



NIH/NIEHS

National Institutes of Health
National Institute of Environmental Health Sciences

WORKSHOP ON

**The Role of Human Exposure
Assessment in the Prevention of
Environmental Disease**

September 22-24, 1999

Doubletree Hotel
Rockville, MD

Sponsored by

National Institutes of Health/National Institute of Environmental Health Sciences
National Toxicology Program

National Institutes of Health/Office of Rare Diseases
National Institutes of Health/National Cancer Institute

Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health

Centers for Disease Control and Prevention/National Center for Environmental Health

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

American Industrial Health Council

Overview

Knowledge of human exposures to agents of potential public health concern is critical for a successful and scientifically sound approach to the evaluation of human health risks resulting from environmental and occupational exposures. This workshop will focus on the exposure-dose-response-disease paradigm and will describe current opportunities and challenges in exposure assessment research, provide usable information on disease-specific chemical exposures that will enhance integration of exposure assessment with epidemiology and toxicology studies, and highlight approaches for further research and the development of effective prevention and intervention strategies. The goals will be to describe current opportunities and challenges in exposure assessment research; enhance integration of exposure assessment with epidemiology and toxicology studies; define research needs, strategies and funding mechanisms; and develop partnerships and mechanisms for increasing stakeholder and community input.

Program

The Role of Human Exposure Assessment in the Prevention of Environmental Disease

September 22-24, 1999 – Doubletree Hotel, Rockville, Maryland

Wednesday, September 22

7:30 AM	Registration/Continental Breakfast	(Foyer, Plaza Ballroom)
8:45 AM-9:30 AM	Opening of Workshop <i>Dr. George Lucier, NIEHS</i>	(Plaza Ballroom)
8:45 AM	Welcome <i>Dr. Kenneth Olden, NIEHS</i>	
9:00 AM	Opening Remarks: Human Exposure Assessment and Environmental Disease <i>Dr. Samuel Wilson, NIEHS</i>	
9:15 AM	Workshop Charge: Utility and Applications of Exposure Assessment <i>Dr. Scott Masten, NIEHS</i>	
9:30 AM-12:15 PM	Plenary Session I: Exposure Assessment in Perspective <i>Chair: Dr. Norine Noonan, USEPA</i>	(Plaza Ballroom)
9:30 AM	Exposure Analysis and Assessment: Progress and Challenges to Achieving Growth in Research and Applications <i>Dr. Paul Lioy, EOHSI</i>	
10:15 AM	Break	(Foyer, Plaza Ballroom)
10:45 AM	Human Exposure Assessment: Challenges and Opportunities for Improving the Linkage between Exposure and Disease <i>Dr. Howard Hu, Harvard University</i>	
11:30 AM	Exposure Assessment: Regulatory and Legislative Issues <i>Dr. Lynn Goldman, Johns Hopkins University and NIEHS</i>	
12:15 PM	Lunch	
1:30 PM- 3:00 PM	Plenary Session II: Emerging Issues in Exposure Assessment <i>Chair: Dr. Gwen Collman, NIEHS</i>	(Plaza Ballroom)
1:30 PM	Gene-Environment Interactions: Bringing Together Molecular Epidemiology and Exposure Assessment <i>Dr. John Groopman, Johns Hopkins University</i>	
2:15 PM	Disease Prevention and Intervention: Role of Exposure Assessment <i>Dr. Richard Jackson, NCEH</i>	
3:00 PM	Break	(Foyer, Plaza Ballroom)
3:30 PM- 5:00 PM	Plenary Session III: Some Federal Initiatives in Exposure Assessment <i>Chair: Dr. Ken Sexton, University of Minnesota</i>	(Plaza Ballroom)
3:30 PM	National Human Exposure Assessment Survey (NHEXAS): Opportunities and Lessons Learned <i>Dr. Judith Graham, USEPA</i>	

- 4:00 PM **A National Occupational Exposure Survey: Planning and Implementation**
Dr. DeLon Hull, NIOSH
- 4:30 PM **National Health and Nutrition Examination Survey (NHANES): A National Biomonitoring Strategy**
Ms. Elaine Gunter, NCEH
- 5:30 PM- 7:30 PM **Poster Session and Reception**
(Twinbrook & Montrose Rooms – Posters; Gazebo & Atrium – Reception)

