Air Toxics Exposure and Health: HEI Studies

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Lovelace Respiratory Research Institute
2425 Ridgecrest Drive SE, Albuquerque, NM 87108

- **Air toxics**
  - **Are air pollutants that may pose a risk to human health or the environment. They include 188 chemicals listed under Section 112(b) of the CAA as hazardous air pollutants (HAPs).**
- **EPA approach to air toxics:**
  - **Identify and list HAPs**
  - **Develop technology-based standards**
  - **Implement risk-based program to assess residual risks after standards are met.**

- **Historically**
  - **We have assessed the toxicity of single compounds**
    - **In the environment: 6 criteria pollutants**
    - **In the workplace: various occupational compounds**
- **Now**
  - **We are faced with assessing the toxicity of 188 air toxics (33 are the "dirty thirty").**
  - **Some listings, such as polycyclic organic matter, include hundreds of possible compounds.**

Traditional Approaches are Designed for Single Compounds

- **Hazard Identification**
  - **What toxicities can be caused by the agent?**
- **Dose/Response**
  - **How much of the agent is required to cause the toxicities?**
- **This information is used along with exposure assessments to complete risk characterization.**

We already have information on some compounds because of occupational concerns

- **Benzene**
- **Butadiene**
- **Metals**
- **Some aldehydes**
- **Acrolein**
- **Hexane**
- **Phosgene**
- **Toluene**
- **Vinyl chloride**
- **Lead**

How Much is in the Ambient Air?

	1,3 Butadiene	Benzene
Baltimore[a]	90 ppt	1.3 ppb
Rural Maryland[a]	9 ppt	0.3 ppb
Cigarette smoke[b]	~1 ppm	~ 5 ppm
Inside toll booth (AM)[c]	1.6 ppb	2.6 ppb
Outside tool booth (AM)[c]	6 ppb	7.7 ppb

[a]Based on 1996 EPA model, median level.
[b]Pankow *et al., Chem. Res. Toxicol. 17*: 805-813, 2004.
[c]Sapkota *et al., Environ. Sci. Technol.* (in press).

Disadvantages of Single Compound Approach

- **Time**
  - **We have spent decades on the six criteria pollutants.**
  - **How long will it take to get the information we need for 188 air toxics?**
- **Reality**
  - **People inhale mixtures, not single compounds.**

An Alternative Approach for Environmental Pollutants

- **Sources emit mixtures of air pollutants**
- **Sources can be regulated to reduce emissions**
- **Test for toxicity of source-specific mixtures**

Regulatory Needs

- ***Urban Air Toxics***
- ***Indoor Air Toxics***
- ***Stationary Source Air Toxics***
- ***Mobile Source Air Toxics***

Urban Dirty 33

Acetaldehyde	*Coke Oven emissions*	*Mercury Compounds*
Acrolein	*1,3-Dichloropropene*	*Methylene Chloride*
Acrylonitrile	*Dioxin*	*Nickel Compounds*
Arsenic Compounds	*Ethylene Dibromide*	*Perchloroethylene*
Benzene	*Ethylene Dichloride*	*Polychlorinated biphenyls*
Beryllium Compounds	*Ethylene Oxide*	*Polycyclic Organic Matter*
1,3-Butadiene	*Formaldehyde*	*Propylene Dichloride*
Cadmium Compounds	*Hexachlorobenzene*	*Quinoline*
Carbon Tetrachloride	*Hydrazine*	*1,1,2,2-Tetrachloroethane*
Chloroform	*Lead Compounds*	*Trichloroethylene*
Chromium Compounds	*Manganese Compounds*	*Vinyl Chloride*

Indoor Air Toxics

Acetaldehyde	*Carbon Tetrachloride*	*Formaldehyde*
Aldrin	*Chlordane*	*Heptachlor*
Arsenic	*Chloroform*	*Methyl Chloride*
Benzene hexachloride	*Dichlorvos*	*Pechloroethylene*
	Dieldrin	*Trichloroethylene*

