



Children's Environmental Health Centers: Research Translation Informing and Evaluating Policy

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Science Questions

Can a relationship be established between adverse health outcomes in young children, such as developmental delays, and the sources of pollution in a community setting? How do susceptibility factors, for example, genetic polymorphisms, play a role in this relationship? Can these research findings be translated and used by policymakers? Can prenatal exposure to pollutants be linked to the early onset of chronic illnesses, such as childhood asthma? Can biomarkers be developed to help elucidate the key steps linking prenatal exposures to adverse outcomes? Can interventions reduce the negative health effects resulting from early life exposures?

Research Goals

The EPA/ NIEHS Children's Environmental Health Research Centers engage in translational research to identify biomarkers of exposure and bioindicators of effect to evaluate the effectiveness of intervention research projects and government supported risk mitigation actions. These centers use integrated, multidisciplinary approaches to conduct research that examines key events in the dose to exposure to health outcome continuum, and ultimately, ties these events to environmental policies and actions.

Researchers Involved

Deborah Segal, Richard Callan, and Chris Saint (NCER); Brenda Eskenazi, Asa Bradman and Nina Holland (University of California, Berkeley); Gloria Coronado and Clem Furlong (University of Washington); Frederica Perera, Robin Wyhatt, Virginia Rauh, Rachel Miller and Megan Williams (Columbia University); Rob McConnell, Ed Avol, James Gauderman, and Andrea Hricko (University of Southern California); Mary Wolff, Gertrude Berkowitz, Jia Chen, and Barbara Brenner (Mount Sinai School of Medicine)

Through targeted translation efforts, community-based exposure and health effects research can have a direct and sustained impact on public health and environmental policy for the protection of children's health. Key findings can be honed to inform policy and practice at the local, state, regional and federal levels.

Developing biological indicators of chemical exposure and adverse effect— and employing them in tandem— may provide multiple ways to evaluate the success of a local intervention or broader policy change.

Findings and Conclusions

Integrating genetic and lifestage susceptibility indicators in epidemiological studies may help elucidate variation in phenotypic presentation and biological response to environmental threats—further informing risk management.

Designing the use of multiple indicators which link source to exposure to biological effect within a prospective study offers tremendous potential to assess the effectiveness of risk management decisions.

The Children's Center's approach to designing studies linking indicators and outcomes— ultimately tying indicators to risk mitigation actions— is broadly applicable to other areas of environmental health research and environmental policy.

Impact and Outcomes

Each Children's Research Center has a **Community Outreach and Translation Core** staffed by scientists, community partners, and public health professionals who translate research findings for clinicians, local policy makers and other stakeholders. The following are examples of **direct** impacts the Centers have contributed to public policy at the local, state and federal levels.

Research findings and subsequent testimony on Integrated Pest Management—non-toxic, environmentally-based approaches to interrupting pest lifecycles— by Mount Sinai investigators influenced the passing of:

• **NYC Pesticide Reduction Law (Intro 329A)**— promotes alternatives to pesticides in all city owned and leased properties, banning all EPA Class 1 chemicals by Feb 2007

• **Neighborhood Notification Law (Intro 328A)**— requires 48-hour notification to adjacent neighbors before spraying non-residential, outdoor insecticides.

California Air Resources Board's **Emissions Reduction Plan for Ports and Goods Movement (2006)** cites multiple peer-reviewed air pollution and health effects articles of the USC Children's Center.

Providing evidence of the take-home pathway, the findings of the University of Washington's Exposure Pathway's Project were influential in **EPA's decision to phase out azinphos-methyl (Class 1)** by 2011.

EPA's **FIFRA Science Advisory Panel** incorporated epidemiological findings on children's birth and developmental outcomes from 3 of the Children's Center cohorts where low-dose exposures to Chlorpyrifos during pregnancy were shown to have adverse effects on childhood development.

Future Directions

By strengthening the community outreach and translation core components of the Children's Centers, ORD/NCER will strongly encourage our research partners to inform local, state and federal policy, particularly in incorporating new knowledge of genetic susceptibility to air toxics and pesticides into regulatory decision. The new Children's Centers program is designed to more rapidly translate molecular evidence of toxic action into bioindicators of exposure or effect which can be used in evaluating policy effectiveness.



Background

Basic Science and Susceptibility Measures

Indicators of Exposures and Health Effects

Intervention Policy Change

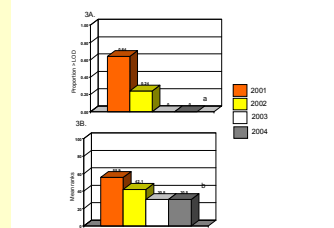
Measuring changes in the environment and public health

Northern Manhattan Birth Cohorts Household Pesticide Studies



EPA and NIEHS support two birth cohorts in New York City, both of which conduct community-based research on pesticide exposures and effects during and after pregnancy for mothers and children. Previous published data showed that 100% of study participants were exposed to household pesticides.

- Associations between diplotypes and PON1 activity in mothers and neonates (Chen et al. 2005)
- Cohort specimens were used to develop a functional approach to genetic susceptibility (Wetmur et al 2005, 2008 and Wallenstein et al, 2006)

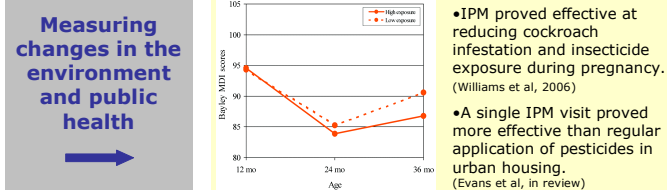


Percent of meconium samples with TCPy concentrations > LOD (3a.) and mean TPCy ranks (3b.) by year of sample collection (Whyatt et al, 2008)

- Adverse birth outcomes associated with OP metabolites** (Berkowitz et al, 2004)
 - smaller head circumference
 - low birth weight and shorter length
- Growth and developmental outcomes** (Rauh et al, 2006)
 - prenatally highly exposed demonstrated mental and motor delays at age 3.
 - behavioral problems at age 3 observed in highly exposed group.

