Communication-Understanding the Community

Thomas Schlenker, MD, MPH
Public Health Madison-Dane County



Lead Human Exposure and Health Risk Volume 1, July 2007

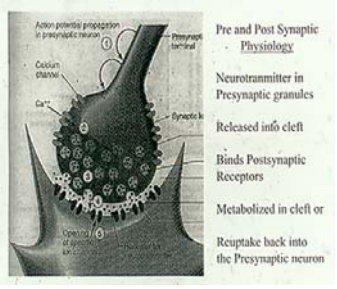


- Sources
- Pathways
- Routes
- Populations
- Internal Disposition
- Endpoints
- Risk Metrics

Community-based Risk Assessment: Lead

- Benjamin Franklin
- Voluminous Research
- National Strategies
- Substantial Funding

Bone, Blood, CNS



Internal Disposition
- Harmless/harmful
- Hgb, RBCs and breast feeding
- Developing brain and synapse story

Chips vs Dust

Sources
Pathways
- Pica
- Child growth/dev
- Housing
- Weather
- Abatement
- Dust wipes

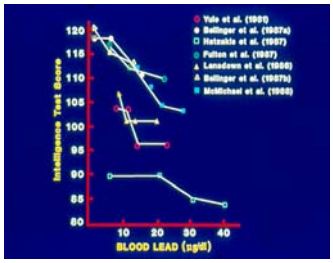
Mothers, babies, doctors and public health

Routes

Populations

- "community-based research framework and a transparent process to instill confidence and trust among community members"
- **"Effects of Lead in Milwaukee's Water."** Wis Med J 1989;88:13

IQ and high school graduation



Risk Metrics

- Herb Needleman in Somerville, Mass

Community-based Risk Assessment: Manganese

Sources
Pathways
Routes
Populations
Internal Disposition
Endpoints
Risk Metrics

EPA Resources

- **Health Effects Support Document for Manganese**, **2003**: HRL = 0.30 mg/L
- **Drinking Water Health Advisory for Manganese**, **2004**: lifetime health advisory value
- **Teach (Toxicity and Exposure Assessment for Children's Health) Manganese Chemical Summary**, **2007**: infant formula
- **Occurrence of Manganese in Drinking Water and Manganese Control** (EPA/Awwa Research Foundation): "aesthetic problem…relates more to consumer complaints rather than protecting health."

Sludge vs Sediment

Pathways

- Wells
- Mains
- Laterals
- Hose bibs

Food, Drink, Osteo-Bi-Flex

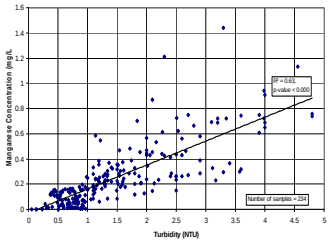


Figure 1. Regression of turbidity against manganese concentration in end-of-flush samples from hydrants.

Sources
- Concentrations
- Bioavailability
- Volume
- Consumer Products

At Risk vs Worried Well

Populations
- "Population factors that differentially affect exposure or toxicity, and in some cases, resiliency to environmental contaminants."
- Infant formula: "contains 50 to 300 ug/L of manganese" (Collipp et al,1983)

Human Impact

Endpoints

Risk Metrics
- Parkinson's Syndrome
- ADHD
- Hair analysis?

It must be the water!

Risk Communication

Perspectives, issues and needs in community-based risk assessment

USEPA Workshop on Research Needs for Community-Based Risk Assessment
October 19, 2007, Research Triangle Park NC

George Bollweg PhD
USEPA Region 5 Air and Radiation Division
bollweg.george@epa.gov
312-353-5598

Outline for this talk

- One definition of community-based risk assessment (CBRA)
- Some CBRA conceptual approaches
- Influence of participant perspective on needs
- Issues and needs encountered in risk assessments with community participants (organized per 2003 USEPA Framework for Cumulative Risk Assessment)
- USEPA tools and approaches for CBRA
- Summary

One definition of community-based risk assessment

According to the Workshop website,

"**Community-based risk assessment** is a model that addresses the multiple chemical and non-chemical stressors faced by a community, while incorporating a community-based participatory research framework and a transparent process to instill confidence and trust among community members."
(http://www.scgcorp.com/riskassessments/index.htm)

1996 NRC "Understanding Risk" p. 28

(http://books.nap.edu/openbook.php?isbn=030905396X)

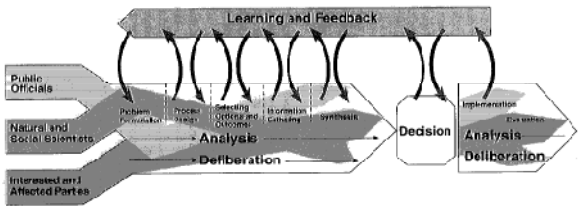
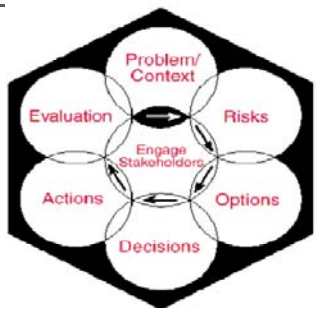


FIGURE 1-2. A schematic representation of the risk decision process.

1997 Presidential/Congressional Commission on Risk Assessment and Risk Management vol. 1

(http://www.riskworld.com/Nreports/1997/riskrpt/pdf/EPAJAN.PDF)



2003 USEPA Framework for Cumulative Risk Assessment, p. 13

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

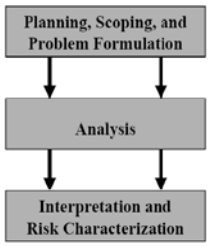


Figure 1-3. Framework for cumulative risk assessment.

Analytic focus/orientation - agent/stressor, community/host

(2003 Framework for Cumulative Risk Assessment, p. 1-2)

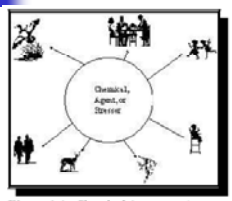


Figure 1-1. Chemical (or stressor) focused assessment starts with a source and evaluates how the chemical gets to various populations or ecological targets. Individual assessments may choose to pursue some or all pathways, media, or population segments.

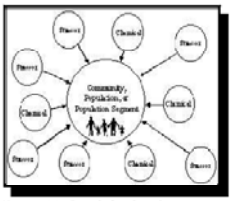


Figure 1-2. Population-based assessments start with the receptors, and determine what chemicals, stressors, or other risk factors are affecting them.

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CBRA-oriented toxicity assessment might put prior slide in the following words:

"...Our guiding thesis is that toxicity is not simply an inherent property of the toxicant but derives from an assortment of jointly acting variables bound implacably into the individual."

Weiss B, Bellinger DC. Social ecology of children's vulnerability to environmental pollutants. 2006 EHP 114, 10: 1479-1485

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Needs: influence of a hypothetical CBRA participant's perspective

- Community members – need timely "answers"
- Research scientists – need timely publications
- Industry participants – need to persuade affected parties that risks are "acceptable"
- USEPA managers – need to address management priorities (e.g. GPRA goals)
- State, Regional risk assessors – need to conduct credible assessments that address participant needs

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General CBRA needs - examples

- **Resources:** community assessment can require big, multi-disciplinary commitment and follow-through (expertise, people, organization, time, etc.)
- **Host- and media-integrated human health risk assessment methods** that unify stressor- and host-focus as well as USEPA Programs fragmented by environmental medium or law (relevant parts of Superfund, RCRA, Pesticides, Air, Water, RAF etc. methods?)
- **Air Program:** combined metric for criteria pollutant and noncriteria pollutant hazards or risks: is "composite risk characterization" (separate presentation) enough?

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Should metrics be combined?

- **Yes: if needed, feasible and if "combining" is logically consistent and interpretable**
- **No: if "combining" results in excessive information loss, hidden incompatibilities, subjectivity, interpretability/ communication problems, false precision, etc.**

(Figure from Greg Paoli; http://www.iom.edu/?id=32160)

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General CBRA needs - examples

Exclusion of "background" stressor exposure or susceptibility ---> incremental assessments irrelevant to some participants. Possible remedies:

(a) address site-specific "background" susceptibility and/or stressor exposures; or

(b) lacking site-specific information, derive a **"**reference human exposure profile" to [median??] environmental pollutants to which incremental exposures could be added (e.g. use Exposure Factors Handbook and Pesticides Program info??)

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CBRA planning, scoping and problem formulation: example issues, needs

1. Methods for choosing participants from "the community"? (in addition to technical experts and self-selectees)
2. Scoping: facilitated meeting among…(?) to formulate analytic problem(s) and scope
3. **Getting right science** (e.g. info on substandard housing, neighborhood crime) as well as **getting science right** (i.e. pollutant exposure concentrations)
4. How to include **"background" stressor exposures, pollutant and/or nonchemical**
5. Update July 1997 planning and scoping "Guidance" (http://www.epa.gov/OSA/spc/pdfs/cumrisk2.pdf)?

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2002 USEPA "Lessons Learned on Planning and Scoping": some orienting questions

(http://www.epa.gov/OSA/spc/pdfs/handbook.pdf, p. D-7)

1. Who are the parties proposing the assessment?
2. Are there other interested or affected parties?
3. **What questions do the parties want the assessment to answer?**
4. What analysis will be done to answer these questions?
5. Who will conduct the analysis?
6. When are the assessment results needed?
7. Who will pay for the assessment?
8. How will the assessment results be used?

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CBRA analysis: example issues, needs

1. More timely IRIS assessments/reassessments (also needed: evaluation of organizational and political influences [levels of review; executive branch process control] on IRIS productivity?)
2. MOA determinations e.g. for benzene
3. Short term RfCs e.g. benzene, naphthalene
4. Limits of Haber's Rule
5. **Assertion that local residents' health is "poorer than national averages"** and not addressed in USEPA exposure and toxicity estimates - how to evaluate this in CBRA context? If true, how to address?

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CBRA analysis: example issues, needs

1. Are ~20-yr old meteorology datasets appropriate for simulating local weather patterns 30-70 years in the future?
2. Appropriateness of data from fixed-site air monitors as surrogate for human exposure concentrations (e.g DEARS Detroit study)
3. Synergistic or antagonistic toxic effects – how likely in some mixtures?
4. Feasibility of an all-species (including humans) hazard quotient or hazard index

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CBRA risk characterization and interpretation: example issues, needs

1. Better communicate hypothetical vs. actuarial numeric risks (e.g. provide lifestyle-risk context?); accurate and balanced characterization (i.e. not just "the number")
2. Characterizing and communicating "cascading" uncertainty, e.g. formal vs. descriptive methods
3. What are **attributes of successful/unsuccessful deliberative processes** (e.g. CARE experiences)?
4. Should a formal **evaluation** step (per 1996 NRC, 1997 PCCRARM) be included in USEPA risk assessments?
5. Expectations management? i.e. USEPA role in addressing socially-embedded issues

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Examples of CBRA approaches, guidance and tools available through USEPA

- **Community Action for a Renewed Environment, CARE** (http://www.epa.gov/care). Competitive grant program to help communities organize and take action to reduce toxic pollution in local environment
- **Community Air Screening How-To Manual** (http://www.epa.gov/oppt/cahp/pubs/howto.htm)
- **ATRA vol. 3–Community-Scale Assessment** (http://www.epa.gov/ttn/fera/risk_atra_vol3.html), especially Chapters 10-12, a sort of "CARE how-to" guide
- **RAGS Part A supplement-Community Involvement in Superfund Risk Assessments** (http://www.epa.gov/oswer/riskassessment/ragsa/pdf/ci_ra.pdf)
- **RCRA Public Participation Manual** (http://www.epa.gov/epaoswer/hazwaste/permit/pubpart/manual.htm)
- **OSA/SPC/RAF Cumulative Risk Assessment Program** http://www.epa.gov/OSA/spc/2cumrisk.htm

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Summary

- CBRA attempts to address real-world human susceptibility, exposure and risk with inclusive, often resource-intensive deliberative process
- Some CBRA conceptual approaches and tools are already available
- CBRA needs to:
  - process multiple, diverse participant input to better identify and formulate problems;
  - help unify fragmented disciplinary “silos”;
  - acquire needed science to address questions/issues of participant concern (long term commitment)

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October 19, 2007

USEPA Workshop on Research Needs for Community Based Risk Assessment

Closing Remarks

Michael A. Callahan
U. S. EPA Region 6
Dallas, Texas

A Brief Cumulative Risk History

- 1970s – knowledge without ability
- 1983 – NRC Red Book
- 1980s – Environmental Justice questions
- 1996 – Food Quality Protection Act
- 1996 – Browner Memo on Cumulative Risk
- 1999 – Risk Assessment Forum Tech Panel on Cumulative Risk Assessment formed
- 2000s – Pesticides assessments, NATA, DBPs, etc.
- 2003 – Framework for Cumulative Risk Assessment
- 2007 – RAF Case Studies Report

Cumulative Risk Technical Panel Phase 2

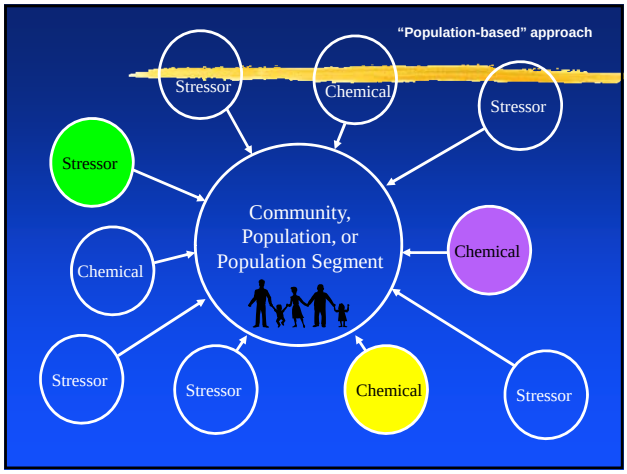
- **Issue Papers (***EHP* mini-monograph *Frontiers in Cumulative Risk Assessment*, Vol. 115 No. 5, May, 2007)
  - If Cumulative Risk Assessment Is the Answer, What Is the Question? (Callahan & Sexton)
  - A Phased Approach for Assessing Combined Effects from Multiple Stressors (Menzie et al)
  - Vulnerability as a Function of Individual and Group Resources in Cumulative Risk Assessment (deFur, et al)
  - Assessing Cumulative Health Risks from Exposure to Environmental Mixtures - Three Fundamental Questions (Sexton & Hattis)
  - Using Biomarkers to Inform Cumulative Risk Assessment (Ryan, et al)
- **Issues, Case Studies, and Research Needs in Cumulative Risk Assessment (late 2007)**

Why Should We Invest in Community Based Cumulative Risk Assessment?

- Communities are asking for it
- EPA's relevance with the public is at stake
- Fairness
- What kind of investment?

Communities are asking for it

- NEJAC
- CARE
- Three communities in past two months in Region 6
- Not asking for "total risk"



Communities are asking for it

- NEJAC
- CARE
- Three communities in past two months in Region 6
- Not asking for "total risk"

We can do some parts of it now

"Risk Assessment doesn't work for us…"

- Why? Some things are left out, e.g.,

  Cascading effects:

  Eco: Erie Canal

  Human: EJ Community

"Risk Assessment doesn't work for us…"

- Why? Some things are left out, e.g.,

  Non-conventional Stressors

Some Losses Potentially Not Covered…

Unreconciled Loss: Physical and Symbolic

Loss of land	Loss of language	Loss of spirituality
Loss of extended family relationships	Loss of sense of belonging	Loss of autonomy
Loss of rights	Loss of self-sufficiency	Loss of social structure
Loss of connection to land	Loss of culture and tradition	Loss of identity
Loss of sovereignty	Loss of history	Loss of control
Loss of cultural pride	Loss of community	Loss of trust

Loss of life: Multiple traumatic deaths related to disease, violence, genetic risk factors...

Source: Lemay and Piotrowski, 2002

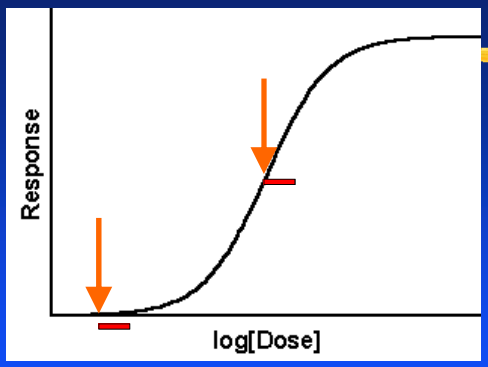
But what about "mission creep?"