Stationary Source Air Toxics

Acetaldehyde	*Dioxane*	*Methyl Ethyl Ketone*
Acrolein	*Dioxins*	*Methyl Isobutyl Ketone*
Acrylonitrile	*Epichlorohydrin*	*Methylene Chloride*
Antimony	*Ethylene Dibromide*	*Naphthalene*
Arsenic	*Ethylene Dichloride*	*Nickel Compounds*
1,3-Butadiene	*Ethylene Glycol*	*2-Nitropropane*
Benzene	*Ethylene Oxide*	*PAHs*
Cadmium Compounds	*Formaldehyde*	*Perchloroethylene*
Chlorine	*Furanes*	*Phenol*
Chloroform	*Glycol Ethers*	*Styrene*
Chloroprene	*Hexane*	*Toluene*
Chromium Compounds	*Hydrochloric Acid*	*Toluenediisocyanate*
Cobalt	*Hydrocyanic Acid*	*1,1,1-Trichloroethane*
Cresol	*Lead Compounds*	*1,1,2-Trichloroethane*
Cumene	*Manganese Compounds*	*Trichloroethylene*
Dibenzofurans	*Mercury Compounds*	*Vinyl Acetate*
Dibutylphthalate	*Methanol*	*Xylene*
Dichloroethyl	*Methyl Chloride*	

Mobile Source Air Toxics

Acetaldehyde	*Dioxin/furans*	*MTBE*
Acrolein	*Ethylbenzene*	*Naphthalene*
Arsenic Compounds	*Formaldehyde*	*Nickel Compounds*
Benzene	*n-Hexane*	*Polycyclic Organic Matter*
1,3-Butadiene	*Lead Compounds*	*Styrene*
Chromium Compounds	*Manganese Compounds*	*Toluene*
Diesel Particulate + Diesel Exhaust Organic Gases	*Mercury Compounds*	*Xylene*

Key Issues

- **High-to-low dose extrapolation**
- **Inter-species extrapolation**
- **Sensitive subpopulations**
- **Complex mixtures**
- **Multiple sources**
- **Multi-media exposure**
- **Environmental contamination**

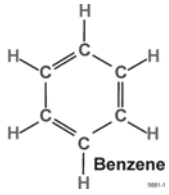
Key Research Questions

- ***What are the sources of air toxics?***
- ***What are the roles of transport, fate, and chemistry on air toxin concentrations?***
- ***What are the effects of exposure to air toxics on human health?***
- ***What are the hazards and dose-response relationships of air toxics?***
- ***What are the risks of air toxics to the environment?***
- ***How can risks from air toxics be prevented and managed cost effectively?***

HEI Studies

Mobile Source Air Toxics

Mobile Source Air Toxics: Benzene



Known human carcinogen

- **Acute nonlymphocytic leukemia**
- **Possibly chronic nonlymphocytic leukemia and chronic lymphocytic leukemia**

Noncancer effects

- **Hematotoxicity and immunotoxicity**
- **Decreased lymphocyte count**

Research issues

- **High to low dose extrapolation**
- **Sensitive subpopulations**
  - **Metabolism differences**

HEI Research: Benzene

- **Metabolites as biomarkers (Melikian)**
- **Low dose metabolism (Turteltaub)**
- **Chromosomal markers and mechanism (Eastmond)**
- **Biomarker validation in human population (Qu)**

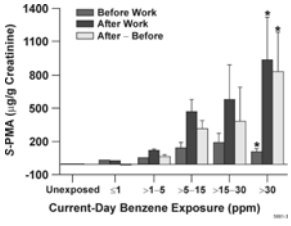
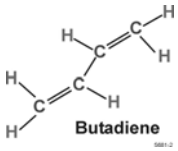


Figure 14. Urinary S-PMA levels (mean ± SE) among all unexposed subjects (n = 51) and exposed subjects (n = 130) grouped according to the current-day benzene exposure. *P: 0.001, test for exposure-response trend based on an ANOVA linear contrast.

From: Qu et al 2003. HEI Research Report Number 115

Mobile Source Air Toxics: 1,3-Butadiene



Known human carcinogen

- Leukemias

Noncancer effects

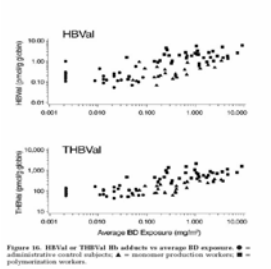
- Ovarian atrophy in mice
- Hematological effects (mice, high concentration)

Research issues

- Inter-species extrapolation
- Confounding exposures

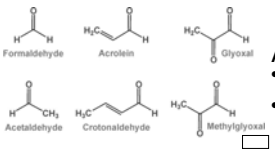
HEI Research: 1,3-Butadiene

- Development of biomarkers for exposure to 1,3-butadiene
  - DNA adducts (Blair)
  - mutation spectra (Recio, Walker)
  - hemoglobin adducts (Swenberg)
- Biomarker validation in human population (Albertini)
- Mechanism (Henderson)



From: Albertini et al 2003. HEI Research Report Number 116

Mobile Source Air Toxics: Aldehydes



Formaldehyde

- Reduced weight gain
- Probable human carcinogen
- Limited evidence humans; sufficient evidence animals (2 strains rats, 1 strain mice). Squamous cell carcinomas

Acetaldehyde

- Degradation of olfactory epithelium (rats, inhal)
- Probable human carcinogen (nasal, laryngeal tumors rodents; inadequate data humans)

Acrolein

- Gastrointestinal toxicity, high exposures (rats), and increased mortality
- Nasal lesions (rats, inhalation) w/ supporting hamster
- Inadequate animal, human cancer data

Research issues

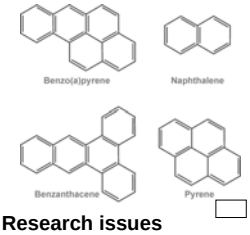
- Exposure
- Sensitive subpopulations

HEI Research: Aldehydes

- Sensitive detection (Zhang, Charles)
- Measuring indoor, outdoor, and personal exposures; influence of outdoor sources on personal exposure (RIOPA: Turpin, Weisel, Zhang)*
- Real-world automotive exposure (Grosjean)
- Hotspots (Fujita, Lioy, Spengler, Smith, Harrison)

* With Mickey Leland National Urban Air Toxics Center

Mobile Source Air Toxics: PAH



Tough nut

- Complex mixture
- Mutagenic and carcinogenic compounds
- Associated with particles and with gas phase

HEI Research

- Toxicity of atmospheric transformation products (Arey)
- Chemical and toxicity characterization of atmospheric transformation products from diesel emissions (Zielinska)

Research issues

- Cross-species comparisons
- High-to-low dose extrapolation
- Bioavailability

Mobile Source Air Toxics: Diesel PM and Exhaust Organic Gases

Critical issues

- Diesel PM and exhaust gases as a complex mixture
- Changing technologies
- Need for a marker specific for diesel (versus gasoline, non-mobile)
- Long latency period for lung cancer

HEI gasoline PM and diesel PM research

- Trying to understand the toxic components of ambient PM (including diesel PM)
- Chronic exposure
- Acute exposure

Mobile Source Air Toxics: Metals

Metals

- Arsenic
- Chromium
- Lead
- Manganese
- Mercury
- Nickel

Other metals

- Cerium and other metals introduced in control technology
- MMT as possible gasoline additive?

Research issues

- Toxicity at low exposures
- Biopersistence

HEI research

- Dose to target tissue
- Literature evaluation

What Next? HEI Research and Review Activities

Noncancer effects

- Hot spot studies
  - Exposure studies to confirm hot spots
  - RFA for health studies

- **HEI Air Toxics Review**
- Special Panel to review and summarize
- Special Report will
  - Summarize the health effects of exposure to the 21 mobile source air toxics defined by the EPA. This information will be gathered from the peer-reviewed literature.
  - Critically analyze the literature for a subset of mobile source air toxics selected by the Panel.
  - Assess and summarize research gaps and unresolved questions, as understood in the context of the current regulatory agenda.

HEI Air Toxics Review: Special Panel

Thomas Kensler (Panel Chair)
Johns Hopkins University

H. Ross Anderson
London University, St. George's Hospital Medical School

Michael Brauer
University of British Columbia

Elizabeth Delzell
University of Alabama, Birmingham

Mark Frampton
University of Rochester

Helmut Greim
Institute of Toxicology and Environmental Hygiene, Technical University of Munich

Rogene Henderson
Lovelace Respiratory Research Institute

Brian Leaderer
Yale University School of Medicine

Bill Rom
New York University Medical Center