Thursday, September 23

- 7:30 AM **Registration/Continental Breakfast** (Foyer, Plaza Ballroom)
- 8:30 AM- 5:30 PM **Breakout Sessions**
- Group 1: Aggregate and Cumulative Exposure and Risk Assessment** (Plaza III)
Co-Chairs: Dr. Clifford Weisel, EOHSI, UMDNJ; Dr. Edo Pellizzari, Research Triangle Institute; Dr. Joseph Jacobson, Wayne State University; Dr. George Lucier, NIEHS
- Group 2: Disproportionate Exposures and Disease Impact** (Regency Room)
Co-Chairs: Dr. Allen Dearry, NIEHS; Dr. George Friedman-Jimenez, New York University
- Group 3: Assessing Environmental Influences on Children's Health** (Plaza II)
Co-Chairs: Dr. Steven Galson, USEPA; Dr. Elaine Faustman, University of Washington; Dr. Lynn Goldman, Johns Hopkins University and NIEHS
- Group 4: Integrating Exposure, Dose, Response, and Susceptibility** (Conference Theater)
Co-Chairs: Dr. Martyn Smith, University of California-Berkeley; Dr. Generosa Grana, UMDNJ
- Group 5: Exposure Assessment in Occupational and Environmental Epidemiology** (Plaza I)
Co-Chairs: Dr. Kyle Steenland, NIOSH; Dr. Jonathan Samet, Johns Hopkins University
- 10:00 AM **Break** (Foyer, Plaza Ballroom)
- 12:00 PM **Lunch**
- 1:30 PM **Breakout Group Presentations and Discussion Continued**
- 3:00 PM **Break** (Foyer, Plaza Ballroom)
- 5:30 PM **Adjourn**

Friday, September 24

- 7:30 AM **Registration/Continental Breakfast** (Foyer, Plaza Ballroom)
- 8:00 AM **Public Comment Session** (Plaza Ballroom)
- 9:15 AM-1:15 PM **Plenary Session IV: Conclusions** (Plaza Ballroom)
Chair: Dr. George Lucier, NIEHS
- 9:15 AM **Closing Address: A Public Health Perspective**
Dr. Bernard Goldstein, EOHSI
- 10:00 AM **Break** (Foyer, Plaza Ballroom)

10:30 AM **Reports of the Breakout Groups and Open Discussion** (Plaza Ballroom)

Group 1: Aggregate and Cumulative Exposure and Risk Assessment
 Len Sauers, Procter & Gamble; Kimberly Thompson, Harvard University; Ellen Silbergeld, University of Maryland; Kim Dietrich, University of Cincinnati

Group 2: Disproportionate Exposures and Disease Impact
 Michael Lebowitz, University of Arizona; Bob Lynch, University of Oklahoma

Group 3: Assessing Environmental Influences on Children’s Health
 Mary Kay O’Rourke, University of Arizona; Linda Sheldon, USEPA; Patrick Breyse, Johns Hopkins

Group 4: Integrating Exposure, Dose, Response, and Susceptibility
 Gayle DeBord, NIOSH; Stephen Rappaport, UNC

Group 5: Exposure Assessment in Occupational and Environmental Epidemiology
 Freja Kamel, NIEHS; Laurie Piacitelli, NIOSH

1:00 PM **Wrap-Up and Closing Remarks**
 Dr. George Lucier, NIEHS

1:15 PM **Workshop Adjourns**

Scientific Organizing Committee

George Lucier, NIEHS, Co-Chair	Carol Henry, Chemical Manufacturer’s Association
Scott Masten, NIEHS, Co-Chair	Jane Hoppin, NIEHS
Gwen Collman, NIEHS	Kumiko Iwamoto, NCI
Allen Dearth, NIEHS	Freja Kamel, NIEHS
Gayle DeBord, CDC-NIOSH	Michael Lebowitz, University of Arizona
Lynn Goldman, Johns Hopkins University and NIEHS	Paul Lioy, EOHSI, UMDNJ
Bernard Goldstein, EOHSI, UMDNJ	Laurie Piacitelli, CDC-NIOSH
Judy Graham, USEPA	Len Sauers, Procter and Gamble
John Groopman, Johns Hopkins University	Ken Sexton, University of Minnesota
Bryan Hardin, CDC-NIOSH	Tom Sinks, CDC-NCEH
La Sonya Harris Hall, NIEHS	John Spengler, Harvard University