Relevance/Credibility

- EPA Priorities:
  - Legislated mandates
  - Court orders
  - Political issues/Media circuses
  - Public need
- Public needs:
  - Federal government as a monolith
    - » Can't help with problem
    - » Paternalism = change the problem
    - » Understand and help
- Risk assessments that consider part of the problem

Fairness: Vulnerability

- **Vulnerability: The state of being open to harm due to the inability to cope with a hazard because of biological susceptibility, prior exposure or disease state, or lack of the resources for resilience.**
- **Vulnerability = Hazard + Inability to cope**
- **Vulnerability can mean that the exact same exposure can result in widely different effects**



Result of "Background" Exposure

Levels of Coping

- First Stage: *Non-erosive Coping*, includes insurance, risk-minimizing, loss management, loans, reduction in dietary intake, cheaper foods, reduction of meals, sale of small stock and non-productive assets
- Second Stage: *Erosive Coping,* includes disposal of productive assets, shark loans, sale of large livestock, land and tools, bonded labor arrangements, child labor
- Third Stage: *Failed Coping*, results in destitution, dependency on charity, out-migration, and in extreme cases prostitution, or even sale of children. (WHO, 1998)

What Type of Investment?

- **Needs:**
  - **Methods – start with screening methods**
  - **Non-chemical stressors – what's important?**
  - **Vulnerability – What factors? How important?**
- **Not all or nothing**
- **It starts step by step**

So Why Invest?

- **Demand starting now and will increase**
- **Invest in Agency's relevance/credibility**
- **Fairness**
- **Not mission creep**
- **Can start to buy in at modest levels**

Let's Go for It!

U.S. EPA Workshop on Research Needs for Community-Based Risk Assessment

U.S. Environmental Protection Agency
Main Campus, Building C
Research Triangle Park, NC

October 18–19, 2007

SUMMARY

INTRODUCTION AND OVERVIEW

The U.S. Environmental Protection Agency (EPA) Workshop on Research Needs for Community-Based Risk Assessments was held on October 18–19, 2007, in Research Triangle Park (RTP), North Carolina. The workshop brought together researchers from academia, private industry, regulatory agencies, and government to discuss ongoing and potential research on community-based risk assessments. The workshop also served as a stimulus for increased collaborations among the various researchers and agencies and resulted in improved knowledge of toxins in the environment. Approximately 85 individuals attended the workshop.

Ms. Deborah Segal, EPA, opened the meeting. She welcomed the participants, explained the logistics of the RTP meeting site, and introduced Dr. Hugh Tilson, EPA, National Program Director for Health.

DAY 1: OCTOBER 18, 2007

Welcoming Remarks
Hugh Tilson, U.S. EPA

Dr. Tilson welcomed participants to the meeting and to the RTP facility, which is one of EPA's greener facilities. He explained that there are many Office of Research and Development programs that involve human health, but the Human Health Research Program (HHRP) is the only crosscutting program that addresses multimedia and regional issues. The main objective of the HHRP is to reduce uncertainties associated with the risk assessment process by providing a greater understanding of exposures to environmental stressors and the basic biological changes that follow. The four Long-Term Goals (LTGs) of the program address crosscutting issues that most EPA offices and regions must manage. LTG 2, regarding characterization of aggregate and cumulative risk assessment, is the LTG most applicable to this workshop. EPA is increasingly being called to provide risk assessments for "super chemicals" and to determine how these interact with nonchemical stressors. There are several scientific questions driving research on cumulative risk, including those regarding available biomarkers, exposure models, and information about mode of action and exposure that can improve risk assessments. The question of how cumulative risk can be assessed at the community level has emerged in the previous 2–3 years. This workshop is important for participants to help EPA identify and address priority issues in this area. The program's goals regarding this issue are to: (1) develop tools and a framework to assess interaction of environmental chemical and nonchemical stressors at the community level, (2) support research on assessing exposure and health risk of tribes as a result of cultural practices, and (3) evaluate tools for use in assessing community risk.

Keynote Address: A Perspective on Community-Based Risk Assessments
Linda Sheldon, U.S. EPA

The fundamental concepts regarding community-based risk assessments (CBRA) are that: (1) not all communities are the same, (2) different communities can have differential risks as a result of exposure to environmental contaminants and other stressors, (3) the same community can have differential risks over time, (4) many of EPA's regulations do not consider these differences, and (5) many communities may be at higher risk because they are not adequately protected through environmental regulations and/or distribution of social benefits. Obvious environmental problems prompted the formation of EPA, and the Agency has addressed many environmental concerns successfully, but some communities still remain at risk. The Food Quality Protection Act defines cumulative risk as involving exposure to two or more pesticides, but it is important to consider nonchemical stressor impacts as well. For the purpose of this workshop, cumulative risk can be defined as the combined risks from aggregate exposures to multiple agents or stressors. Cumulative risk assessment is an analysis, characterization, and possible quantification of the combined risks to health or the environment from multiple agents or stressors.

Risk assessors must consider the following questions: (1) How do we identify the most important risks in these communities? (2) How do we assess the cumulative risk in these communities? (3) How do we develop appropriate risk mitigation procedures? (4) How do we demonstrate that we made a positive impact? During the past 3–4 years, the National Exposure Research Laboratory (NERL) expanded its aggregate risk research to include cumulative risk. In doing so, researchers then needed to consider multiple stressors and community conditions. Ecologists always consider communities (i.e., ecosystems) and the entire range of stressors and the condition of the ecosystem as a result of cascading effects. Ecologists have developed models and GIS tools that should be applicable to human health risk assessment; ecologists are valuable resources and potential partners for risk assessors.

During the recent International Society of Exposure Analysis (ISEA) 17th Annual Conference, a number of scientists, including Drs. Marie Lynn Miranda and Marc Serre, presented data on the application of advanced statistical, GIS, and modeling tools to understand exposure and risk. Dr. Miranda is applying spatial tools to CBRA research, and Dr. Serre is examining the spatial and temporal distributions of stressors in the community that allow estimates of pollutants in the community over space and time.

Science, tools, communication, partnerships, and trust are needed to advance CBRA research. To build the science, the source-to-health outcome continuum (environmental release, environmental concentrations, exposures concentrations, target organ dose, early biological effects, adverse outcomes) should guide the core research that is conducted to determine exposure and health risks. An emphasis should be placed on building the tools, including simple and low-cost monitoring methods, GIS tools, models for exposure, comparative databases, tools for interpretation, and primers for conducting assessments and using the tools. These tools must be developed for and used by the community. To build communication with the community, scientists must "keep it simple." Researchers must listen to the community, hear its concerns, and know how the community is different and how this difference impacts community risk. Researchers should describe the science in simple terms, including the issues, what is known, and what can be changed. All researchers must be involved with the community at some level.

A paradigm shift for the Agency is the transformation from decision-making to providing technical assistance to help communities make decisions. Exposure and risk analysis has shifted from analysis done for the community to partnering in a deliberative process. Communities want to know what the possible exposures are and have concerns regarding exposures addressed; this often is more subjective than objective. CBRA is important because researchers have an opportunity to make a difference. It is hard work because CBRA is multidisciplinary, communities must be involved, and impact is an important issue. Technology exists that makes CBRA research possible, and it is improving steadily. This workshop is focused on bringing all of these factors together to improve CBRA research.

Summary of Session—"Exposure Assessment Methods in Community-Based Risk Assessment" From the International Society of Exposure Analysis (ISEA) 17th Annual Conference

Brad Schultz, U.S. EPA

Mr. Schultz summarized the session that he co-chaired with Dr. Valerie Zartarian at the recent ISEA Conference. The session started with a brief overview of the Community Action for a Renewed Environment (CARE) Program, which coordinates EPA program and regional offices and the Centers for Disease Control and Prevention (CDC) via a memorandum of understanding; the program also supplements EPA regulations to support community-driven risk assessment and risk management. One level of CARE research includes risk prioritization and the selection of risk reduction activities, whereas a second level involves risk reduction and quantification of effects. The session also included a CARE technical issues overview by the environmental health assessment co-chair, EPA Regions 1 and 6 case studies, the status of EPA cumulative assessment guidance, and an overview of EPA work on the National Children's Study (NCS). A NERL principal investigator provided a summary of exposure tools research; collaborations with health scientists, risk assessors, and the CARE Program; NCS exposure assessment research; and research involving measurement methods and modeling. One attractive idea that was discussed was the use of Google Earth as a possible CBRA tool. Following these overviews, the session included a discussion regarding community needs and research needs for community-based cumulative risk assessment. Needs identified included: low-cost techniques for community monitoring; methods to assess the impacts on health following an action; information on nonchemical stressors and vulnerability; determination of the value of monitoring and modeling results; better methods to quantify local nonchemical information; tools to characterize dietary exposures at the community level for unique cultural groups; inventories and protocols for assessing nonchemical stressors; and research that is directly usable by the community or its local health or environmental department.

The important issues identified by session participants are as follows: (1) Community-driven assessment is of great importance. (2) Research needs to be usable by communities and their local health departments. (3) Cumulative risk assessment, including nonchemical stressors and vulnerability, is important. (4) Researchers should focus on the main contributors to risk and health impacts and recurring community questions to address cumulative risk. (5) Protocols for nonchemical stressors are needed, and low-cost measurements are important. (6) Dose-response for risk prioritization is important, including comparison with other chemical risks and nonchemical stressors. (7) Quantifying benefits is important for future applications by communities.

SESSION I: DATA NEEDS AND MEASUREMENT METHODS FOR COMMUNITY-BASED RISK ASSESSMENT

Development of Nanoscaled Sensor Systems for Detecting and Monitoring Environmental Chemical Agents

Desmond Stubbs, Oak Ridge Center for Advanced Studies

The Oak Ridge Center for Advanced Studies (ORCAS) is a nonprofit organization operating at the Oak Ridge National Laboratory as a Department of Defense and Department of Energy corporation. ORCAS is a "think and do" consortium of research universities, government, industry, and nongovernmental organizations (NGOs) that partners with local educational institutions to perform research. It focuses on critical issues with strong science and technology content. Problems are framed broadly, taking into account their scientific, technical, economic, social, and policy dimensions to develop research and integrated strategies for addressing those challenges. ORCAS attempts to ensure that its ideas and research are translated into action.

The organization held a workshop in April 2006 entitled "Nanotechnology Applications in Environmental Health: Big Plans for Little Particles" that introduced nanomaterials/nanosensors to the environmental

and ecological health communities. The workshop explored the "art of the doable" in terms of nanotechnology and fostered a discussion of the possible environmental health effects, exposure assessment, and ecological health applications. The result of the workshop was better informed communities with increased likelihood of beneficial interactions in the future. Additionally, Dr. Michael Strano, formerly of the University of Illinois at Urbana-Champaign, published a commentary, *The Case for Nanotechnology*, which provided a list of wants and needs of nanotechnology researchers, including low-detection limits, fluorescence-based techniques, and detection technologies based on nanosystems. The commentary also points out that shelf life varies as a function of the sensing layer, real-time detection is a common feature of nanosensing technology, and binding mechanisms for the sensor platform determine useful life of the technology. Following the workshop, researchers determined several factors that need to be included in a universal system, such as location and activity sensors, an electronic diary, wearable sensors, and portable sensors.

ORCAS and its partners are conducting research on several devices for use in exposure assessment, including passive radio-frequency identification (RFID) tags, an electronic nose (i.e., "dog-on-a-chip"), microelectromagnetic sensors, and interferometric optical sensors. The vapor phase sensor system currently being researched is a piezoelectric, surface-sensitive device. The surface sensitivity is important in vapor detection, and the devices can be used in an array to detect multiple chemical agents. In this system, antibodies to a selected chemical change the three-dimensional signal following detection. Antibodies are immobilized on gold electrodes as a result of their high binding affinity for the antigen. The multi-analyte, multicantilever detection system employs arrays of sensors on a single chip with selective coatings for application-specific programmable sensors. Eighty different chemicals can be detected on a single chip. An array of 300 chips can be formed on one wafer at a cost of $3 per wafer. Built-in redundancies in this system allow comparison, and built-in telemetry provides remote sensing capabilities. The system was tested successfully via a chip implanted in the necks of rats that measured blood-alcohol levels.

The dog-on-a-chip technology was explored as a method for detecting trinitrotoluene (TNT), because the ability to detect TNT is key to reducing fatalities from the 100 million land mines scattered across the planet, tracking explosives materials, and addressing environmental concerns such as water and soil contamination. Two TNT analogs are musk oil and ammonium nitrate; the Transportation Security Administration's current methods are unable to distinguish between TNT and the two analogs. ORCAS researchers used six TNT analogs to perform its proof of concept testing. Three-dimensionally plotting data points over time consistently and definitively distinguished TNT from the five other analogs. This method has the potential to be a universal platform to distinguish various analogs and provide useful data.

Discussion

A participant asked which monitoring device would be most useable in the community. Dr. Stubbs responded that all of the devices are sensitive devices that can be used in the community for acute sensing, but there is a saturation issue that must be considered with long-term use. The participant asked if the $3 cost includes tailoring, to which Dr. Stubbs replied yes.

A participant asked if a library or inventory of chemicals that can be detected is available. Dr. Stubbs responded that an abstract had been published with the inventory, which includes mercury, pesticides, and explosives.

A participant asked if these devices could be used internally to detect stress steroids and endogenous chemicals. Dr. Stubbs responded that investigators currently are exploring internal human use. Assays have been developed but not tested, but this is the direction in which research is heading.

A participant asked for additional information on technologies that can be used for continuous monitoring. Dr. Stubbs stated that an algorithm to measure various factors over time can be built into these devices. Passive RFID tags allow the ability to retrieve data at any point in time. Using array technology also provides the advantage of monitoring over time; however, difficulties arise as a result of size and saturation issues. Researchers are working on a way to purge the device to manage these difficulties. Over-time, near-real-time, and real-time monitoring algorithms can be built into the selective layer.

A participant asked for comments on the known limits to the technology. Dr. Stubbs responded that as these are vapor-measuring devices, they are limited by vapor pressure. How analytes in solution are presented to the device is important. For example, the dog-on-a-chip cannot function in solution, but the RFID tag can be used in liquid by changing the configuration of the electrode. This, however, causes a loss of sensitivity.

A participant commented that the ability to detect the presence and the viability of pathogens is necessary and asked if the research has examined microbial detection. Dr. Stubbs answered that interdisciplinary research that includes microbiologists is necessary, and there has been some work completed on glycoproteins in the cell wall. Chip researchers can collaborate with microbiologists to determine if there is a marker that can be used to indicate viability.

A participant asked what the ease of use is for the community and if these technologies are appropriate for those communities exposed to Superfund sites. Dr. Stubbs replied that the objective of developing these technologies was for this type of exposure. The devices are designed to be wearable, relatively inexpensive, remotely sensed, small, unobtrusive, and without the need for user literacy.

Data Collection Platforms for Integrated Longitudinal Surveys of Human Exposure-Related Behavior
Paul Kizakevich, RTI International

Dr. Kizakevich described research that addresses the need for an electronic diary that was identified following the April 2006 ORCAS workshop described by Dr. Stubbs. He explained that the need for integrated data collection is prompted by the various routes and modifiers of exposure. The overall objective of his research is to develop a personal data collection system that integrates data input streams for collection of human exposure-related behaviors, supports EPA human exposure assessment models, can be easily adapted for other human exposure assessment studies, and possesses sufficiently low burden that most members of the general U.S. household population will be willing to participate in the study for at least 1 week per season for 1 year. At a very basic level, the approach is to: develop diary methodologies for data collection; develop sensors and automation to reduce burden; evaluate methods in the general population; assess, improve, and enhance developments; reevaluate methods and technologies; and facilitate system use for future research studies. The researchers are exploring different methods of collecting data and evaluating these methods by collecting feedback from the population. Four types of diaries—paper, electronic menu, voice, and photo—are being explored via automated technologies such as global positioning systems for outdoor location and movement, wireless beacons for indoor residential locations, wireless Polar chest belts for heart rate monitoring, and accelerometers for movement and compliance monitoring.

Paper, electronic menu, and voice diaries were used to collect dietary data. Paper and electronic menu diaries and automated wireless beacons were used to collect consumer product data. For wireless beacon collection, a fob was assigned to inventoried products; fob-initiated time-stamps were recorded for each product-use event, and an accompanying electronic (PC Pocket) questionnaire was answered by the user. The fobs are a low-burden item to collect data, and the Pocket PC was designed with familiar Web-style menus for ease of use. Additionally, the Pocket PC measures the length of time that it takes users to operate the Pocket PC. Menus can be tailored to each individual user's activities. The photo diary is a

passive diary worn on the belt and takes pictures of the wearer's environment every 2 minutes. The user has the ability to delete photos before uploading to the EPA Consolidated Human Activity Database (CHAD); CHAD is used to categorize the locations in the photos. Another technology employed is locator beacons that are placed throughout the residence in study-designated rooms. The locator beacon syncs with the Pocket PC worn by the user and records the length of time spent in designated locations within the residence.

A pilot evaluation of the above technologies was employed to evaluate the technical performance of technologies and systems as well as participant and analyst burden for various diary modes. The study included 48 participants who for 7 days each used paper, electronic menu, voice, and photo data collection methods; agreed to heart rate and residential location beacon monitoring; and used wireless fobs to record product-use events. Participants represented a range of ages and education levels. Dr. Kizakevich showed examples of activity and dietary data, statistical integration of one individual's activity for 1 day, the top 15 activities reported by mode, and the top 10 food items reported by mode. Participant-reported compliance was underreported compared to the literature and may reflect a training issue. The perceived data-entry burden was greater than actual burden for activity and product-use data collection but lower for pesticide-use data collection. The data-coding burden was recorded as the amount of time the analyst needed to code the data.

The researchers concluded that the burden for menu-based activity and location data entry is low; however, several participants expressed difficulty with the menus. Activity and location reporting were lower than in previous studies. Participants liked using the voice diary, although technical issues affected recording quality. Although most participants liked the photo diary, some participants expressed privacy issues in their workplace. Because some participants reported avoiding activities and limiting diet to reduce entries for paper, voice, and menu diaries, further improvement in menu structures, prompting, and automation may help to improve compliance and avoid behavior modifications.

Discussion

A participant asked if the researchers were moving toward a plan to recommend any of these diaries or a combination of them and if the 7-day data will be available. Dr. Kizakevich responded that the data will be made available following the next round of monitoring. Originally the goal was to determine the best method, but now the plan is to release the data and let individual researchers use this knowledge to determine what method is best for their needs.

A participant asked if any consideration had been given to measuring exposures in children. Dr. Kizakevich replied that some of the diary methods could be simplified and made very specific for children. Activity sets can be tailored to children's activities. The voice method, combined with random prompting throughout the day, is a good method for children.

A participant asked if the resolutions needed to compute exposure for the different approaches had been calculated. Dr. Kizakevich answered that this had not been done in a formal manner. An advisory panel is providing guidance for the modeling studies, and this information may be available following the next round.

A participant asked how easy the sensors were for senior citizens to use. Dr. Kizakevich responded that this type of information has not been separated out, but one senior citizen who originally was confused by the technology became one of the best at using it.

A participant asked if a pictorial version would be available for children, those with language differences, or elderly individuals who cannot see words as well. Dr. Kizakevich answered that this has been discussed. All menu items are database driven and can be translated easily into other languages. One

problem with a pictorial approach is choosing pictures that have universal meaning so that there is no confusion. The platform is designed to be flexible enough to adapt to the needs of children and the elderly.

A participant commented that compliance as a function of education level could be investigated. He asked if there was a problem with care of the devices. Dr. Kizakevich responded that some were dropped, and battery longevity was a problem.

Assessment Methods for Community-Based Risk Assessment
Elaine Faustman, University of Washington

Three types of studies were examined to understand which pesticide exposures were occurring in children. The three types of studies were a community-based participatory research (CBPR) project, a longitudinal multiple sampling project aimed at understanding between- and within-family variability, and a longitudinal cohort study. The community was a unit of analysis as well as the individual. Researchers have only crude statistics of organophosphate and carbamate pesticide usage in various counties in Washington State, whereas the communities have better knowledge of usage. The study investigated four Washington State counties: Yakima, Benton, Franklin, and Walla Walla. Significant amounts of organophosphate and carbamate pesticides are applied each year to apples and potatoes, but the amounts vary each year and are unpredictable.

The CBPR project examined 12 communities, where community is defined as a town or a labor camp. The project utilized the Environmental Public Health Continuum adapted from Dr. Hal Zenick, which helps to facilitate understanding of potential sources and how these sources might lead to exposures at the individual, community, and/or population levels. The Continuum is a framework to educate the public regarding exposures and risks. Project researchers educated more than 6,000 community members at more than 250 events, such as community health fairs. Additionally, community members held more than 1,000 home health parties, and the overall number of participants in all levels of community activities was more than 18,000. Researchers handed out toys to children while teaching them simple things to help reduce their exposure to pesticides. Second and third grade students were invited to enter a drawing contest about methods to reduce exposure, and the winning entries were included in a calendar. Children also were taught handwashing songs. Following the interventions, children were asked evaluation questions to determine if they were receiving the message.

Another project received crucial input from the community regarding vehicle dust. As a result of the community's suggestion, the project model was changed, and this greatly improved the study. This underscores the importance of involving the community during the earliest planning stages. This project used chlorpyrifos metabolites as biomarkers of exposure to understand between-person and mother-child variability. A framework into which factors can be input is necessary to understand this variability. Quantifiable levels of two or more organophosphates in dust were found in 36 percent of homes and 42 percent of cars, and 60 percent of households (defined as home and vehicles together) had evidence of two or more organophosphates in collected dust. Results also indicated that 86 percent of children had quantifiable levels of at least one dialkyl metabolite, and 36 percent had quantifiable levels of both dimethyl and diethyl metabolites. Evidence of a take-home pathway was determined via the observation that workers who thinned crops were more likely than those who did not thin to have detectable levels of azinophos-methyl in their house dust and vehicles, and children of thinners also were more likely to have detectable levels. Contrary to expectations, workers who reported mixing, loading, or applying pesticides had lower incidence of detectable pesticide residues in their homes, vehicle dust, and in their children's urine; this may be a result of mandated safety training for this occupation versus thinners. These data were compared to National Health and Nutrition Examination Survey (NHANES) data, which showed that community farmworkers and their children possessed higher urine concentrations of metabolites versus the NHANES population. Farmworkers and their children also have higher concentrations when

compared to nonfarmworkers and their children within the same community. Year-to-year and crop-to-crop variability also existed. The take-home pathways that increased children's exposure to pesticides were examined so that effective interventions could be planned.

Two longitudinal studies of organophosphate metabolites were used to estimate within and between variability of 3,5,6-trichloro-2-pyridinol (TCP), the major degradation product of chlorpyrifos and chlorpyrifos-methyl pesticides. Multiple measurements in the same person across time permit estimation of both within- and between-person variability. TCP measurements below the limit of detection were treated as left censored in statistical analyses. Results indicated that this method has a poor ability to detect exposure to chlorpyrifos and chlorpyrifos-methyl pesticides. Sources of uncertainty for this method include stochasticity and parameter and model uncertainties. The collection design included three to five sampling events in each of the thinning, harvest, and nonspray seasons. Genotypes and gene expression are being examined in farmworkers versus nonfarmworkers and in parent-child pairs. Biomarkers of susceptibility, exposure, and effect are being determined. A viable framework that integrates these data is needed to educate the community; the methodology underlying this integrated framework tool is complicated. Ascertaining the genotype and phenotype for key chlorpyrifos metabolic genes will improve prediction of exposure response and at-risk individuals in agricultural communities. Determining polymorphisms is important as well. The community asks simple questions (e.g., Can I eat vegetables from my garden?) that have complicated answers; experiments must be designed to answer these relevant public health questions.

Discussion

A participant asked if study participants request and receive individual results. Dr. Faustman replied that all individuals receive their results with a detailed explanation.

A participant asked how researchers managed more complex questions, such as those regarding risk when it is not known, and how doctors in the community were involved. Dr. Faustman responded that pediatricians in the community already are associated with migrant clinics, and there are a lot of collaborations with community doctors. Study participants who are identified as having life-threatening conditions or those who researchers feel need follow-up (i.e., those participants whose risk is unknown) are sent to community doctors.

Dr. Elaine Cohen Hubal, EPA, asked what plans for gene expression had been made. Dr. Faustman answered that no analyses had been completed, but the profiles will be examined together. In this manner, variability should be explained and will be approached in an investigative framework.

A participant asked if drinking water was a possible exposure source. Dr. Faustman replied that her project examined one particular source, but the National Oceanic and Atmospheric Administration (NOAA) was performing similar studies in drinking water.

A participant asked how much has been done to intervene at different points in the cycle. Dr. Faustman explained that interventions are set up to educate people to change their clothes before entering their vehicle or house. The community knows the message, but researchers have not yet worked with the community to take the next step. The participant commented that the EPA framework can be used as a resource to assist with the interventions.

A participant commented that the researchers' plan of explaining all biological results could affect the design of the entire research project. Dr. Faustman explained that it is important to explain the individual results, and the community knows that the researchers are committed to them.

SESSION II: THE BIOLOGICAL IMPACT OF NON-CHEMICAL STRESSORS AND INTERACTION WITH OTHER ENVIRONMENTAL EXPOSURES

Social Stress, Stress Hormones, and Neurotoxins
James Herman, University of Cincinnati

Social stressors do not deprive an individual of essential needs such as oxygen, but these man-made stressors do affect human physiology. Stress responses can be anticipatory or reactive. Anticipatory responses are caused by possible threats to homeostasis and involve innate programs and learning. Reactive responses, caused by direct threats to homeostasis, are generated by reflexive pathways and are true emergencies. Stress responses are remarkably conserved and can be studied in mammals to construct meaningful predictions in humans. Behavior systems, the sympathoadrenal system, and the hypothalamic-pituitary-adrenal (HPA) axis mediate stress responses and release of glucocorticoids. Glucocorticoids are ligands; therefore, where receptors are present, physiological reactions can occur. These receptors are ubiquitous in numerous cell types throughout the body.

The HPA stress axis initiates a redistribution of physiological resources, the short-term benefits of which are energy mobilization and diversion, immune response limitation, and central nervous system (CNS) arousal. Constant stimulation of the stress response has several long-term consequences, such as metabolic disease, obesity, musculoskeletal atrophy, hypothalamic-pituitary-gonadal problems, immune dysfunction, depression, and possibly post-traumatic stress disorder (PTSD). The neurobiological consequences of stress are numerous. Stress-related affective disease states (e.g., depression, PTSD) affect 10 percent of the population in any given year. Stress exacerbates other affective disease states, such as schizophrenia and bipolar disease, and other organic disease processes. Stress hormone secretion can contribute to cell loss and cognitive decline in aging and dementia.

It is important to note that stress and glucocorticoids inhibit neurogenesis, and social stress produces a structural change in dendrites, causing them to shrink, in the hippocampus of nonhuman primates. These observations are consistent with glucocorticoid affects on memory and learning. Additionally, stress reduces neurotrophic factor expression in the cortex and hippocampus of rodents. Researchers also have determined that stress experienced by adults is not the only significant factor; stress experienced *in utero* can lead to depression-related syndrome. Stress can cause changes in the distribution of types of fat that affect obesity and diabetes; the percent of visceral fat is increased on recovery from stress. Following head trauma, glucocorticoids mediate resulting neurological effects; RU486, a potent glucocorticoid inhibitor, has been shown to be protective. Because stress is a predisposing factor in neurodegeneration, stress can be considered a risk factor for Parkinsonism. Stress is a predisposing factor in other neurodegenerative models, including epilepsy, stroke, aging, and Alzheimer's disease. Additionally, toxins have the ability to modulate circulating glucocorticoid levels; exposure to lead leads to elevated circulating glucocorticoids.

In terms of stress as a co-morbid condition, the implications for toxicology are immense. Stress enhances relapse of addictive behaviors (e.g., smoking, alcohol, other drugs of abuse), and social stress promotes abdominal obesity. Prenatal stress interacts with lead exposure to alter brain neurochemistry, behavior, and HPA axis drive. Finally, stress represents one of the "hits" in the multi-hit hypothesis of toxicity. In terms of risk assessment, it is important to note that substance abuse and obesity are prevalent in lower socioeconomic status (SES) populations, and these populations have disproportionate exposure to some environmental toxicants (e.g., lead). Environmental toxicants can modulate glucocorticoid secretion, which in turn enhances neurotoxic processes. Toxins can magnify stress on neurons, and stress can potentiate the effects toxins have on nerves. Therefore, stress and toxins can initiate synergistic effects on nerves.

Discussion

A participant asked if stressors accelerate disease state and aging. Dr. Herman responded that they did, and they also affect metabolic capacity. Another participant asked what effects result from diet, vitamin supplements, and exercise. Dr. Herman replied that antioxidants have been shown to be neuroprotective. Exercise is interesting in that it increases stress on the body while being performed, but decreases stress between exercise periods. It has been shown to have a number of positive effects on various processes.

A participant asked what measurement limitations exist. Dr. Herman answered that the ability to measure stress hormones in an at-risk population in real-time is not yet possible. Blood pressure and heart rate have daily variability and, therefore, are not reliable. Some hormones can be measured in saliva. The participant asked if baseline variability data are available. Dr. Herman responded that inter-individual variability is very high, and he is not aware of any available intra-individual data.

A participant asked if the degenerative process can be reversed after stress is removed. Dr. Herman explained that the best that can be done is to stop the degenerative process; it cannot be reversed.

A participant asked if there are factors that offset stress. Dr. Herman answered that data support that some factors can buffer some of the negative impacts of stress. Exercise and small natural rewards (e.g., sucrose snacks) improve the tone of the HPA axis. The participant asked if multiple stress factors worked together in a synergistic manner. Dr. Herman responded that intensity is a factor, and increased intensity causes increased wear and tear on the body.

A participant asked what is known about changes in stress response with recurrent acute stress. Dr. Herman stated that this was examined in a social stress model. Animals experiencing unfamiliar stress have increased stress response when compared to familiar stress. There is built-in habituation to similar stress and sensitization to other stress.

Intersections of Social Ecology, Neurobehavioral Development, and Environmental Contamination
Bernard Weiss, University of Rochester School of Medicine and Dentistry

Dr. Weiss displayed a chart of rates of return to human capital investment originally devised by Dr. James J. Heckman, a renowned economist; this graphic illustrates the finding that an increase of opportunities at an early age increases benefits during later life, whereas increasing the delay in providing opportunities for youth decreases benefits. Abecedarian academic outcomes indicate that early investment in children increases college graduation rates and decreases the rate of children held back a grade. Rodent experiments showed that enriched environments initiated a change in brain biochemistry and subsequent behaviors; these enriched environments promote neurogenesis in a variety of ways. An important question is whether such effects are counterbalanced by exposure to environmental contaminants.

Dr. David Rall, a renowned environmental health scientist, introduced the concept of the overt effect when he posed the question about whether people would be aware of the toxic potency of thalidomide if the drug did not have overt consequences and instead reduced affected children's intellectual potential by 10 percent. Today, there are a wide variety of human exposures to neurotoxic agents such as heavy metals, pesticides, organic solvents, food and cosmetic additives, air pollutants and endocrine disruptors. Lead exposure is one example of the consequences of not being observant of mounting evidence and/or placing economic concerns above health. There is a direct correlation between increased blood lead levels and decreased IQ. Even a small shift in IQ distribution has significant effects on the population, with a 57 percent increase of those labeled "mentally retarded." Research indicates that blood lead increases reading-level deficits in children, and bone lead increases aggression and delinquency and decreases attention span. The academic and social costs of lead exposure are high, and from an economic standpoint, the cost of low levels of exposure to U.S. society has not been measured. It is the lower SES

groups that bear the brunt of the cost, including increased risk of drug dependency and jail time and decreased lifetime earnings. Low income has been correlated with increased blood lead levels, lower math scores, and increased antisocial behavior when compared to those in higher income levels.

One current perspective on lead is that there is no discernible threshold for lead toxicity. Neurotoxic effects grow more rapidly at low exposure levels, and behavioral disorders are at least as measurable as IQ deficits. Lead toxicity is a lifetime issue; its effects, including cognitive deficits and osteoporosis, persist with aging. The appropriate level of concern should be any value above zero, and lead exposure may diminish the effects of environmental enrichment. Environmental tobacco smoke (ETS) has a similar effect to that of lead. ETS and material hardship have a synergistic effect on the Bayley Mental Development Index, and children of mothers who smoked during pregnancy average a 3 percent drop in IQ. Using 1994 data and extrapolating back to 1964, this drop in IQ translates into a total earnings loss of $720 billion for those 30 years. Insecticide use and prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) also have similarities to lead and ETS exposure. There are commonalities between toxic exposures and social disadvantage; poverty is linked to high exposures to ETS and PAHs as well as lead and other developmental neurotoxicants. Social disadvantage embodies multiple dimensions. Income also affects relative risks of CNS disorders; increases in income and education decrease the effects of affective and anxiety disorders and substance abuse.

Many of the above issues can be linked to deficiencies in maternal care. Low mother-infant interaction is a risk factor for both social-emotional competence and verbal IQ in 4-year-old children. Maternal care has epigenetic consequences. A study on epigenetic changes induced by different styles of maternal behavior revealed that maternal fostering behaviors are nongenomically transmitted to the next generation of female offspring; daughters behave like their mothers. Other studies have shown that prenatal stress increases the effects of lead exposure; some are gender specific and involve altered male sexuality. Layered, cumulative risks exist in disadvantaged communities that deplete cognitive potential. Small changes can accumulate and have effects on the disadvantaged community that exceed effects seen in advantaged communities. A 3 percent rise in IQ would induce reductions in social risks and have enormous benefits on societal outcomes.

Discussion

A participant asked how a proposal to lower the level of concern of lead from 10 μg/dL to 2 μg/dL would translate in practical terms. Dr. Weiss replied that one example would be to remove lead-contaminated drinking water fountains from schools.

A participant asked how to deal with the increasing frequency of potentially contaminated products that are not being measured before import into the United States. Dr. Weiss stated that stabilizing or increasing the budgets of EPA and the Consumer Product Safety Commission would be a start.

A participant asked how decreasing the lead level of concern would be beneficial. Dr. Weiss stated that there is no apparent threshold for lead toxicity.

A participant commented that metals of concern change over time and asked if it would be necessary to address all metals at the same time to be proactive. Dr. Weiss replied that additional research is necessary for all metals and other potential neurotoxicants.

A participant asked about the hypothesis that small levels of toxicants are beneficial because they activate repair. Dr. Weiss explained that depending on the toxin, more negative effects may be seen at smaller doses than at moderate doses. Lead has no threshold, and alcohol has no fetal threshold. This 50-year-old doctrine should be re-examined.

Dr. Tilson commented that in terms of prioritization, quantifying risks so that communities can make decisions is necessary. A national calculation may be a good guideline, but some communities will deviate from this. Dr. Weiss added that disadvantaged communities have increased exposure compared to advantaged communities.

Social Environment as a Modifier of Chemical Exposures
Robert Wright, Harvard School of Public Health

Construction of the CNS, which begins *in utero* and continues throughout childhood, involves the production of 100 billion nerve cells and 1 trillion glial cells; these cells migrate, differentiate, and form synapses. Glial cells are the primary regulator of synapse formation. Synapses transmit signals between neurons. Environmental stimuli cause neurons to fire; neuronal/synaptic firing is a signaling process to mold the synaptic architecture of the brain. The brain builds its network in a partially stochastic manner. Synapses are made by the billions, and in some respects randomly, between neurons. Net gains in synapses occur from fetal life until age 2, and then the number of synapses in the human brain begins to decrease. Synaptic networks are created in a learned process. When synapses fire, neurotransmitters are released into synaptic junctions, which in turn release growth factors and provide a signal that this firing is an important neuronal connection; functional synapses release growth factors, whereas nonfunctional synapses do not release growth factors.

It has been demonstrated that environmental chemicals affect neuronal development. At "low" doses of blood lead (approximately 5–10 μg/dL), lead interacts with protein kinase C and stimulates neurotransmitter release; therefore, neurons fire in the absence of an appropriate environmental stimuli. Additionally, lead mimics calcium, a critical component of nerve signal transmission. Calcium enters neurons during depolarization, but lead blocks calcium channels. The net effect is that lead stimulates nerves to fire in a more stochastic fashion and also inhibits both appropriate and inappropriate neurotransmission. In this manner, lead decreases the efficiency of the underlying synaptic architecture.

Plasticity is the brain's capacity to diminish the effects of toxic insults through structural and functional changes via processes similar to synaptic selection. Plasticity allows for new connections to be made that improve function following an insult. It has been demonstrated that social environment affects neurodevelopment as a result of chronic stress that impairs memory and learning capacity. The handling paradigm of rat behavior illustrates this point; rats that exhibit behaviors that stimulate stress in their offspring have fearful offspring with a brisk HPA stress response. Although the behaviors tend to cluster in family lines, researchers determined that environment, not genetics, plays a large role in influencing the behaviors. Prenatal and early life exposures increase the risk of late-life disease (e.g., hypertension and obesity), and the handling paradigm is an example of neuroprogramming.

Genes are influenced by histone methylation, which usually turns off genes, and histone acetylation, which usually turns on genes. Epigenetics refers to heritable changes in gene expression, such as histone acetylation and methylation, that do not involve changes to the underlying DNA sequences. Epigenetics plays an important role in synaptic pruning via environmental stimuli, and epigenetic marks within neurons change with synaptic activity. This "epigenetic opening" of synaptogenesis to the environment is maximal during childhood, and it is the source of the exceptional cognitive adaptability of humans and possibly the source of its fragility.

A study in rodents examined the effects of social environment and lead. Rats poisoned with lead during lactation (at levels seen clinically in humans) and kept in social isolation had less memory and learning function when compared to lead-treated rats raised in groups with social stimulation. This raised a question about whether reducing stress can be considered a treatment. One study examined mothers' self-esteem when their children were 24 months old; covariates included blood lead, mother's IQ and education, and child's gender. The research showed that the effects of lead varied by mother's self-

esteem; therefore, a positive social environment may mitigate the effects of lead. Another pilot study investigated *in utero* ETS exposure and respiratory outcomes and measured exposure to violence (ETV) and scores on the Wisconsin Card Sorting Test, a neurocognitive test. Children with *in utero* ETS exposure and ETV had significantly lower test scores than those without such exposures. This work led to the establishment of a new birth cohort that will study stress, lead, iron deficiency, and neurodevelopment from a holistic perspective. The long-term goals of that study are to: (1) identify factors that increase and/or decrease metal toxicity, (2) understand the biology of metal neurotoxicity, (3) prevent toxicity, and (4) treat toxicity after it has occurred by finding the appropriate intervention(s).

Discussion

A participant commented on the holistic framework of salutogenesis and the ability of some people in a normal population to overcome exposures. The positive factors that allow them to do this must be explored. He asked what Dr. Wright would like to see more of to further this type of research. Dr. Wright responded that he would like to see Superfund issues considered in risk assessments. Also, society as a whole can decrease the emphasis on economics. There is no budget for social interventions, but there is significant funding for pharmaceuticals. This inequality must be overcome.

Dr. Weiss agreed that interventions later in life are useful because neurogeneration still can occur in the aging brain. It makes economic sense to eliminate contaminants and intervene in cases of contaminated individuals because the plasticity of the brain is great.

A participant asked how EPA could contribute more to risk assessments. Dr. Wright commented that he understood that EPA faces budget cuts and undeserved hostility from the community. If enough research is completed that proves these concepts, the political climate may shift so that there is a mandate for EPA to receive the resources it needs.

SESSION III: STATISTICAL AND MATHEMATICAL MODELING FOR COMMUNITY-BASED RISK ASSESSMENT

Community-Based Risk Assessment—A Statistician's Perspective

Louise Ryan, Harvard School of Public Health

Dr. Ryan reported a past case about Cape Cod citizens living near a U.S. Air Force base who were concerned about excess cancer rates reported on the Upper Cape. There was clear evidence of multiple exposures, but the number of excess cases was small to moderate, the study power was limited by the total population, and no individual exposure assessment was completed. The data were very noisy, and smoothing of the data did not help. It was a very frustrating experience for researchers and the community. Another home allergen study completed in Boston with mother-child pairs found geographical variation in maternal serum immunoglobulin E, but geoadditive modeling suggests a "hotspot" in the city that is confounded by race and poverty. Another study involves cardiovascular response to air pollution that will attempt to determine exposure levels at various points in the Boston area. The goal of the study is to relate predicted exposures to health outcomes (e.g., heart rate variability, arrhythmias, birth weight), and the latent variable formulation is promising. The similarities of these studies include sparse data, a clever combination of data from multiple sources, and the inclusion of spatiotemporal modeling in the study designs.

Mercury is an important human exposure of concern. A controversy arose as a result of conflicting conclusions from two large, well-conducted epidemiological studies. Both studies included prenatal enrollment, had reliable biomarkers of exposure, adjusted for similar important confounders, and measured similar outcomes. The National Academies of Science confirmed the quality of both studies and identified a third. When the focus was shifted from p-values to dose-response estimation, the studies were

less discrepant. Researchers now are using the data to focus on how methyl mercury relates to IQ because IQ has been monetized and relates to other endpoints. A summary of endpoints are available from the three studies and can be divided by domain (e.g., cognition, attention, motor). Graphical representation of all of the data shows that there is not much commonality between the three studies, but adding additional endpoints does show some similarities. Random effects formulation was used to express the data as a set of estimated dose-response coefficients, standard errors, and study and endpoint codes. There are not enough data to reliably estimate separate study and endpoint variance components, so a sensitive analysis was employed as assumptions were varied. This showed that one effect of mercury exposure was decreased IQ. Including the third study's outlying data point made the results appear concordant.

The researchers learned that uncertainty tends to be large when dealing with data collected in real-world communities, and there is a need to measure characteristics of the community in addition to individuals. There are major benefits to using statistical techniques (e.g., Bayesian) to synthesize information from multiple sources. Good tools, such as spatiotemporal and hierarchical models, exist. Researchers must be cautioned against over-interpreting model results and placing too much emphasis on p-values. Many sensitivity analyses must be performed. In the future, researchers should fine-tune spatiotemporal models and initiate work to adjust available tools for combining information so that they are able to handle multiple scales, levels of accuracy, and so forth. Researchers also should design studies about neglected topics. One such project is working on developing strategies for ingenious subsampling to maximize information and minimize cost; another project involves extensions to spatial setting. Spatial design in general is very interesting; including a spatial and a temporal piece allows space and time effects to be separated.

Discussion

Dr. Weiss commented that one of the differences between the two controversial studies was that one examined fish and the other examined whales, which are much more contaminated. The fish study separated the effects of polychlorinated biphenyls, and Dr. Weiss asked if it is possible to separate factors out when they truly are tangled. Dr. Ryan replied that if the characteristics of the studies themselves can be built, then separation of effects and confounding factors may be possible. If the unit of observation is the community, then more communities are needed. Hierarchical models, however, do not have the potential to do this.

A participant asked what was meant by measuring more characteristics of the community. Dr. Ryan replied that examples would be levels of community violence, racism, poverty, and so forth. The sample size is related more to the number of communities than to the number of individuals in the community.

A participant asked if data were being collected to validate the model to ensure that the researchers were not underestimating exposure concentrations and exposures. Dr. Ryan replied that in developing a statistical methodology, agents to test possible underestimation are employed. Her colleagues are beginning to examine this, and it is a complicated issue.

A Multi-Site Time Series Study of Hospital Admissions and Fine Particles: A Case-Study for National Public Health Surveillance
Francesca Dominici, Johns Hopkins University Bloomberg School of Public Health

One broad goal of environmental health scientists is the creation of a national system for tracking population health. Currently, multiple government databases contain substantial amounts of information on the environmental, social, and economic factors that determine health. Research on population health could be rapidly advanced by integrating these existing databases and designing new statistical models that could describe major threats and their causes. These integrated databases and new analysis tools would create a national system for population health research.

Fundamental research topics regarding air pollution and health include determining if there is a risk at current pollution levels, how the risk can be estimated, how large the risk is, and what causes the risk. The objectives of a research project dealing with the health effects of fine air particles are to: (1) assemble a national database of time-series data for the period of 1999 to 2005 on hospital admissions rates for cardiovascular and respiratory diseases, fine particulates, and weather for 204 U.S. counties; (2) develop state-of-the-art statistical methods; (3) develop maps that illustrate relative risk of hospital admissions associated with short-term changes in fine particles; and (4) illustrate how integration and analysis of national databases can lead to a national health monitoring system. National data sources include: the National Claim History Files (NCHF), the Medicare Current Beneficiary Survey, EPA's AirData database, the NOAA Weather Monitoring Network, and the U.S. Census. The project is examining the 204 U.S. counties for which there are matched data. This national cohort is a national study of fine particles and hospital admissions in Medicare. Data include billing claims (NCHF) for everyone older than the age of 65 and enrolled in Medicare, date of admission/doctor's visit, treatment, disease, costs, age, gender, race, and place of residence (by ZIP code and/or county). The study design includes a large sample size to identify sample effects. Thus far, researchers have noted seasonality of hospitalization for chronic obstructive pulmonary disease in Los Angeles, California.

Multi-site time-series studies compare day-to-day variations in hospital admission rates with day-to-day variations in pollution levels within the same community. The study design avoids the problem of unmeasured differences among populations, and key confounders are the seasonal effects on infectious diseases and weather. Semiparametric regressions for estimating associations between day-to-day variations in air pollution and mortality and controlling for confounding factors are used for within-city analysis. Hierarchical models for estimating national-average relative rate and regional-average relative rate and exploring heterogeneity of air pollution effects across the country are used for between-city analyses. For any given city, the researchers attempt to estimate a small pollution effect relative to confounding effects of trend, season, and weather. Challenges include the strong role of other time-dependent factors, the high correlation between nonlinear predictors, and the sensitivity of findings to model specifications. Results have indicated that all effects are small but consistent across location. Respiratory data show a lag before the effects of air pollution occur. Determining the mechanisms, size, chemical components, and sources of particulate matter (PM) toxicity is the next step.

Multi-site time-series studies provide strong evidence of short-term association between air pollution and mortality, and preliminary results from Medicare data (1999–2002) indicate that current air pollution levels affect health. It is important to note that national datasets are powerful resources for assessing the health effects of air pollution, there are statistical models that can integrate information across space and time, and the national average estimates for the effect of PM are robust to various model formulations and statistical methods. Researchers need to be able to reproduce previous findings, test assumptions and robustness of findings, check methodology, and then implement and test new methodologies. One method by which researchers can share data and advance the science is to utilize the Internet to build databases and share methodologies from published papers.

Linking national databases and developing statistical methods that can properly analyze them are essential steps for a successful national public health tracking system. Because of the small risks to be detected and the large number of potential confounders, single-site studies generally display increased statistical error. A national system that routinely analyzes data from multiple locations in a systematic fashion is a promising approach for tracking population health. The explosion of information requires reproducibility and expertise in statistical methods and integration of complex databases.

Discussion

Dr. Cohen Hubal asked if there are current methods that allow national data to be used to inform at the community level. Dr. Dominici replied that extrapolation across similar communities is possible.

Dr. Cohen Hubal clarified that it is possible to borrow strengths of other characteristics that are more relevant and asked if at some point community-level data are too sparse to accomplish this. Dr. Dominici answered that much information may be available in some communities but very little in others. The choice can be made to extrapolate the data and account for differential variations.

A participant asked if having multiple sites gives power to the data. Dr. Dominici responded in the affirmative. The participant commented that layers can be added, but it is limited by hospital admissions. Dr. Dominici replied that this is true, and in terms of linking data together, mortality data also can be acquired, and geographical resolution can be linked with other confounders. The participant asked if that meant that statistical methods are built in. Dr. Dominici replied that they were not at this point, but increased integration makes analysis easier.

A participant commented that this method appeared to work for communities in the range of a population of 1,000–30,000 individuals and asked what the role is for statistics in a community-based setting. Dr. Dominici responded that the goal is to be as practical as possible and link only community data with other available data. The participant asked if it is ever possible to state specifically what factors are responsible for what endpoints. Dr. Dominici answered that it is possible to address data in one community by using other community data to increase power. Dr. Ryan added that complexity depends on what factors are being examined. It is beneficial to reduce citizens' focus on cause and effect, and instead quantify how much risk people may have. A participant stated that context-driven data still are needed.

Dr. Cohen Hubal noted that one goal of this workshop is to identify tools and the gap between tools and answering questions at the community level. It is necessary to be aware of weaknesses and the characteristics of communities that are linked to increased risk of chemical exposure, as well as how more holistic techniques can be used to determine risks. What types of research can and should be done must be determined. One outcome of the workshop should be to determine how research can be done to move forward to answering CBRA questions in a better way.

Risk Assessment/Risk Communication: Understanding the Community
Thomas Schlenker, Public Health Madison-Dane County

Accurate and valid risk assessment cannot be performed unless there is an understanding of the community and communication between the community and researchers. A current CBRA involves human exposure to lead and the associated health risk and will analyze sources, pathways, routes, populations, internal dispositions, endpoints, and risk metrics. There is an enormous history related to lead, which was recognized as a risk by Benjamin Franklin more than 200 years ago. There is much research about lead, and national lead strategies involving EPA and the U.S. Department of Housing and Urban Development have been successful. Substantial funding is available for lead research.

When communicating with communities, it is necessary to tell a story about the "life" of lead in the body to engage them instead of merely providing data and scientific jargon about internal disposition about lead in blood, bone, and the CNS. Community research must involve the knowledge of how people live and their housing, SES, and behavior patterns. In Milwaukee, Wisconsin, community members and the media were focused on lead in water, which was a large distraction because researchers were attempting to focus on other routes of exposure. Policymakers, confused by the media, confounded the problem. Researchers eventually performed a simple study that indicated that there was no correlation between the age of the house and lead in water; this allowed them to focus on the issue of lead in paint. It has been established that increased exposure to lead causes a decrease in IQ; in one cohort, Dr. Herbert Needleman also determined that children not exposed to lead had a seven times higher rate of high school graduation than children with lead exposure.

Manganese is considered beneficial in small doses. In Madison, Wisconsin, manganese in water is a concern because manganese is precipitated out of the water by chlorine and settles into pipes. When there is a change in hydraulics, the manganese re-enters the water and enters homes as a thick, brown sludge. Researchers in Madison used the same model to examine manganese as was used to examine lead. EPA's 2003 *Health Effects Support Document for Manganese* established the health reference level for manganese to be 300 μg/L; in 2004, EPA's *Drinking Water Health Advisory for Manganese* established a lifetime health advisory level, which is much more useful as it defined the concepts of short- and long-term exposure. In the Madison case, one well was perceived as the worst offender in terms of manganese exposure, but two different wells a great distance from the perceived offender had higher levels of manganese. Brown water had unsafe levels of manganese, and some clear water with no visible signs of manganese also had unsafe levels. Additionally, manganese is present in infant formula; foods such as nuts, grains, tea, and soy; and over-the-counter supplements. The predigested form of infant formula contains manganese at the maximum health reference level. Human endpoints for exposure to manganese are generally unknown, but long-term effects are associated with Parkinson's Syndrome and Attention Deficit Hyperactivity Disorder.

Discussion

A participant commented that models that are developed to bring exposure risks to the community level must be understood by community stakeholders and asked how researchers can approach the need to take complicated models and move them into a context where they can be trusted and understood by the community. Dr. Schlenker replied that providing examples of how it has been or can be used at the community level would be best. It is helpful to have community guidance and advice. A participant added that community members do not need to have a technical knowledge of the models to understand the scientific narrative if it is explained in simple terms. Dr. Faustman noted that helpful guidance is available to assist in determining what information is needed to answer community questions.

DAY 2: OCTOBER 19, 2007

Perspectives, Issues, and Needs in Community-Based Risk Assessment
George Bollweg, U.S. EPA

This workshop's definition of CBRA is "a model that addresses the multiple chemical and nonchemical stressors faced by a community, while incorporating a community-based participatory research framework and a transparent process to instill confidence and trust among community members." The National Research Council's 1996 *Understanding Risk* was the first well-organized approach to this type of research. It recognized that not just technical experts perform risk assessment and established steps for synthesis and implementation. CBRA researchers should consider including an evaluation step at the end of each research project. The 1997 *Presidential/Congressional Commission on Risk Assessment and Risk Management, Volume 1*, identified risk management in addition to risk assessment and stressed the importance of the problem/context step of the process. The 2003 EPA *Framework for Cumulative Risk Assessment* provides a useful, streamlined process. Traditional assessments focused on chemical stressors, whereas a new focus is population-based assessments, which emphasize that toxicity is influenced by factors surrounding an individual and not by the toxicant alone.

Different CBRA participants have different needs. Community members need timely answers, whereas researchers need timely publications. Industry participants need to persuade affected parties that risks are "acceptable," and EPA managers need to address Agency management priorities. Additionally, state and regional risk assessors need to conduct credible assessments that address participant needs. Community assessment can require substantial, multidisciplinary commitment and follow-through. Integrated human health risk assessments are necessary that combine the various EPA programs having different focuses and different methods of doing business. For example, the Air Program combines metrics for criteria and

noncriteria pollutant hazards or risk, but some programs may find that combining metrics results in excessive information loss, hidden incompatibilities, subjectivity, interpretability and communication problems, false precision, and so forth.

What may be considered "background" exposures are in the foreground for those exposed; fragmented EPA programs that have a single focus may not consider this. Exclusion of background stressor exposure or susceptibility results in incremental assessments that are irrelevant to some participants. This can be solved by addressing site-specific background susceptibility and/or stressor exposures or, if site-specific information is lacking, deriving a reference human exposure profile to which incremental exposures could be added.

Methods for choosing participants from the community are needed. Additionally, "getting the right science" and "getting the science right" are equally important. CBRA problem formulation must include background (pollutant and/or nonchemical) stressor exposures. What questions the community and the researchers want answered must be considered during the CBRA planning and scoping process. Organizational and political influences (e.g., levels of review, executive branch process control) on EPA's Integrated Risk Information System (commonly known as IRIS) productivity should be evaluated; the levels of review have become too lengthy. The limits of Haber's Rule also must be addressed. In cases where a community's health is determined to be poorer than national averages but is not addressed in EPA exposure and toxicity estimates, an epidemiological investigation is necessary. The problem is how to evaluate this in a CBRA context, and if the assertion is true, how this situation can be addressed. CBRA research needs to examine synergistic or antagonistic toxic effects, determine the feasibility of an all-species hazard index, ascertain the appropriateness of using old datasets for future predictions, establish attributes of successful and unsuccessful deliberative processes, and determine if a formal evaluation step should be included in EPA risk assessments.

CBRA attempts to address real-world human susceptibility, exposure, and risk with inclusive, often resource-intensive deliberative processes. Some conceptual approaches and tools are available, but CBRA needs to process multiple, diverse participant input to better identify and formulate problems; help unify fragmented disciplinary "silos"; and acquire needed science to address questions and issues of participant concern.

Discussion

A participant asked what a graph of return on EPA investment in single agents versus mixtures would look like. Dr. Bollweg responded that he did not know, but it would probably depend on an individual's needs, as some are exposed to single toxicants and some to mixtures.

A participant asked from a cost perspective whether it is better to create a healthy exposure profile or a reference exposure profile. Dr. Bollweg answered that the purpose of the reference exposure profile was to include items that normally were excluded. It is specific to areas and exposures (e.g., dust exposure of individuals living near roads).

A participant noted that comments from communities near contaminated sites show that the communities instinctively understood that their present condition is not good in terms of health and wellbeing. He asked whether Dr. Bollweg purposely excluded the need to satisfy regulations and laws from his presentation. Dr. Bollweg replied yes, because although difficulties have arisen as a result of permit requirements, the situation, especially with Superfund sites, is improving. There is a need to satisfy the goal of the Superfund as well as the conflicting needs of the community; CBRA may be able to integrate these differing needs.

A participant commented that local health departments need to be involved in CBRA projects and asked how to go about securing their participation, as well as the participation of other agencies. Dr. Bollweg answered that resource commitment is important. Also, determining the availability of data is important because some agencies are not authorized to share some data. Prior knowledge that obtaining information is a complex and complicated process may decrease frustration.

Overview of Breakout Groups
Yolanda Sanchez, Association of Schools of Public Health (ASPH) Fellow, U.S. EPA

Ms. Yolanda Sanchez reiterated the definition of CBRA that Dr. Bollweg introduced in his presentation. The three breakout session themes follow the three session topics of the previous day: (1) data needs and measurement methods for CBRA, (2) biological impact of nonchemical stressors and interaction with other environmental exposures, and (3) statistical and mathematical modeling for CBRA. Each breakout group should: (1) identify tools and approaches that may be applied to conduct CBRA, (2) discuss how to incorporate community-based information into traditional EPA risk assessments, and (3) evaluate the research needs for CBRA. To facilitate dialogue in the breakout session, the organizing committee produced charge questions that have been included in the workshop materials.

CONCURRENT BREAKOUT SESSIONS

Breakout Session 1: Data Needs and Measurement Methods for Community-Based Risk Assessment
Moderator: Elaine Cohen Hubal, U.S. EPA
Recorder: Jennifer Hurlburt, The Scientific Consulting Group (SCG), Inc.
Attendees: See Addendum

Dr. Cohen Hubal showed slides depicting two different conceptual models and a list of vulnerability factors to help facilitate thoughts about data needs and measurement methods. Important questions for the group to address are: (1) Are there data currently available? (2) What are the data sources? (3) When is it necessary to collect data in the community? (4) What are the characteristics of the environment and of the individual environmental indicators that researchers must consider?

One issue that is confusing to many, including scientists and those conducting assessments, is how to link individual-level environmental exposures to community-level factors. The actual assessments are conducted on the individual level, but one method to connect the two is to group the individuals together for the analysis of the community-level factors, as they were in the distribution curves from Dr. Faustman's study.

Dr. Faustman asked Dr. Cohen Hubal about the Conceptual Model for Considering Vulnerability in Cumulative Risk Assessment. She wondered about the best method to incorporate the information from Session II: The Biological Impact of Non-Chemical Stressors and Interaction with Other Environmental Exposures into this type of model. For example, where do the potency factors enter for a given stressor, whether it is chemical or nonchemical? Dr. Cohen Hubal responded that that particular model was not intended to represent exposure length. The model's focus was on classification of all of the different factors; there are many issues (e.g., temporal aspects) that must still be addressed in the study.

Mr. Matthew Lakin, EPA, spoke about the distinction between vulnerability and susceptibility. One school of thought is that vulnerability and susceptibility are two different things. Susceptibility includes the biological factors that make a person more predisposed to some type of effect or adverse outcome. Vulnerability includes the environmental characteristics that might lead to a higher level of exposure. These appeared to be only one category in the displayed conceptual model. Dr. Cohen Hubal explained that in that particular study, susceptibility was categorized as a vulnerability.

Dr. Alesia Ferguson, University of Arkansas for Medical Sciences, mentioned that a speaker the previous day had mentioned a theory related to resilience. Would resilience be considered a vulnerability or a susceptibility? Mr. Kent Thomas, EPA, answered that resilience would be considered a susceptibility. Resilience occurs on two levels: (1) at the individual level, resilience is lessened as a person ages, so repeat exposures may be more harmful to older individuals; and (2) at the community level, the community as a whole may have less resiliency to recover from exposures. Dr. Cohen Hubal explained that in her study susceptibility was defined as genetic susceptibility or developmental stage susceptibility. She explained that researchers traditionally have studied the source-to-outcome paradigm, but this breaks down when multifactorial issues are examined. She maintained that researchers need to move from a pathway focus to a focus that includes other issues that are present with these exposures. Dr. Faustman did not agree that the framework necessarily breaks down with these issues. She has worked with engineers who use some interesting vulnerability diagrams, and many issues are involved. For example, community location or conditions are important factors. Dr. Cohen Hubal commented that a researcher could define a system as a community and then specifically examine particular individuals or particular sources, depending on how the boundaries are drawn. If the intent is to identify multiple factors, the researcher must draw the boundaries to ensure that all the inputs and outputs are considered.

Dr. Cohen Hubal explained that she presented the conceptual models as examples to stimulate discussion. What are the important factors at the individual and community levels? Mr. Thomas explained that four categories of data are needed for a cumulative risk assessment: (1) physical environment, (2) social environment, (3) chemical environment, and (4) health (as an outcome or as a risk factor). Dr. Ferguson asked if data needed to be defined to represent risk quantitatively. Mr. Thomas replied that in terms of a screening-level assessment, researchers are able to determine some of the major stressors in the community. The next step is to work toward understanding the relative risk associated with these stressors.

Dr. Cohen Hubal asked if the participants knew of publicly available data that could serve as a starting point for researchers. Dr. Danelle Lobdell, EPA, responded that the data available depend on the research question and on the community. Dr. Faustman asked if any of the participants knew of an example of a known stressor other than air pollution that had been linked to specific communities. Dr. Dina Schreinemachers, EPA, replied that data on various toxicants are available in four states. She suggested that researchers start with ecologic studies and then move to subject-based studies. A series of multilevel, multidisciplinary studies is needed. Dr. Faustman mentioned that the CDC conducts surveillance projects in partnership with universities across the country. Dr. Socoby Wilson, University of South Carolina, added that he recently submitted a proposal to EPA to develop national health indicators.

Dr. Cohen Hubal asked those with experience working in communities if they often found the data they needed when they began their work. She asked for examples of the types of data found and whether the data were general or community-specific. Are there efficient, cost-effective ways to obtain these data? Dr. Ferguson responded that it depends on the chemical of interest and the location. For example, some states collect extensive lead-related data, whereas others collect no lead-related data. Mr. Thomas suggested that researchers start by determining the community's data needs. The next step is to determine what data are available. Dr. Mari Eggers, Montana State University, added that it would be helpful if there were guidelines detailing where different types of data could be found. Mr. Lakin said that he and his CARE Program colleagues currently are drafting guidelines, but there are a lack of data on many topics, and even if data exist, access often is an issue. Dr. Ferguson suggested that data be extrapolated from one community to another. Mr. Lakin added that this approach would involve quantifying the differences between the communities (e.g., accounting for a higher smoking rate in one community). Dr. Faustman suggested compiling a list of available data. Mr. Lakin agreed that a list could be helpful but added that the ultimate goal is to identify quantitative relationships. Dr. Ferguson mentioned the study conducted by Dr. Zartarian as a potential model; Dr. Zartarian and her colleagues identified 100 factors and performed a stacked quantitative analysis. Dr. Wilson suggested developing spatial indices. He

mentioned some other potential models, including the social vulnerability index and a project in California related to risk and environmental health disparities. Mr. Lakin noted that there still is difficulty in linking the information to environmental risks.

Dr. Wilson pointed to the importance of collecting qualitative data as well as quantitative data. Quantitative data alone will miss many important issues, such as the effects of living in a stressful environment. Mr. Lakin agreed that there is value in both quantitative and qualitative data. Mr. Thomas noted that people often do not understand the risks associated with environmental stressors. The perceived risk might be very different from the actual risk. Dr. Ferguson pointed out that perceived risk still is very important, and Mr. Thomas clarified that he was not discounting perceived risk. Dr. Pamela Rao, Farmworker Justice, commented that, as a social scientist, her work always begins with the people in the community; their perceived risks are the starting point. Mr. Lakin asked Dr. Rao if she thought better information on community cohesion, sense of identity, and other factors linked to perceived risk were needed. She agreed that better data are needed and emphasized the importance of starting with qualitative data; without qualitative data the work will have no direction.

Dr. Cohen Hubal asked the participants to share their thoughts on measurement methods. Dr. Faustman commented that GIS data are very useful. GIS data can be used to ensure that areas are not missed in risk assessments. Alternatively, researchers need to be careful when using these data to determine specific risk areas. For example, a 1-mile radius might be identified as an area of concern, but what about the people living just outside of that 1-mile radius? Dr. Wilson pointed out that this is where the qualitative data is useful. Dr. Rao emphasized that research cannot be performed at a distance; it must be done in the community.

Dr. Ferguson asked if there is a point at which there are too much data. Mr. Lakin thought that a better question might be: What is the right amount of assessment? In his work, Mr. Lakin has found that the answer depends on the community. Dr. Cohen Hubal added that the information collected would be based on the community's concerns and conditions present in that community. Dr. Rao suggested starting with the research question. Mr. Thomas pointed out that from EPA's perspective, the question is: Where does the chemical and biological pollutant risk fit into that context? Mr. Lakin stated that it would not be inappropriate to begin a risk assessment by focusing on specific chemical stressors; that can be one of the solutions offered to the community, and if the community identifies other problems, others can be brought in to address those issues.

Dr. Faustman warned that risk comparisons can be dangerous. It is important not to ease the pressures on industry; they are responsible for keeping the environment clean. Dr. Cohen Hubal noted that there are still many compounds in the everyday environment about which little is known. Dr. Lobdell offered lead as an example; it is still not known if any level of lead in the blood is safe.

Dr. Faustman gave an example of a multifaceted problem that would require a multidisciplinary approach: the loss of traditional diets in Native American communities. This loss has resulted in serious health problems for this population. Loss of salmon, a staple of the Native American diet, from the waterways has contributed significantly to this problem. This loss can be represented with data. One aspect of improving the health of Native Americans involves ensuring that the waterways are clean to allow salmon to thrive. This problem requires that various agencies work together.

Mr. Thomas noted that some of the studies presented the previous day had indicated that the effects of exposure could be magnified because of certain attributes and vulnerabilities. What data are needed to understand those vulnerabilities? Dr. Rao asked if he was referring to taking the analysis to the chemical or environmental level. Mr. Thomas clarified that he was referring to the understanding that in a community there are multiple risks, and many of them have little to do with chemical and biological exposures.

Dr. Cohen Hubal asked Dr. Rao about a comment she had made earlier about the difficulty of measuring and characterizing the location of certain groups (e.g., migratory farmworkers) and their related risk. What are the limitations? What measurements are needed? Dr. Rao clarified that she was referring to cumulative risk issues that are not dependent on the individual's geography. Given that, Dr. Cohen Hubal asked how a researcher could define, track, and characterize the community. What should be measured? Dr. Rao responded that in many cases the data needed are not readily available. In her work with pesticides, she and her colleagues have had to use sales records and other clues to gain a better understanding of farmworkers' exposure. Dr. Wilson noted that different data are available on the national and local levels. The CDC has performed much work collecting environmental public health data, and EPA has state-level environmental indicators in areas such as air and water. Dr. Wilson added that the data frequently must be collected at the local level.

A participant asked if there were any case studies of comprehensive cumulative risk assessments that could be used for guidance. Dr. Faustman replied that there are some good examples, including *Community Risk Profiles and Understanding Risk.* Dr. Ferguson commented that as the risk assessments become more advanced, multidisciplinary approaches are needed. Mr. Lakin commented that, from a research needs perspective, taking a community-based participatory research approach is one method by which to ensure a multidisciplinary approach. He stated that more demonstration projects are needed to advance the work in this area. Dr. Wilson mentioned a book called *Street Science* by Jason Corburn that includes examples of community groups using EPA's exposure risk model.

Dr. Schlenker explained that most of his work involves starting with a health outcome and moving backward to find the cause. For example, in Madison-Dane County, as in the nation as a whole, the infant mortality rate (the rate of infant deaths occurring before age 1) for African Americans was more than twice the Caucasian rate. Since 2000, however, the African American infant mortality rate has steadily decreased in Madison-Dane County and is now comparable to the rate for Caucasians. What changed? Dr. Schenkler said that answering that question would involve qualitative research comparing the African American mothers currently in Madison-Dane County to African American mothers in other counties or comparing them to the group of mothers experiencing the high infant mortality rate.

Mr. Lakin mentioned the public availability of certain data, such as the mapping information available through Google Earth. The availability of this information makes it more difficult to mislead the public, but there still is a need to further expand these types of tools in terms of community access to data and interactivity. Dr. Faustman cautioned that with the current accessibility of certain data, researchers must be careful to protect people's privacy. In one case, for example, breast cancer data were mapped by house in a neighborhood, allowing everyone in the neighborhood to see who did and did not have breast cancer. Mr. Lakin thought that address-level data could be very useful in risk assessments.

Dr. Lobdell reminded the group that risk assessments must take into account the realities of the people living in those areas. For example, a factory may be a major polluter, but if the livelihoods of the people in that area depend on that factory, they may not want to address the pollution problem for fear that they might lose their jobs. Dr. Wilson added that many people do not have any other employment options. Dr. Faustman emphasized that communities should not feel as if pollution control is their burden; it is industry's responsibility. Dr. Ferguson said that for health outcomes, it is known that multiple stressors can contribute to health outcomes, even independent of one another. Thus, a chemical stressor could be removed, and the community could still have the same health outcome. If EPA finds that the chemical stressor is not the major problem in a community, then other agencies will need to be involved. Dr. Faustman suggested that other agencies be included from the beginning. Mr. Lakin pointed out that EPA's Ecological Program focuses on many of these multifactorial issues (e.g., how urban sprawl affects the environment); much of this work is performed in partnership with other agencies.

Dr. Wilson suggested using the environmental justice framework. He gave an example of a community in North Carolina that blocked the building of a highway by submitting a complaint to the Department of Justice arguing that their civil rights would be violated if the highway was built because they would not be able to access basic amenities. Are there other innovative approaches like this that could be used to affect change? Mr. Lakin agreed that this was one way to approach the problem. He asked what the research needs are. What is the missing component in terms of current scientific understanding? Dr. Wilson responded that, in this case, the community performed its own cumulative risk assessment. Mr. Lakin encouraged the other participants to think about ways to reproduce this type of success story in other communities.

Breakout Session 2: The Biological Impact of Non-Chemical Stressors and Interaction With Other Environmental Exposures
Moderator: Carrie Knowlton, ASPH Fellow, U.S. EPA
Recorder: Kristen LeBaron, SCG, Inc.
Attendees: See Addendum

Ms. Knowlton explained that the group's first charge was to identify tools and approaches that could be applied to CBRA. Mr. Gary Bangs, EPA, noted that some researchers have obtained access to difficult-to-access datasets. Perhaps a preconstructed, integrated database could be made available by those researchers who have broken barriers. Mr. Ravishankar Rao, EPA, added that Census data could be included. Ms. Kathy Sykes, EPA, mentioned the Interagency Forum on Aging-Related Statistics and noted that there may be a parallel dataset with families and children. Mr. Michael Callahan stated that there are many data in the literature about stress-causing impacts, the effects of violence on asthma, and other topics that EPA normally does not study. Dr. Robert MacPhail, EPA, agreed that there is a significant amount of data on psychoneuroimmunology topics.

Ms. Kacee Deener, EPA, asked if data on biological stressors or social stress in combination with environmental stressors were available. Dr. MacPhail responded that data on both, but primarily on biological stressors, existed. Ms. Deener asked if data on toxins other than lead were available. Dr. Peter deFur, Virginia Commonwealth University, commented that other toxins were included in a background paper.

Mr. Rao noted that some common data are available that may address community concerns. Mr. Bangs shared Mr. Callahan's concern that the right data may not be considered, and some data related to stressors, housing, measurement endpoints are not necessarily found in PubMed. Dr. Weiss stated that the number one factor in health risk is poverty.

Ms. Knowlton asked participants to identify models and technologies in addition to data sources. Mr. Michael Wright, EPA, suggested an examination of group-level effects separate from individual-level effects. Mr. Callahan noted that the Tool for Health and Resilience in Vulnerable Environments, an index of social capital commonly known as THRIVE, is one available tool.

Dr. deFur asked if models in this context were defined as computer-predicted or conceptual. Ms. Knowlton replied that she interpreted the question as computer-predicted, but conceptual models could be considered if necessary. Dr. Robert Hubal, RTI International, explained that one possible method is high-performance computing that simulates community impacts after an event. Dr. deFur added that some comparative behavioral science technologies may be useful, as well as some in the strict ecological sciences. Behavioral science may be a closer topic area that will not necessitate too many interpretations. Dr. MacPhail asked if the ecological science technologies were nonhuman-based. Dr. deFur responded that this was the case and that he was referring to the topic of experimental ecology in which the science examines large animal populations and ecosystems that have population changes as a result of stress (e.g., fragmentation of the ecosystem). These data can be indirectly translated into human systems.

Dr. MacPhail commented that field research provides the opportunity to perform mesocosm studies and gain control over stressors. Dr. deFur agreed that mesocosm studies have potential.

Mr. Bangs asked if social coping models were available that examined the addition of stressors and what factors lead to a failure or breakdown of coping at either the individual or the community level. Dr. Weiss stated that there is a large amount of information in medical and social science literature about the effects of stress on behavior and biology, but there are very few islands of data that have examined the joint effects of these types of displacements and chemical exposure.

Mr. Nigel Fields, EPA, commented that not many researchers were working on these types of effects. He mentioned the Broken Windows Theory, which explores social problems in the community that increase stress, and the Weber Theory, which states that African American women over time experience different impacts on their health than women of other races, and these impacts affect their children as well. There are a number of social models and theories that can be explored.

Dr. Weiss noted the difference between health and conceptual models. A given population has certain parameters and then is stressed by a chemical exposure; the biological basis for this effect has not been examined. This is a whole new field. He cited the example of a Montreal group that is examining an epigenetic model and maternal exposure to chemicals.

Ms. Knowlton summarized that social and environmental information need to be integrated. Dr. deFur commented that much of the research is attempting to address different questions. Dr. Weiss stated that the research addresses nonchemical stressors that are not usually considered by EPA. Mr. Bangs described a workshop in February 2007 that discussed microbial insult of nonimmunocompetent individuals and how these individuals respond. Dr. deFur described work that examines specific contaminants, how the contaminants affect community by source, and how disease affects response.

Dr. MacPhail noted that the stress experienced by home caregivers has not been examined and this phenomenon will increase over time. It is possible that environmental factors could be involved. Stress could result in accelerated aging in the caregiver. Ms. Sykes added that premature death also could be a result.

Mr. Ross Highsmith, EPA, added that epigenetic studies could be added to the toolbox. Mr. Wright suggested that simulation-based techniques and approaches across disciplines could be included.

Ms. Debbie Lowe Liang, EPA, asked if there was a deadline for providing suggestions and input to EPA about these topics. Ms. Deener responded that EPA would accept input for the next month. Ms. Liang asked if input from individuals who did not attend the workshop was acceptable. Ms. Knowlton responded that is was.

Ms. Knowlton moved the discussion to the second charge question and asked the group to consider how CBRA could be added to traditional EPA risk assessments.

Ms. Deener stated that the community can be important in identifying the exposure pathway. Ms. Sanchez, ASPH Fellow, added that the community also can identify exposure sources. Dr. Highsmith commented that they can describe lifestyles that may be outside of expectations. Mr. Wright noted that unique diets could be identified by the community. Ms. Liang stated that community input regarding social stresses is important.

Dr. deFur noted that several methods are presently in use at EPA. The 2003 EPA Community Involvement Conference, which might have identified successful methods regarding community focus

groups and meetings, could be a potential resource. Existing social structures (e.g., church) can be used as a gathering tool to obtain community input.

Dr. Weiss described a Web-based system for CBRA that he developed 10 years ago as the result of an EPA initiative. The reference for the resulting publication is: Weiss B. A Web-Based Survey Method for Evaluating Different Components of Uncertainty in Relative Health Risk Judgments. *Neurotoxicology* 2001;22(5):707-721.

Mr. Fields cited the Casa de Salud in Massachusetts as an example of building community infrastructure and knowledge. Researchers worked with the community and set up house parties to address household chemicals and asthma. It took approximately 3 years to escalate, but it has become a significant health movement about a variety of health topics such as diabetes, HIV/AIDS, and so forth. The mayor has incorporated it into the city's mainframe. Originally, this was a large, disenfranchised population that did not know how to be included but has increased its involvement. Additionally, Drs. Barbara Harper and Anna Hardy are exploring nontraditional routes of exposure during religious rites.

Dr. MacPhail asked if the group's definition of community included a cross-section with all ages, races, gender, education, and so forth represented. Mr. Callahan indicated that this was not necessarily the case. Mr. Bangs stated that the community of interest includes affected individuals, and this might be a very specific group. Dr. deFur added that geography might be one classification.

Dr. Weiss advised that the term community must be defined. He is involved in a community advisory board that has varied members from industry, academia, and county health, who cover all constituents of the community. The community provides input so that the board can determine their environmental health needs. EPA could construct a paradigm in which community representatives are approached and included in an advisory board. Dr. deFur stated that EPA facilitates such committees at cleanup sites. Ms. Sanchez asked if Superfund sites were included. Dr. deFur stated that cleanup sites include both Superfund and non-Superfund sites, as well as states mandated with the Comprehensive Environmental Response, Compensation, and Liability Act (commonly known as CERCLA). There has been mixed success with this approach, and he is not aware of any studies regarding why certain attempts succeed or fail.

Ms. Knowlton asked participants to consider how the information obtained from the community can be used.

A participant asked about the CARE Program. Ms. Knowlton replied that the CARE Program provides communities with tools to determine their most important stressors and technical assistance to implement programs to reduce their own environmental problems. It does not use traditional risk assessment methods.

Mr. Callahan stated that if new information (i.e., community input) is being placed into an old framework (i.e., EPA traditional risk assessment process), then stakeholders and researchers must determine a method to make EPA decision-makers realize that it is in their best interest to consider it, or this will not happen. Dr. deFur agreed that this problem must be solved at the beginning; the same holds true for motivating the community. The inertia of encouraging citizens to be involved and inducing decision-makers to care must be overcome. Dr. Weiss suggested identifying community members who are active and approaching them. Mr. Callahan stated that decision-makers need a reason for change to happen; this is how to attract them.

Dr. Hubal stated that specific, real-time data can be gathered from individuals in the community; EPA managers can be shown the real-time data to drive policy decisions that need to be made. One method may be an interactive survey. Dr. Highsmith cautioned that some individuals and communities have been oversurveyed. It may be possible to find people in the community who have better questions.

Ms. Deener suggested increasing the level of trust between communities and EPA. Dr. deFur agreed that researchers must know the community, or the whole effort will fail. Mr. Fields added that understanding the linkages and social cohesiveness is necessary. Some communities provide services and support for each other; these services make the group functional. It is necessary to characterize the connections and know who provides what services to whom. Dr. deFur summarized this as assessment of social capital.

Mr. Bangs stated that the needs of the EPA risk manager and the needs of the community must be satisfied, or the effort is a failure.

Dr. deFur suggested changing and reshaping the risk management process so that it is not so rigid and stepwise, so that new types of information or processes can be inserted. Currently, the process does not work if it becomes necessary to work backward. The source-to-outcome paradigm cannot be used because the research is not starting with the source.

Ms. Knowlton asked the group to consider ways that this discussion could be expanded to include nonchemical stressors. Dr. Weiss stated that nonchemical stressors have biological effects. This can be the baseline with which to start. Having national standards that may not apply to all communities is not effective. Some communities will be more susceptible because of current health standards. Ms. Sanchez commented that within the environmental justice movement the issue that equal exposure does not equate to equitable exposure has been argued for more than 15 years. Dr. Weiss wondered if it had been argued on a biological basis.

Mr. Bangs replied that a common complaint is that there is no metric. Ms. Sanchez thought that Dr. Faustman currently was involved in a water quality standards decision that affects a tribal community and whether or not the community should have lower standards because of their lifestyle. Mr. Bangs and Dr. deFur asserted that the states of Oregon and Washington had lowered standards; there is a precedence for this type of decision based on community lifestyle.

Dr. MacPhail stated that local newspapers have good knowledge of their own community. They are able to collect and disseminate information that might be useful.

Dr. deFur commented that a review board, comprised of community members with local knowledge, needs to be instated because local knowledge can be a modifier of quantified data. The local community might have a different perspective than what statistics indicate. Mr. Fields agreed and cited the example of a community in which political leaders did not know the practice of Santeria existed; the practice was a source of mercury exposure that would have been otherwise unknown without local knowledge.

Ms. Liang commented that the technique might not work with national standards, but community advisory boards could help EPA determine the most impacted communities. Dr. MacPhail agreed that these boards could help identify at-risk communities, but they will not be able to help researchers understand why the communities are at risk; that is a scientific question. Mr. Callahan stated that community knowledge often is surprising. Ms. Knowlton added that community members know their own health and nonchemical stressors. Dr. MacPhail said a distinction between “identify” and “understand” must be made.