- Personal air monitoring
- Urinary metabolites
- Maternal and cord blood
- Meconium Validation Study

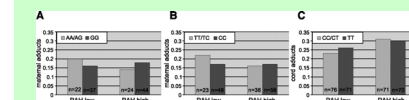
- Integrated Pest Management research and city-wide implementation (2006)
- 2001 phase out of Diazinon and Chlorpyrifos



- IPM proved effective at reducing cockroach infestation and insecticide exposure during pregnancy. (Williams et al, 2006)
- A single IPM visit proved more effective than regular application of pesticides in urban housing. (Evans et al, in review)

New York City Traffic-Related Air Pollution

The Columbia study cohort has shown 100% of subjects having exposure to PAHs in the air during pregnancy and 40% reporting ETS exposure. PAH exposure in this urban cohort of nonsmokers is largely due to traffic sources and ETS. Researches and community partners successfully campaigned to introduce a cleaner bus fleet and permanent air monitors in Northern Manhattan

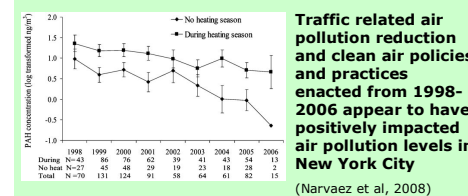


Investigators explored interactions between prenatal PAH exposure and 17 polymorphisms in the genes and haplotypes on PAH-DNA adducts in cord blood of 547 newborns and in maternal blood of 806 mothers. (Wang et al, 2008)

- Methods include:**
- Personal monitoring for PAHs
 - Stationary monitoring of elemental carbon, PM 2.5 and metals
 - Spatial and temporal distribution analysis of PAH, PM2.5 and metals
 - Blood and cord blood analysis of PAH-DNA adducts

- Adverse Birth Outcomes** (Choi et al, 2008)
 - Intrauterine growth restriction and small size for gestational age
 - Head circumference
 - Pre-term birth
- Developmental delays** (Perera et al 2006)
 - PDI at 36 months
 - Decreased IQ at age 5
- Increase in Cancer Risk** (Bocsky et al 2005)
 - Significant increase in PAH-DNA adducts from prenatal exposures

- Pre-DERA Voluntary Action (2000-2006)
- Introduction of cleaner bus fleet using ULSD and CNG



Traffic related air pollution reduction and clean air policies and practices enacted from 1998-2006 appear to have positively impacted air pollution levels in New York City (Narvaez et al, 2008)

Farm-worker cohorts and Agricultural Communities

Two community-based agricultural studies are investigating susceptibility and the take-home pathway for multiple pesticides.



Paraoxonase (PON1) detoxifies OP pesticides in blood. PON1 activity is lower in newborns than adults, with especially low levels in the certain genotypes. For Diazinon, some newborns may be up to 65 times more susceptible than adults with highest enzyme levels. For Chlorpyrifos, a 50-fold difference in susceptibility among newborns was predicted; some newborns may be 130-164 times as susceptible as the highest adults. In follow-up studies, worse health outcomes are associated with vulnerable genotypes. (Holland and Furlong, 2006)

- Methods include:**
- Lifespan exposure modeling and assessment
 - Household measures
 - Blood, urinary, breast milk and saliva measures of OPs
 - Novel analytical tools for a panel of pesticides
 - Analysis of take-home exposures
 - Spray-drift analysis
 - Genetic and enzyme analysis
 - Transgenic animal models

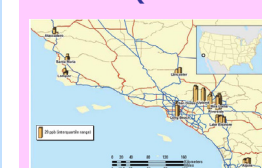
- Exposure Studies found** (Bradman et al, 2006, 2007):
 - Higher OP metabolites in pregnant women living in an agricultural area
 - Toddlers exposed to 2x pesticides of crawlers
 - Levels of agricultural pesticides in indoor and outdoor air are correlated
- Health Effects studies found** (Eskenzai et al, 2007):
 - Prenatal OP exposure to be associated with poorer MDI at 24 months, and developmental disorder at and beyond 24 months

- US EPA Worker Protection Standards
- Field-based intervention studies to break the take-home Pathway



Wearing WPS-recommended clothing, handwashing with soap and wearing gloves were associated with lower levels of malathion urinary metabolites in farmworkers. Despite these protective behaviors, participants had significantly higher exposure compared to a national reference sample. (Salvatore et al, 2008)

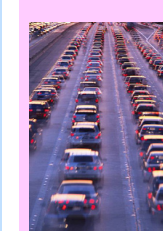
Greater Los Angeles (Urban Air Toxics)



Researches at USC are studying the childhood determinants of respiratory susceptibility to air pollution and tobacco smoke in several Los Angeles area cohorts.

Phase II enzyme and antioxidant gene-environment interaction studies (Islam et al, 2008, Gilliland et al 2004, 2006)

- *In utero* exposure to tobacco smoke was associated with increased risk of asthma among children with GSTM1 null genotype.
- Individuals with GSTM1 null or the GSTP1 I105 wildtype genotypes showed greatly enhanced nasal allergic responses in the presence of diesel exhaust particles.
- