# Air Toxics Exposure and Health: HEI Studies


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## HEI Annual Meeting

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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*

*Acrolein*

*Acrylonitrile*

*Arsenic Compounds*

*Benzene*

*Beryllium Compounds*

*1,3-Butadiene*

*Cadmium Compounds*

*Carbon Tetrachloride*

*Chloroform*

*Chromium Compounds*

*Coke Oven emissions*

*1,3-Dichloropropene*

*Dioxin*

*Ethylene Dibromide*

*Ethylene Dichloride*

*Ethylene Oxide*

*Formaldehyde*

*Hexachlorobenzene*

*Hydrazine*

*Lead Compounds*

*Manganese Compounds*

*Mercury Compounds*

*Methylene Chloride*

*Nickel Compounds*

*Perchloroethylene*

*Polychlorinated biphenyls*

*Polycyclic Organic Matter*

*Propylene Dichloride*

*Quinoline*

*1,1,2,2-Tetrachloroethane*

*Trichloroethylene*

*Vinyl Chloride*

# Indoor Air Toxics

*Acetaldehyde*

*Aldrin*

*Arsenic*

*Benzene hexachloride*

*Carbon Tetrachloride*

*Chlordane*

*Chloroform*

*Dichlorvos*

*Dieldrin*

*Formaldehyde*

*Heptachlor*

*Methyl Chloride*

*Pechloroethylene*

*Trichloroethylene*

# Stationary Source Air Toxics

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

# Mobile Source Air Toxics

*Acetaldehyde*

*Acrolein*

*Arsenic Compounds*

*Benzene*

*1,3-Butadiene*

*Chromium Compounds*

*Diesel Particulate + Diesel Exhaust Organic Gases*

*Dioxin/furans*

*Ethylbenzene*

*Formaldehyde*

*n-Hexane*

*Lead Compounds*

*Manganese Compounds*

*Mercury Compounds*

*MTBE*

*Naphthalene*

*Nickel Compounds*

*Polycyclic Organic Matter*

*Styrene*

*Toluene*

*Xylene*

# Key Issues

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

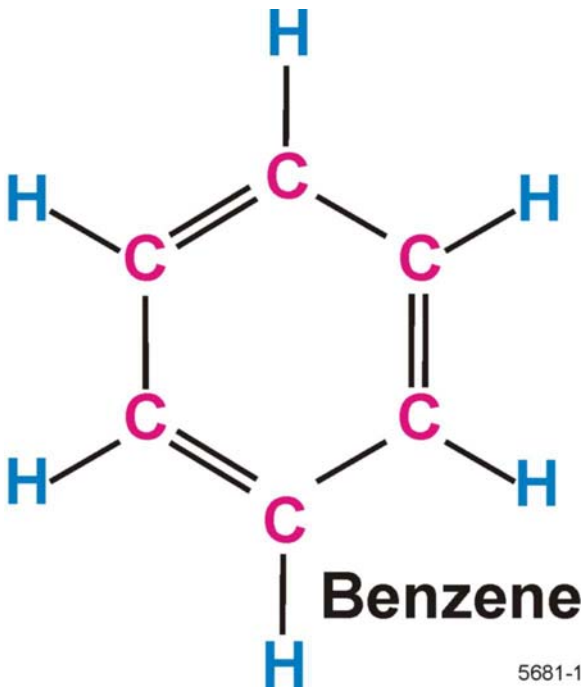
# Key Research Questions

- ***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)**

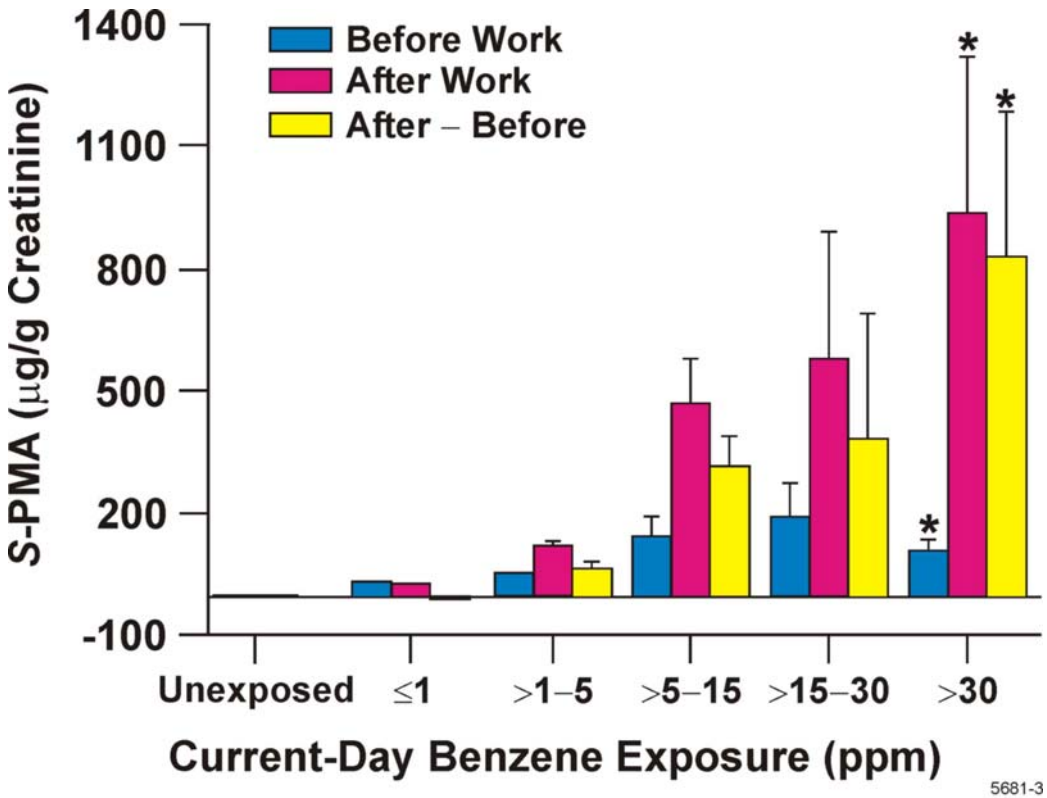
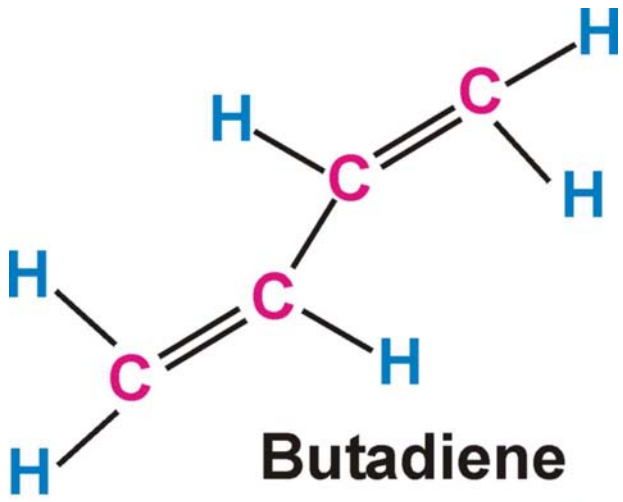



Figure 14. Urinary *S*-PMA levels (mean ± SE) among all unexposed subjects ($n$ = 51) and exposed subjects ($n$ = 130) grouped according to the current-day benzene exposure. *$P \leq 0.001$, test for exposure-response trend based on an ANOVA linear contrast.