Ms. Knowlton asked the group to consider the third charge question, which asks participants to evaluate research needs for CBRA.

Dr. Highsmith stated that many factors result in stress. The two questions to consider are: Is there a relative potency of stress? What is the relevance of stress to susceptibility? Susceptibility appears to be an issue because it changes how exposures affect susceptible individuals. Mr. Callahan thought that by

taking the approach of relative potency, it is similar to saying that stress is a carcinogen. A different approach must be taken.

Dr. deFur stated that there are decades of clinical and laboratory research on stress response. The largest gap is that no one has asked questions that are specifically applicable to the issues being discussed. Data about stress and about certain environmental contaminants are available, but there are no data regarding how to combine this information or about what factors make individuals or groups more vulnerable. The question of vulnerability can be answered indirectly by gathering data from the individual parts and overlaying or combining them. The research question that has not been asked is what makes individuals in the community more vulnerable; in this regard, community is defined geographically or demographically. He thinks of vulnerability as a specific exposure concentration and of susceptibility as having a biological basis. Dr. Highsmith clarified that vulnerability means sensitivity and that susceptibility is a biological term. Mr. Callahan responded that the 2003 *Framework for Cumulative Risk Assessment* defined vulnerability, susceptibility, and sensitivity. Sensitivity and susceptibility are biological, whereas differential exposure, differential ability to recover, and differential preparedness are not.

Dr. deFur commented that social capital can crumble as a result of changes in infrastructure; therefore, this is one topic that can be considered.

Ms. Deener asked about the usefulness of laboratory animal studies versus community or epidemiological studies. Mr. Callahan replied that epidemiological studies in small communities are not useful because there is not adequate power. What is needed is a combination of laboratory research and community studies. Dr. MacPhail stated that the most beneficial features of laboratory research are the ability to control stressors and to collect tissues and other samples. Stress markers in the brain can be linked to urine and blood, which in turn can be linked to the community.

Dr. Hubal commented that the military is studying PTSD in returning soldiers; this could be a potential source of data. This is a specific community that can be studied, and laboratory data are available because the military is starting to collect them. Dr. MacPhail added that the military is collecting baseline, predeployment data so that comparisons can be made. This community is exposed to many stressors, so it might become too prohibitive to study all of them. Dr. deFur stated that the myriad of combinations also makes it prohibitive.

Dr. MacPhail stated that it is necessary to have a simplified design that can measure complex systems.

Ms. Knowlton asked the group to consider the second part of the charge question regarding important methodological gaps for incorporating nonchemical stressors into traditional EPA risk assessments.

Mr. Bangs commented that a holistic approach is needed. Ms. Deener speculated whether a discussion about incorporating nonchemical stressors into traditional EPA risk assessments can occur if the basic questions are not known. Mr. Fields commented that one gap includes determining what amount of epigenetics and other research will be studied before moving into the community.

Dr. deFur stated that research that tests assumptions is needed, especially the source-to-outcome paradigm. Mr. Callahan commented that the cumulative risk paradigm does not use the source-to-outcome paradigm, so this does not need to be addressed. Research is needed to determine which chemical stressors are important. Dr. MacPhail asked if a ranking for stressors had been investigated. Dr. deFur replied that such a ranking was published in the May 2007 issue of *Environmental Health Perspectives*. Ranking items such as psychosocial factors could change the quantification component or increase efficacy at the receptor level. Ranking also can change the dose-response curve in many ways that could result from vulnerability. There is no mathematical distinction between the ability to respond and the ability to recover, but there is a biological difference.

Mr. Bangs commented that basic biological and epigenetic research about multistressors, as well as a more ecological approach to risk assessment and risk management, is needed. Mr. Callahan agreed that this is how cumulative risk assessment must be done. Dr. deFur commented that specific ecological activities must be considered, and eventually cumulative risk must be a combination of both human health and human ecological risk assessment.

Mr. Callahan stated that there must be a plausible link between cause and effect (i.e., more than random data) for decision-makers to act. Dr. MacPhail added that regulators must realize that this is an exceedingly complicated issue.

Breakout Session 3: Statistical and Mathematical Modeling for Community-Based Risk Assessment
Moderator: Pasky Pascual, U.S. EPA
Recorder: Mary Spock, SCG, Inc.
Attendees: See Addendum

Mr. Pasky Pascual thanked participants for attending the session and asked them to introduce themselves. After the introductions, he noted the need to formalize and quantify data for use in decision-making. There should be a difference between the analytical component in the model and the modeling form itself, because the latter is what informs communities about their risks. If the modeling form is transparent, community members can follow the narrative of the science without needing to understand the analytical component behind it. Duke University is conducting interesting research in this area and has produced very simple, accessible modeling forms that lay people can understand, despite the sophisticated set of analytical techniques behind the models.

Dr. David Reif, EPA, agreed that it is important to present data to communities in a manner that does not involve excessive technical language. How a solution to a problem is represented is more important than the underlying method used to reach the solution. One approach is to use easily accessible infographics, maps, graphs, and pictures.

Mr. Pascual suggested that the HB Model is a ready answer to the first question, which asked participants to identify tools and approaches that could be applied to CBRA. Mr. Schultz responded that HB is a tool that works well for spatial representation of levels but does not incorporate some of the nonchemical stressors or human activity patterns that might affect nonspatial factors such as mixtures, activities, and community practices. Mr. Pascual recommended that the group parse the first bullet point and determine the various issues involved.

Dr. Paloma Beamer, University of Arizona, stated that researchers need better dose estimates and better methods for interpreting biomonitoring. Researchers must get closer to what they are measuring to access risk.

Dr. Janis Johnston, AAAS Science and Technology Policy Fellow, noted that researchers need to account for, quantify, and assess social variables, and these do not easily lend themselves to the process. For instance, if community members are asked to rank a variable from one to five, this creates noncontinuous data; however, if asked to rank a variable from one to 100, the task often seems too difficult and information may be lost. Researchers must decide how to determine which social and contextual variables are important and apply these to the model.

Mr. Pascual agreed that pertinent social variables must be identified in each case and then converted into measurable indicators to include in a model. Dr. Bollweg added that researchers must identify and parameterize variables.

Dr. Reif noted that if researchers have, for example, a suite of measured, quantitative airborne exposures and a suite of questionnaire data, then perhaps a decision tree is a useful approach. This would be an explicit representation of the interaction between a quantitative variable and a socioeconomic variable.

Dr. Beamer mentioned a paper by Ms. Rhona Julien published in the *Journal of Exposure Science and Environmental Epidemiology*, "Pesticide loadings of select organophosphate and pyrethroid pesticides in urban public housing," in which these types of classification regression trees were used to examine pesticide levels in Boston public housing.

Ms. Eloise Mulford, EPA, explained that Native American tribes tend to distrust models provided by EPA. A situation pertinent to tribes is the desire to return to previous diets that consist of more fish. Risk assessment, however, will examine their current diet, the majority of which might be store-bought groceries and not fish from a contaminated river. Researchers therefore must determine how to incorporate the tribes' planned dietary changes into risk assessment models. Another variable has not been included in previous risk assessments for political reasons; Native American tribe members, unlike other Americans, cannot relocate to avoid contaminants. This variable increases risk for this population. Additionally, some tribes have only 100 or 1,000 members, and this is another variable often missed in risk assessment. Researchers must communicate effectively the risk of 1/1000 to a tribe of only 100 members. Dr. Reif responded that perhaps risk could be presented specifically in terms of the risk per 100 fish from the contaminated river.

Mr. Pascual noted that Ms. Mulford's point was consistent with Dr. Johnston's statement: As researchers attempt to formalize problem scoping, they must include the typically nonquantifiable values.

Ms. Mulford explained that tribal members tend to be process-oriented. They care about what is included in the input for risk assessment and also want to know how researchers use the input. Dr. Bollweg interpreted this as a communication challenge. "Black box" processes are not acceptable to tribes, so researchers must improve their ability to communicate complex ideas and the extremely mathematically complicated models behind them.

Mr. Pascual explained that based on the workshop's definition of CBRA, the session participants had been focusing on chemical and nonchemical stressors but needed to examine the two additional building blocks, participatory-based research and transparency. Research starts with a holistic perception of the problems, but analytical modeling tools (such as Analytica and Stella) can identify the primary factors of interest and allow researchers to choose arrows of association and causation.

Dr. Bollweg stressed that modelers must be able to explain their technically complex models in plain English. Mr. Pascual suggested that community members be engaged in building the models, using standard conceptual modeling tools to determine what factors are important. Dr. Beamer added that one of the goals of modeling is to develop a structure that can be applied from one community to another. Ms. Mulford added that researchers frequently explain only simple facts to the public, but the knowledge and understanding of communities should not be underestimated.

Mr. Pascual summarized the important needs that the group had identified:

- Better geospatial characterization of the communities.
- Greater ability to deal with multiple scales (temporal, spatial, or data from multiple sources).
- Greater ability to deal with mixtures versus single insults.
- Better measures of physical variables (e.g., dose).

- Greater ability to identify which social variables to measure and to turn those variables into something quantifiable.

- Better measures of quantified social variables.

- Greater ability to explain models and/or to build them in collaboration with the community to ensure transparency.

Dr. Tilson asked how researchers can validate complex models to ensure they are working. Mr. Pascual commented that working with communities starting from model conception would be useful because different people have different versions of reality. If researchers chart out important variables in a group, they can ascertain that the versions of reality match in a qualitative, consensual manner. Mr. Pascual added that he prefers using Bayesian mathematical approaches to examine the likelihood of the model against data that emerge over time. This provides a formal way to test the ability of the model to capture reality.

Dr. Reif stated that the usual method researchers use to build risk assessment models involves prespecification. This approach works if the community has identified a problem, but if the problem is not known, researchers must measure a number of variables and use an empirical model. He wondered if communities would be amenable to research that determines what is important based on what the collected data show. The important issues might not be those the community initially thought were important, so the strength of the model must outweigh prior conceptions about the problem. Mr. Pascual added that under this premise, when in the laboratory, the goal is to capture all possible data. In the community setting, however, data are expensive, and this approach may not be possible. Dr. Reif explained that there would still be an underlying hypothesis that what researchers are measuring is relevant; determining how factors are important differs from the determination that they are important.

Mr. Pascual added that another significant set of research needs involves verifying and increasing the credibility of models.

Mr. Schultz noted that when communicating with communities regarding dose, interpretation of what the dose means in terms of effect is important. Mr. Pascual added that when building exposure models, researchers must link the dose to both the effect and the source.

Dr. Winona Victery, EPA, mentioned that researchers should consider using data collected by the CDC's Environmental Public Health Tracking Program, which is attempting to link environmentally measured situations with health records. Mr. Pascual agreed that pooling data is beneficial when combining data from multiple sources.

Ms. Segal advised that regarding CBRA and nonchemical stressors, dose-response will shift when other factors are considered. Different communities will show different dose-responses and effects based on socioeconomic disparities.

Dr. Beamer noted that exposures cannot occur without activities that lead to them, and there has been insufficient examination of these activity patterns, such as lead exposure as a result of hand-to-mouth activity, which might be higher in poorer children with fewer toys.

Mr. Pascual mentioned that a key point regarding national models had been raised at previous sessions. The basic approach of HB is to say that there is a common model that applies nationwide, but the value of HB is in viewing the model not as fixed but as stochastic; if data from a certain community are entered, the value can change. There may be a common model with parameters that vary from location to location.

Researchers then can determine why they vary. HB models are single models working on many scales, not numerous different models.

Dr. Johnston advised that when researchers display a map, often some Midwestern states have no data listed, and the people living in those areas will perceive the model as irrelevant. Dr. Roy Whitmore, RTI International, stated that researchers conducting a community-based study from one of those areas could still incorporate data from that area into the model but would need less local data if using related data from other geographic areas. This concept could be explained to the community.

Mr. Schultz asked for clarification on whether Mr. Pascual suggested that researchers use HB methods for the whole process (from chemical concentration to the health effects) or specifically for estimating localized concentrations. Mr. Pascual explained that he was working on a project that was attempting to link societal behaviors and physical changes and determine the valuations, but this was not entirely based on HB methods. One specific set of issues is related to combining data over several dimensions. He asked for assistance from the group on accounting for the interactions of multiple stressors.

Dr. Reif noted that when combining multiple data types, decision tree-based models could be effective. The approach is nonparametric, so these models are not affected by sample size, as are many others. They also are easy to interpret. Dr. Tilson agreed that this approach is reasonable and asked if research had been conducted using physiological measures of stress, such as steroid hormones, in subpopulations to determine if stress is a factor. Dr. Victery noted there was a study that examined cortisol levels and exposure to violence. Ms. Segal mentioned studies by Dr. Cory-Schlecta evaluating the interaction of lead and corticosteroids. Dr. Tilson added that many nonchemical stressors will produce a fairly generic stress response.

Dr. Beamer suggested that researchers incorporate physiologically based pharmacokinetic (PBPK) and physiologically based pharmacodynamic (PBPD) models into CBRA. For instance, if there is a known hormone level shown under stress, researchers could incorporate this with another variable with a physiological basis.

Mr. Pascual added that socioeconomic factors are difficult to desegregate at the individual chemical level and wondered how researchers could handle this issue. Dr. Reif explained that each individual would have a decision tree, and if, for example, there were five causes leading to a particular outcome, community members could be partitioned into five groups. Dr. Pascual stated that the particular behavior activity could serve as a proxy to estimate exposure to mixtures. Researchers might only be able to study the effects of mixtures on a cellular mechanistic level. Dr. Beamer explained that this is why more pharmacodynamics of the PBPD models, as well as data to validate them, are needed. There is a relationship between physiological and sociological responses, and researchers can use mathematics to describe physiological factors.

Dr. Tilson noted that regarding the interaction of chemical and nonchemical stressors, if the stress of the environment produces a response, there will be a differential response to chemical stressors in that population, which offers some biological plausibility about the interaction. Dr. Beamer added that models also can incorporate the unique physiologies of different communities.

Mr. Pascual stated that the group had not discussed incorporating community-based information into the research. Dr. Reif raised the point that when science is presented to the public, what appears to be a decent weight of evidence to the scientists (such as a 95% confidence interval) is not seen as such by community members, because the concepts of uncertainty and variability are not widely understood. Scientists must communicate these concepts so that people understand that the data do apply to them; how to best accomplish this is unclear.

Dr. Bollweg responded that people simply want to know if a stressor is safe or not; they do not want to be given a number. Researchers do not get questions in an objective form, however, and part of the job is to convert these subjective questions into testable variables.

Dr. Victery noted a use for this concept at the local governmental level. For example, during a presentation on manganese in the water supply in Wisconsin, there were questions raised on how the information was ascertained and what indicated that the water was or was not safe. The data should be user-friendly and easy to locate. Researchers have a great deal of information, but it may not be accessible to the affected communities.

Ms. Mulford agreed that communities want to know not only whether the water is safe but how scientists determine this. Dr. Whitmore stated that the answer to whether or not something is safe is not always "yes" or "no." Mr. Pascual agreed that the binary approach does not always work. Using an analytical hierarchical process, researchers might not be able to put a number on what people prefer, but they can decide in an ordinal way what factors are important, weigh different options, and analyze the tradeoff. Communities need to know that scientists frequently do not deal in certainties. In one study, Mr. Pascual worked with fishermen in the Philippines, and decision-making was conducted in the form of a board game. Fishermen learned about the stochasticity of decision-making by playing the game 10 times and making strategic decisions that led to various outcomes.

Ms. Mulford explained that if agencies list options for tribes in terms of pollution cleanup standards, the answer they receive may be that none of the options are sufficient, and only zero pollution is acceptable. A better approach with a community is for the Agency to ask where they should begin to cleanup, and honor that preference.

Mr. Pascual summarized that the four main areas the group had discussed were: (1) selecting the proper analytical tools; (2) using these tools to link exposure back to emissions and forward to effects; (3) taking better measurements on the physical and social sides to feed into the analytical tools; and (4) building up credibility and learning better ways to verify the models used (i.e., "meta" issues).

Dr. Bollweg pointed out that in terms of modeling exposures to mixtures, there are some new methods, such as toxicity testing prioritization using high-throughput methods. Researchers can learn which mixtures (and what concentration of these mixtures) are found repeatedly in large areas. Dr. Reif added that this is being done for toxic gas, and researchers are attempting to extend the method to other domains. Dr. Beamer offered that combining PBPK with Bayesian methods might be a way to integrate some of the issues discussed.