NIEHS Conference Support Staff

Anna Lee Sabella	Roxanne Hall	Angie Wilson	Alma Britton
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Breakout Group 1

Aggregate and Cumulative Exposure and Risk Assessment

Overview

To achieve scientifically credible and realistic exposure and risk assessments, exposure to harmful agents from all possible sources, through all possible routes, and to agents within a chemical class or of structural similarity which may exert their toxic effects via a similar mode of action must be considered. Chemicals acting by different mechanisms to produce a similar response or adverse health effect and common co-exposures are also important to consider for risk assessment, but for this scenario, an integrated assessment of exposure and risk is far more complex. This session will present current approaches for performing aggregate and cumulative exposure assessments and through case examples will address some of the key issues encountered.

Aggregate Exposure Assessment

Session Chairs

Edo Pellizzari, Research Triangle Institute
Cliff Weisel, EOHSI

Rapporteurs

Len Sauers, Procter & Gamble
Kimberly Thompson, Harvard University

Discussants

Paul Lioy, EOHSI
Stephen Olin, International Life Sciences Institute
Mike Jayjock, Rohm & Haas
Lance Wallace, US EPA
John Adgate, University of Minnesota
Ronald Melnick, NIEHS
David Wallinga, Natural Resources Defense Council

Description

This session will attempt to develop a conceptual framework for which aggregate exposure assessments can be conducted, review the technical design issues that need to be addressed to improve the quality of these assessments, and develop a strategy to address these issues. The product of this session will be a list of potential research projects that would lead to a fundamental scientific improvement in this area. Three presentations will be made to facilitate the discussion. The first two will outline the scientific approaches and tools currently available to prepare aggregate exposure assessments. Since there has been little work in this area outside the pesticide area, a third presentation will comprise a case example of an aggregate exposure assessment of glucose amides. The hurdles in preparing an appropriate aggregate assessment for this instance include 1) understanding the source of all these exposures, 2) specifically quantifying them, and 3) determining how to use this information to accurately derive an aggregate exposure.

Discussion Topics

- Conceptual framework for aggregate exposure assessment
- Strategies and design issues

- Identify gaps that currently prevent the preparation of technically robust aggregate exposure assessments
- Define the research needed to fill these gaps

Agenda

8:30 AM	<i>Introduction and Session Goals</i> Edo Pellizzari, Research Triangle Institute
8:45 AM	<i>Current Scientific Approaches Used to Prepare Aggregate and Cumulative Exposure Assessments</i> Mike Callahan, US EPA
9:15 AM	<i>Guiding Principles for Preparing Aggregate Exposure Assessments</i> Kimberly Thompson, Harvard University
9:45 AM	<i>Case Example Presentation: Aggregate Exposure Assessment of Glucose Amides</i> Drew Badger, Procter & Gamble
10:00 AM	Case Example Discussion
10:30 AM	Break
11:00 AM	Case Example Discussion continued
12:00 PM	Synthesis and Conclusions
12:30 PM	Lunch

Cumulative Risk Assessment

Session Chairs

Joe Jacobson, Wayne State University
George Lucier, NIEHS

Rapporteurs

Ellen Silbergeld, University of Maryland
Kim Dietrich, University of Cincinnati

Discussants

Mike Callahan, US EPA
Claudia Thompson, NIEHS
Linda Birnbaum, US EPA
Deborah Rice, US EPA
Carole Kimmel, US EPA
Claire Coles, Emory University
Joel Ager, Wayne State University

Description

Cumulative exposure refers to the case where exposure to two or more chemicals affect a common endpoint. In some instances, both substances may operate on a single causal pathway

(mechanism); in others, the same endpoint may be affected by different toxicological processes. Cumulative effects can be additive, synergistic, or "subtractive." In principle, subtractive effects can be "protective", in that the exposure of one substance could "cancel out" the deleterious effects of another (as has been claimed for selenium and mercury in certain contexts). In practice, subtractive effects seem more likely to occur when the effects of two substances are less than additive; that is, an adverse effect may be stronger in the presence of both substances but not as great as the sum of the effects of each exposure alone.

Discussion topics

- How can we determine whether two agents operate through a common mechanism of action?
- When several agents affect a common endpoint, how can we determine the degree to which each is responsible for the observed effect?
- How can cumulative exposure be quantified given that the units of measurement will be different for each substance?
- How can toxicological and epidemiological studies be designed to improve our capacity to evaluate cumulative exposures?

Agenda

1:30 PM	<i>Introduction, Overview of the Problem and Session Goals</i> Joe Jacobson, Wayne State University
1:50 PM	<i>A Framework for Cumulative Risk Assessment</i> Beth Mileson, International Life Sciences Institute
2:10 PM	<i>Common Mechanisms of Toxicity: Organophosphate Pesticides</i> Janice Chambers, Mississippi State University
2:30 PM	<i>Case Example Presentation and Discussion: Evidence of additive and less than additive effects from a study of prenatal exposure to PCBs</i> Joe Jacobson, Wayne State University
3:30 PM	Break
4:00 PM	<i>Case Example Presentation and Discussion: Assessing cumulative neurological effects of exposure to methylmercury and PCBs</i> John Risher, ATSDR
5:00 PM	Synthesis and Conclusions

Breakout Group 2

Disproportionate Exposures and Disease Impact

Session Chairs

Allen Dearry, NIEHS

George Friedman-Jimenez, Bellevue Hospital, New York University

Rapporteurs

Michael Lebowitz, University of Arizona

Bob Lynch, University of Oklahoma

Discussants

LaSonya Harris-Hall, NIEHS

Maureen Lichtveld, ATSDR

Eula Bingham, University of Cincinnati

Richard Jackson, NCEH

Rafael Moure, University of Massachusetts Lowell

Adam Finkel, OSHA

Luz Claudio, Mt. Sinai Medical Center

Sherry Baron, NIOSH

Robert Menzer, US EPA

Stephen Lester, Center for Health, Environment & Justice

Steven Lewis, Exxon Biomedical Sciences

Harvey Checkoway, University of Washington

Michael Alavanja, NCI

Description

A number of factors, including access to and quality of health care, nutrition, lifestyle, occupation, education, and socioeconomic status (SES), all may contribute to the present disparities in disease prevalence and health in particular populations. The underlying cause for many of the above may be the gradient in SES that currently exists in this country. This SES gradient may in some instances lead to disproportionate exposures that some populations may experience, e.g., as a result of living conditions, siting of chemical manufacturing/processing facilities, or employment in occupations where disproportionately higher exposures to hazardous substances may occur. An assessment of exposure situations contributing to health disparities and strategies for development of appropriate intervention strategies is planned for this breakout session. This will allow for development of scientifically credible strategies for evaluating disproportionate exposures in affected communities and assessing their contribution to observed disparities in health.

Discussion Topics

- What strategies can be used to document and identify causative factors in disproportionate exposures and/or disproportionate disease risk in community-based studies?
- How can excess risk be reduced?
- Do traditional epidemiologic or clinic-based approaches work when trying to document disproportionate exposures and a linkage to risk/adverse health outcome?
- How can such studies be improved using current exposure assessment methodology?

Agenda

8:30 AM

Introduction and Session Goals

Allen Deary, NIEHS

8:45 AM *Socio-Economic Status and Health Disparities*
Marsha Lillie-Blanton, Johns Hopkins University (invited)

9:00 AM *Strategies for Assessing Disproportionate Exposure*
Thomas Burke, Johns Hopkins University

9:15 AM *Community-Based Risk Assessment and Communication*
Bryan Williams, University of Arizona

9:30 AM *Case Example Presentation and Discussion: Health Effects and Exposure Assessment in Western Oregon Migrant Farmworkers*
Linda McCauley, Oregon Health Sciences University

10:30 AM **Break**

11:00 AM *Case Example Presentation and Discussion: Lead Exposure from Mining Operations in Native American Children in Oklahoma*
Bob Lynch, University of Oklahoma

12:30 PM **Lunch**

1:30 PM *Case Example Presentation and Discussion: Asthma and Indoor/Outdoor Exposures in Latino Children in Los Angeles*
Carlos Porras, Communities for a Better Environment

2:30 PM *Case Example Presentation and Discussion: Occupational Issues*
Howard Frumkin, Emory University

3:30 PM **Break**

4:00 PM *Case Example Presentation and Discussion: GIS-Based Approaches to Environmental Equity Assessment*
Lance Waller, Emory University

5:00 PM **Synthesis and Conclusions**

Breakout Group 3

Assessing Environmental Influences on Children's Health

Session Chairs

Elaine Faustman, University of Washington (Focus area 1)

Mike Firestone, US EPA (Focus area 2)

Lynn Goldman, Johns Hopkins University and NIEHS (Focus area 3)

Rapporteurs

Mary Kay O'Rourke, University of Arizona (Focus area 1)

Linda Sheldon, US EPA (Focus area 2)

Patrick Breysse, Johns Hopkins University (Focus area 3)

Discussants

Judy Graham, US EPA

Jerry Heindel, NIEHS

Dawn Castillo, NIOSH

Joel Mattson, Dow AgroSciences

Leslie Robison, University of Minnesota

Thomas Sinks, NCEH

Description

Both biological attributes and physical behaviors of children make them uniquely susceptible to potential adverse health effects from environmental exposures. This session will focus on the susceptibility of children from the perspective of increased responsiveness to a given dose, increased exposure and dose, and study approaches utilized to address these issues. Three focus areas will form the basis for discussion during this session:

- 1) Susceptibility related to differential sensitivity.** Developing systems or disease states can make a child more responsive than an adult, even with similar delivered doses.
- 2) Susceptibility related to differential exposure and/or dose.** Children's exposures differ from adults in many ways because of differences in behaviors impacting known or suspected exposure pathways, microenvironments, and pharmacokinetics.
- 3) Approaches to investigating exposures of children.** The investigation of exposure and health outcomes in children presents special challenges, with the greatest difficulties occurring at the earliest ages.

Discussion Topics

- Critical windows of exposure
- Routes and pathways of exposure
- Biologically relevant exposure measurements
- Important endpoints to consider when performing exposure-effect studies in children

Agenda

8:30 AM

Introduction and Session Goals

Lynn Goldman, Johns Hopkins University and NIEHS

Elaine Faustman, University of Washington

Mike Firestone, US EPA

9:00 AM

State of the Science Presentations

Susceptibility related to differential sensitivity
Cynthia Bearer, Case Western Reserve University

Susceptibility related to differential exposure and/or dose
Natalie Freeman, EOHSI

Approaches to investigating exposures of children
Richard Fenske, University of Washington

10:30 AM

Break

11:00 AM

Case Studies Presentation and Discussion

Stachybotrys
Ruth Etzel, USDA

Residential exposure of children in New York City to perchloroethylene
Judy Schreiber, New York State Department of Health

12:30 PM

Lunch

1:30 PM

Case Studies Presentation and Discussion continued

Exposure of children to pesticides
Ken Sexton, University of Minnesota

Exposure of socioeconomically disadvantaged children and their parents to PAHs
Nancy Wilson, US EPA

3:00 PM

Break

3:30 PM

Case Studies Presentation and Discussion continued

Retrospective assessment of children's exposure to particulate matter and ozone
Jack Spengler, Harvard University

Urinary biomarkers of organophosphate pesticide exposure in children
Mary Kay O'Rourke, University of Arizona

5:00 PM

Synthesis and Conclusions

Breakout Group 4

Integrating Exposure, Dose, Response, and Susceptibility

Session Chairs

Martyn Smith, University of California-Berkeley
Generosa Grana, University of Medicine and Dentistry of New Jersey

Rapporteurs

Gayle DeBord, NIOSH
Stephen Rappaport, University of North Carolina

Discussants

Bernard Goldstein, EOHSI
John Groopman, Johns Hopkins University
Larry Needham, NCEH
Scott Masten, NIEHS

Description

The risk of an adverse health outcome after exposure to environmental agents is a function of the type, magnitude, duration and pattern of exposure but also of individual susceptibility to the exposure in question. In addition to factors such as age, nutrition, and socioeconomic status, genetic makeup plays a key role in individual susceptibility. A number of gene products have been found to influence the distribution or metabolism of chemical agents leading to individual variation in internal dose to the target tissue (pharmacokinetics). The spectrum of biological response leading to pathology (pharmacodynamics) is also genetically determined and would be expected to vary between individuals. In a few cases, linkage between expression of variant gene products in the population and individual differences in pharmacokinetics, pharmacodynamics, or the risk of disease have been established. This session will focus on a number of issues relevant to integrating exposure information, biological measures of dose, biological response, and genetic susceptibility from both population-based studies and animal models to improve predictions of risk.

Discussion Topics

- Relating exposure to dose and dose to response
- Incorporating susceptibility into exposure-dose and dose-response assessment
- Linking genetic polymorphisms with gene function and relevant exposures
- Genetic variation in exposure-dose and dose-response relationships as a determinant of risk
- Interaction of increased exposure and increased sensitivity in specific populations

Case studies and Presenters

Integrating from Exposure Forward: Benzene, metabolic polymorphisms, and leukemia risk

Martyn Smith, University of California-Berkeley
Nathaniel Rothman, NCI
Stephen Rappaport, University of North Carolina
Eric Johnson, Tulane University
Bob Sonawane, US EPA

Integrating from Disease Backward: Breast cancer, environmental exposures, and susceptibility factors

Generosa Grana, University of Medicine and Dentistry of New Jersey

Michelle Bennett, NIEHS

Kirsten Moysich, Roswell Park Cancer Institute

Coral LaMartiniere, University of Alabama-Birmingham

Ainsley Weston, NIOSH

Ruth Allen, USEPA/NCI

Agenda

8:30 AM

Introduction and Session Goals

Martyn Smith, University of California-Berkeley

Generosa Grana, University of Medicine and Dentistry of New Jersey

8:45 AM

Exposure to Dose Modeling

Jerry Blancato, US EPA

9:00 AM

Incorporating Susceptibility into Integrated Exposure-Dose-Risk Models

Hisham El-Masri, ATSDR

9:15 AM

Benzene Presentations and Discussion

10:30 AM

Break

11:00 AM

Benzene Presentations and Discussion continued

12:30 PM

Lunch

1:30 PM

Breast Cancer Presentations and Discussion

3:30 PM

Break

4:00 PM

Breast Cancer Presentations and Discussion continued

5:00 PM

Synthesis and Conclusions

Breakout Group 5

Exposure Assessment in Occupational and Environmental Epidemiology

Session Chairs

Kyle Steenland, NIOSH
Jonathan Samet, Johns Hopkins University

Rapporteurs

Freja Kamel, NIEHS
Laurie Piacitelli, NIOSH

Discussants

Jane Hoppin, NIEHS
Carol Henry, Chemical Manufacturers Association
Leslie Stayner, NIOSH
Aaron Blair, NCI
Rebecca Roper, MSHA
Irva Hertz-Piccioto, University of North Carolina
DeLon Hull, NIOSH
Kumiko Iwamoto, NCI
Manuel Gomez, American Industrial Hygiene Association
Joel Bender, Owens-Corning (retired)
Pam Susi, Center to Protect Workers Rights

Description

Occupational and environmental epidemiologic studies represent two approaches to studying associations between exposure to toxic agents and human health effects. An adequate and accurate assessment of exposure to the agent(s) in question is essential for establishing association (or lack thereof) between exposure and health endpoints. The two types of studies deal with different populations, exposures that differ in route and magnitude, and different sources and types of information. This breakout session will compare the two types of studies for the purpose of developing strategies that can enhance the utilization of both in environmental health research. Three case studies will be used as examples: arsenic, diesel exhaust, and radon.

Discussion Topics

- What are the similarities and differences in assessing exposure in occupational and environmental studies?
- What are the advantages and limitations of each study type for relating exposure to health outcomes?
- What tools have been developed in occupational studies that can be applied to environmental studies, and vice versa?
- What difficulties are encountered in extrapolating from high to low exposure scenarios? From workers to the general population?