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

# Mobile Source Air Toxics: 1,3-Butadiene



Butadiene

5681-2

## 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)**

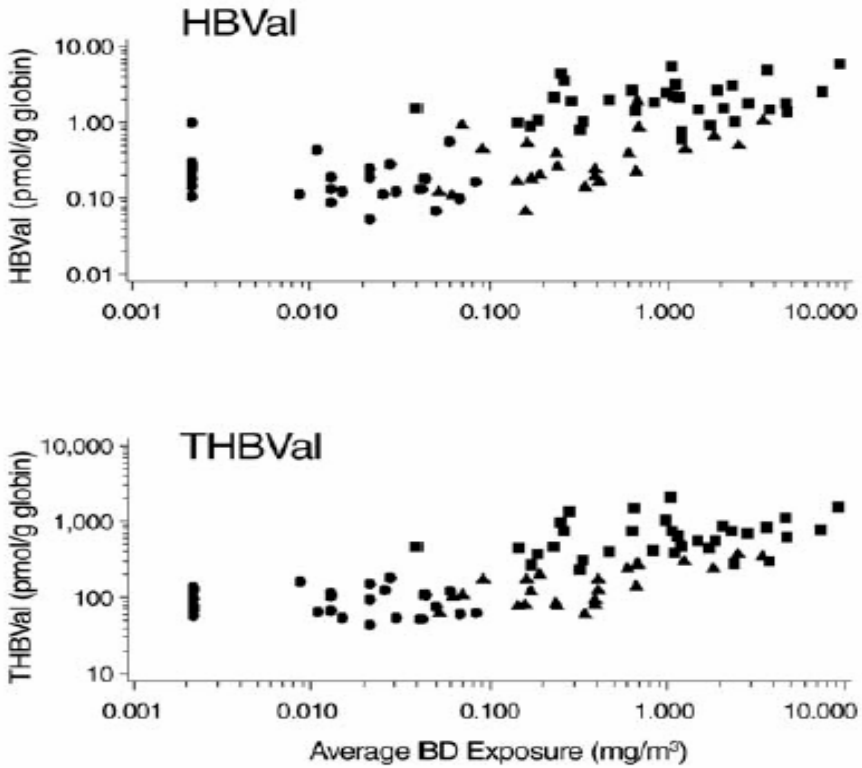
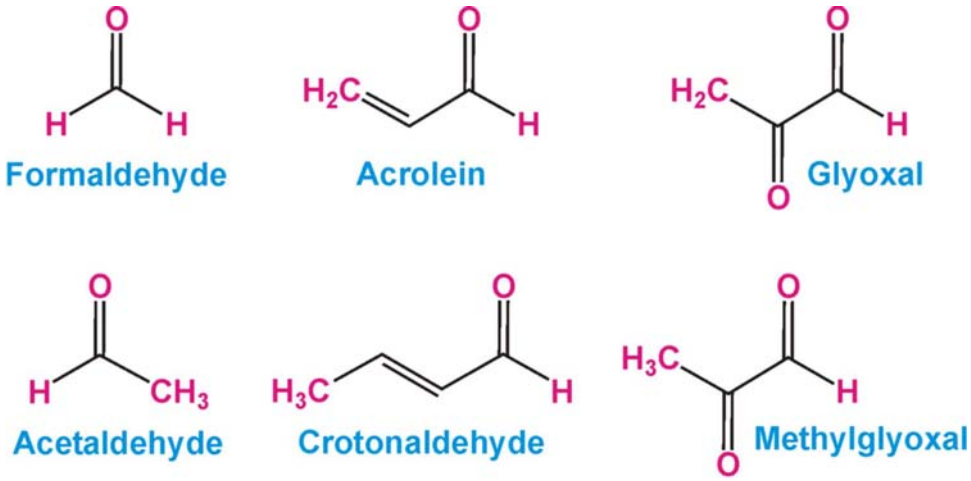



**Figure 16. HBVal or THBVal Hb adducts vs average BD exposure.** ● = administrative control subjects; ▲ = monomer production workers; ■ = polymerization workers.

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

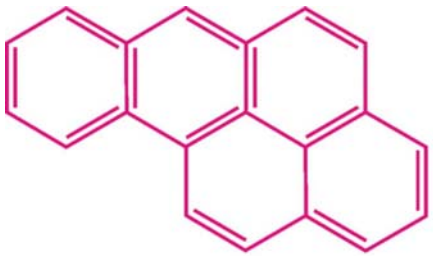
- Exposure
- Sensitive subpopulations

# 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)**

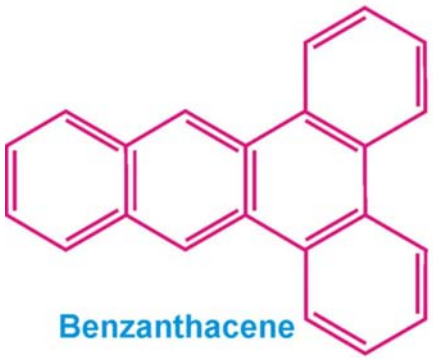

* With Mickey Leland National Urban Air Toxics Center

# Mobile Source Air Toxics: PAH



Benzo(a)pyrene

Naphthalene



Benzanthacene

Pyrene

## Research issues

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

## 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)

# 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