Mr. Pascual suggested that shared, mapable ontologies for organizing data gathered at multiple levels is critical to ensure that information can be shared and located easily using semantic search engines. Dr. Reif added that communities should be able to organize data themselves using a desktop tool. Whoever within a particular community establishes a formal ontology for data sharing can be a contact person at the community level. Ms. Mulford agreed that a tool that the community can operate themselves would be beneficial for tribal communities, many of whom do not like to share data. Dr. Whitmore added that this approach may encourage them to share data, and the National Institutes of Health have developed some relevant data-sharing protocols.

Mr. Pascual concurred that, for example, if Maricopa County in Arizona can see a benefit from using New York data, the community may feel a sense of reciprocation. Shared ontologies allow different versions of reality to be mapped to each other.

CLOSING SESSION

Breakout Reports to the Group
Breakout Moderators

Drs. Cohen Hubal and Faustman summarized the salient points of Breakout Group #1 (See Appendix A, Data Needs Outline). The group identified data needs, especially contextual information. Data needs are driven by community needs. Data access is an issue; existing data may not always be obtainable. A list of available tools would be beneficial. The differences between vulnerability and susceptibility must be explained to the community. Development of indicators and metrics is needed as well as translation of indices to risk. Several options for applying existing tools and developing new tools exist. Detailed case studies are needed, but completion of demonstration projects could address this. One important point is that EPA needs to partner with other agencies, universities, NGOs, and advocacy groups. Communication and the responsibility of a formal report-back to the community are critical, and ethics, training, and education also need to be considered. Additionally, tools and approaches from other fields also should be examined and adopted to CBRA as appropriate.

Ms. Knowlton summarized Breakout Group #2's discussion (See Appendix B, The Biological Impact of Non-Chemical Stressors and Interaction With Other Environmental Exposures Breakout Session Responses). The group discussed scientific and social data that are not integrated and debated the pros and cons of local versus national databases. Participants examined the role of communities in improving data on nonchemical stressors to be used in EPA's traditional risk assessments, including modifying quantitative data and identifying sources and pathways of exposure, activity patterns, and important social stressors and health endpoints. Existing CBPR literature, the 2003 EPA Community Involvement Workshop, and Dr. Barbara Harper's work on Native Americans and treaty rights offer potential models for involving communities. Existing models from the fields of ecology and the social sciences can be built on to incorporate the information gained from national databases and local community input into a risk assessment framework. Participants also suggested that local standards should be developed to accompany national standards, and representatives from the most impacted communities should be present on national advisory boards. Expanded community involvement may not increase the understanding of interactions between chemical and nonchemical stressors, but it will help make associations that drive research. In terms of gaps in knowledge and methodology, more community-based studies and laboratory research are needed to better understand the relationship between environmental and social stress. More research also is needed to determine the most important nonchemical stressors and identify biomarkers of stress and its interactions with chemical exposures. The basic assumptions of the source-to-outcome paradigm must be tested, and researchers must look beyond biological effects and dose-response relationships to incorporate a more ecologic approach, including risk perception and social/economic effects.

Dr. Reif and Mr. Pascual provided the summary of Breakout Group #3's session (See Appendix C, Statistical and Mathematical Modelling). Interpretable solutions exist for answering the question that the community is asking (i.e., translation of results). Credible results are needed, and explanations that underestimate the community's ability and desire to understand must be avoided while respecting the need for nontraditional or advanced methods. Diverse data types, such as environmental, biological, and social, should be included in statistical modeling. The group discussed how to identify relevant data that can be converted to an understanding of indicators, which in turn must be associated with chemical stressors. Data does not need to be stored in one manner as long as it is hierarchical. Analytical issues include how to manage multiple scales and stressors. A general model can be adapted by geographic location and include multiple sources. The Hierarchical Bayesian Model requires more research to increase its ability to add data from multiple sources and scales. One approach to answering the question of mixtures may be to use desegregation techniques to classify lifestyles that serve as proxies for

exposures. It is important to ensure that linkages are appropriate in models. A certain level of transparency is necessary for credibility, and involving the community in building the model will help accomplish this. The preferred outcomes of stakeholders must be identified, and the most important mixtures must be identified and prioritized.

Closing Remarks
Michael Callahan, U.S. EPA

Mr. Callahan commented that he is encouraged that a workshop such as this was organized and noted the quality of the presentations. He provided a brief history of cumulative risk assessment, stating that the first cancer risk report in 1976 has become simplified over the years, and too much emphasis has been placed on some assumptions. Many documents and reports during the subsequent 30 years have provided a revisiting of these assumptions. The Cumulative Risk Technical Panel has commissioned a series of papers regarding issues, case studies, and research needs in cumulative risk assessment. CBRA should be considered a wise investment because communities have begun to request it, EPA's relevance with the public is at stake, and issues of fairness are involved. Environmental justice groups have determined that CBRA is a good tool for communities. Communities are not asking for total risk, and some parts of the assessments the communities desire can be accomplished now.

Some communities perceive that risk assessment does not work for them as a result of items such as cascading effects, nonconventional stressors, and potential losses being omitted from past risk assessments. Physical and spiritual losses that may not be identified in a traditional risk assessment but are important are loss of land, language, spirituality, extended family relationships, sense of belonging, autonomy, rights, self-sufficiency, social structure, connection to land, culture and tradition, identity, history, cultural pride, community, and trust. EPA managers are concerned that including these items contributes to "mission creep," but even under the narrowest view of EPA's mission (i.e., identifying harm as a result of chemical exposures) these factors constitute harm. Public needs are a part of EPA's priority, and EPA needs to respond to the public's question in such a manner that demonstrates understanding and the desire to help.

Vulnerability is the state of being open to harm as a result of the inability to cope with a hazard because of biological susceptibility, prior exposure or disease state, or lack of the resources for resilience. Vulnerability can mean that the exact same exposure can result in widely different effects; equal exposure is not equitable. Three levels of coping exist: (1) nonerosive, (2) erosive, and (3) failed. Risk assessors consider the first two stages but rarely consider the third. This third stage needs to be considered, and communities have known that for quite some time. The third stage provides some range of vulnerability.

CBRA can begin with screening methods that determine important nonchemical stressors and factors that contribute to vulnerability. CBRA is not an all-or-nothing process; it starts step by step. Investment in CBRA is important because demands for it will increase, it will enhance the Agency's relevance and credibility, and it can be entered into in a modest, step-wise manner.

Discussion

Dr. deFur asked what the next step was to continue this discussion on a larger scale and to increase participation by individuals from other parts and outside of the Agency. Mr. Callahan replied that a bottom-up approach was the key; other groups will follow as more dialogues occur.

A participant commented that CBRA is necessary, but quantification is extremely difficult. He asked if quantification is necessary to mitigate risk. Mr. Callahan responded that it is not.

A participant stated that tribes deal with stress in different manners to mitigate final risk. Mr. Callahan agreed that tribal examples are unique, and decision-makers must be aware of the unique harms facing tribes. A participant agreed that community values must be included and prioritized. Mr. Callahan answered that this is what comparative risk assessment is (i.e., how risk is ranked according to values).

A participant suggested that communication within EPA be improved, because frequently after the condition of the environment has been determined, the environment has changed.

A participant agreed with the concept of placing stresses in an economic context because communities need to know the economic consequences of risk. Mr. Callahan noted that poverty is a correlate and may be one way to quantify various issues.

Ms. Segal thanked the presenters for their excellent presentations, which received many favorable comments from attendees. She thanked Dr. Cohen Hubal, Ms. Knowlton, and Dr. Reif for organizing the breakout sessions and Mr. Pascual, Mr. Bangs, Dr. Meta Bonner, Mr. Schultz, and Mr. Lakin for their assistance in organizing the workshop. She recognized Mr. Fields as the impetus for the workshop, and thanked him for his guidance. He and Ms. Deener contributed to the original proposal for the workshop.

Dr. Cohen Hubal thanked Ms. Segal for her organization of the workshop.

The meeting was adjourned at 1:05 p.m.

APPENDIX A: DATA NEEDS OUTLINE

1. Data needs—contextual information

    a. Based on scoping
    b. Community-level concerns
    c. Contextual experts needed
    d. Community-driven versus community-based

2. Data access

    a. Guidance on available sources
    b. Multi-agency
    c. Surveillance (e.g., CDC, multi-university, environmental health tracking)
    d. Indicators
    e. EPA/National Institute of Environmental Health Sciences Children's Centers
    f. Databases that are available and accessible
    g. GAPS AT THE LOCAL LEVEL—AND ACCESS (e.g., NHANES)

3. Definition of community

    a. What important factors characterize similarities/differences among communities (when is extrapolation appropriate)?

    b. What factors are important for characterizing vulnerabilities that may interact to increase risk from chemical exposure?

    c. Geography is not always a defining factor (Not all communities geographically bound, may have shared exposures, vulnerability factors)

4. Development of indicators and metrics

    a. How much data are needed, when do you have enough, when does too much limit interpretation?

5. Translation from indices to risk

    a. What available social indices may be applicable for EPA cumulative risk assessment?
    b. How can these indices be translated in a quantitative way to assess risk?
    c. Importance of both qualitative and quantitative indices

6. Application of existing tools and developing new tools

    a. Geographic information systems have tremendous power but significant limitations in interpretation (often because of data limitations)

    b. Linking with risk

    c. Make tools available and accessible to community (Google Earth-ish)

7. Multidisciplinary teams

8. Case studies

    a. Review, compile
    b. Lessons learned
    c. Use available tools

9. Demonstration projects

    a. Exposure-based (highly exposed)
    b. Outcome-based (specific health issues)
    c. Population-based (particularly vulnerable group)
    d. Solutions-based (identification of positive trend, understand why)

10. EPA needs to partner!! (Responsibility)

    a. National Institutes of Health
    b. CDC/Agency for Toxic Substances and Disease Registry
    c. Department of Housing and Urban Development
    d. Departments of Transportation, Agriculture, Education, etc.
    e. State and local level

11. Partner for context

    a. Universities
    b. Non-governmental Organizations
    c. Advocacy groups

12. Communication

    a. Scoping
    b. Interpretation
    c. Methods of dialogue and interaction

13. Ethics

    a. Balance accessibility with confidentiality
    b. Research needed on de-identifying data to improve access for analysis
    c. Data ownership
    d. Report back
    e. Honor and build off of existing relationships in community!

14. Training/education

    a. Attract more representatives of minority communities to field
    b. Education in academia on how to work with communities and conduct CBPR
    c. Communities need introduction to RA—basic training on environmental health and RA

15. Mining other fields

APPENDIX B: THE BIOLOGICAL IMPACT OF NON-CHEMICAL STRESSORS AND INTERACTION WITH OTHER ENVIRONMENTAL EXPOSURES BREAKOUT SESSION RESPONSES

The following was recorded from the session flipchart.

1. Identify tools and approaches that may be applied to conduct CBRA. (*Workshop participants: We will touch on this question briefly during the breakout session, but if you know of additional research programs or studies that contribute to the body of knowledge, please e-mail them to the facilitator at knowlton.carrie@epa.gov before or after the workshop.*)

- What data are available on biological impact of nonchemical stressors and the associated interaction with environmental exposures?
    - Census data
    - Interagency Forum on Aging-Related Statistics
    - Extensive social/economic data, just not commonly used by EPA
    - Must make a distinction between local data and national databases
    - Stress and caregiver studies give insight into biological effects of stress
- What models exist to help us understand interactions of nonchemical stressors and environmental exposures?
    - THRIVE social capital index
    - Social coping models
    - High-performance computing
    - Epigenetics
- What techniques (i.e., measurement, modeling) can be borrowed from other disciplines to quantify the effects of nonchemical stressors?
    - Computer simulations
    - Methods from social epidemiology
    - Behavioral sciences
    - Ecology (community structure, disturbance)

2. Discuss how to incorporate community-based information into traditional EPA risk assessments.

- How can community-based participatory research frameworks be most useful for identifying important exposures and risks?
    - Modifiers of quantitative data
    - Sources and pathways of exposure

- Lifestyle/activity pattern
- Social stressors/poverty
- Must demonstrate CBRA to be an improvement on traditional risk assessment
- Increased participation → more data

- What methods have been successfully used to collect community-based information regarding nonchemical health issues? Are these methods transferable to any community?
  - Review existing literature and outcome of EPA's community involvement conference
  - *Neurotoxicology* has published an article on a Web-based community risk assessment tool
  - Barbara Harper's work on Native Americans and treaty rights
  - Use of advisory boards representative of communities
  - Create models based on lessons learned
  - Real-time surveys (e.g., sensor technology) can lead to increased participation
  - Need a fundamental change in the risk assessment process
  - Need to look at biological endpoints, not single chemicals
- How can community knowledge be incorporated into EPA's risk management process?
  - Can lead to standards based on local conditions, as opposed to national standards
  - Lead to community-driven programs, designed by and implemented by communities
  - Local media can become involved to disseminate information
  - National risk management and standard setting can incorporate community advisory board with representatives from most impacted communities
- What is the role of community knowledge in understanding the interaction of multiple stressors?
  - Community knowledge may not help us understand interactions but will help make associations that drive research

3. Evaluate the research needs for CBRA.

- What are the most significant gaps in our understanding of the biological impacts of stress and interactions with environmental exposures?
  - Need research on effects of combination of stress and chemical exposure
  - What makes certain communities more vulnerable?
  - Community epidemiological studies need to be combined with animal data and laboratory research

- Biomarkers
- Need to look beyond biological effects at risk perception and social/economic effects
- Need to know which nonchemical stressors are most important

- What are the important methodological gaps for incorporating nonchemical stressors into traditional EPA risk assessments? How can this information be used in risk assessments?
  - Need to test basic assumptions of source-to-outcome paradigm
  - Need an ecologic approach beyond dose-response

APPENDIX C: STATISTICAL AND MATHEMATICAL MODELLING

- Interpretable solutions
- Answer the question the community is asking (translate results)
- Credible results
- Avoid the "black-box" explanation, but respect the need for nontraditional or advanced methods
- Include diverse data types (environmental, biological, social . . .)
- Data sharing (ontologies)
- Can analysis be a two-way street?

ADDENDUM: BREAKOUT SESSION PARTICIPANTS

Breakout Session I

Name	Affiliation
Eggers, Mari	Montana State University at Bozeman
Faustman, Elaine	University of Washington
Ferguson, Alesia	University of Arkansas for Medical Sciences
Hu, Chih-yang	Louisiana State University
Cohen Hubal, Elaine	U.S. EPA
Kizakevich, Paul	RTI International
Lakin, Matthew	U.S. EPA
Lobdell, Danelle	U.S. EPA
Rao, Pamela	Farmworker Justice
Schlenker, Thomas	Public Health Madison-Dane County
Schreinemachers, Dina	U.S. EPA
Thomas, Kent	U.S. EPA
Watkins, Timothy	U.S. EPA
Wilson, Sacoby	University of South Carolina

Breakout Session II

Name	Affiliation
Bangs, Gary	U.S. EPA
Callahan, Michael	U.S. EPA
Deener, Kacee	U.S. EPA
deFur, Peter	Virginia Commonwealth University
Fields, Nigel	U.S. EPA
Highsmith, Ross	U.S. EPA
Hubal, Rob	RTI International
Knowlton, Carrie	ASPH Fellow, U.S. EPA
Lowe Liang, Debbie	U.S. EPA
MacPhail, Robert	U.S. EPA
Rao, Ravishankar	U.S. EPA
Rouse, Tonesia	U.S. EPA
Sanchez, Yolanda	ASPH Fellow, U.S. EPA
Sykes, Kathy	U.S. EPA
Weiss, Bernard	University of Rochester
Wells, Sharon	U.S. EPA
Wright, Michael	U.S. EPA

Session III

Name	Affiliation
Beamer, Paloma	University of Arizona
Bollweg, George	U.S. EPA
Johnston, Janis	AAAS Science and Technology Fellow, U.S. EPA
Mulford, Eloise	U.S. EPA
Pascual, Pasky	U.S. EPA
Reif, David	U.S. EPA
Schultz, Brad	U.S. EPA
Segal, Deborah	U.S. EPA
Tilson, Hugh	U.S. EPA
Victery, Winona	U.S. EPA
Whitmore, Roy	RTI International