Case Studies, Presenters, and Issues

Arsenic

Claudia Hopenhayn-Rich, University of Kentucky (health effects)
Rebecca Calderon, US EPA (environmental exposure sources)

David MacIntosh, University of Georgia (multimedia exposures; NHEXAS)
Michael Waalkes, NIEHS (mechanisms)

Arsenic provides a good example for contrasting exposure pathways in occupational and environmental studies and for discussing the implications for research on health outcomes. Key issues to be addressed include:

- There are different routes for occupational exposure (inhalation) and environmental exposure (ingestion from drinking water or food).
- Measurement issues: organic vs inorganic arsenic, different valence states, multiple exposure routes, and interference from biological interactions. What is the best exposure metric?
- Since arsenic is not a persistent compound in the body, how can we estimate chronic exposure? Can we reconstruct dose? Is it possible to use historical data on arsenic in drinking water to reconstruct cumulative dose? Can we use questionnaires to ascertain exposure history?
- There are health outcomes with significant public health implications: bladder cancer, lung cancer, diabetes, reproductive effects. Why are different outcomes seen for occupational and environmental exposures? Are there ecological correlates?
- Does genetic susceptibility (eg, methylation) affect the relationship between exposure and health outcomes?

Radon

Jonathan Samet, Johns Hopkins University (occupational vs environmental exposures)
Dale Sandler, NIEHS (indoor radon)
William Field, University of Iowa (indoor radon)
David Brenner, Columbia University (mechanisms)

The discussion of radon will focus on the different problems encountered in measuring exposure in occupational and environmental settings and the difficulties of dose extrapolation from one context to the other. Key issues to be addressed include:

- The occupational environment in mines differs from the home environment because other exposures including dust and diesel exhaust are present. These exposures are carcinogenic in themselves and also affect radon exposure, since radon daughters (the active agents) adsorb to particles. These particles serve to keep the radon daughters in the air longer and also act as delivery agents to the lung.
- Activity levels, which can affect respiratory rate and hence exposure, differ between the occupational and environmental settings.
- Ideally radon measurement in environmental studies would require assessment of all former homes but many of these cannot be accessed. Also, dosimeters need to be placed for at least a year.
- Measurement of radioactivity embedded in glass could theoretically provide an integrated measure of exposure in homes, but this measurement is problematic, since deposition of the radioactivity on the glass is affected by airborne particles, for example from cigarette smoke.

Diesel Exhaust

Susan Woskie, University of Massachusetts Lowell (exposure of railroad workers)
Kyle Steenland, NIOSH (exposure of truck drivers)
Aaron Cohen, Health Effects Institute (lung cancer and other respiratory disease)
Joellen Lewtas, US EPA (mechanisms)

The discussion of diesel exhaust will focus on problems encountered in occupational studies and possible lessons for environmental studies. Key issues to be addressed include:

- Retrospective dose reconstruction in occupational studies
- Probabilistic exposure assessment
- What are the difficulties in estimating dose due to variable exposure characteristics? How does exposure vary between sources and over time? What is the best surrogate to represent a complex exposure: respirable particulates? elemental carbon?
- What exposure metric is relevant to the disease process: average, cumulative or peak exposure?
- How well have we defined the relationship between exposure and health outcomes? Are low-dose exposures in occupational studies comparable to exposures in the general population?

Agenda

8:30 AM	<i>Introduction and Session Goals</i> Kyle Steenland, NIOSH
8:40 AM	<i>Overview: Definitions and Issues</i> Jonathan Samet, Johns Hopkins University
9:00 AM	<i>Arsenic Presentations and Discussion</i>
10:30 AM	Break
11:00 AM	<i>Arsenic Presentations and Discussion continued</i>
11:30 AM	<i>Radon Presentations and Discussion</i>
12:30 PM	Lunch
1:30 PM	<i>Radon Presentations and Discussion continued</i>
2:30 PM	<i>Diesel Exhaust Presentations and Discussion</i>
3:30 PM	Break
4:00 PM	<i>Diesel Exhaust Presentations and Discussion continued</i>
5:00 PM	Synthesis and Conclusions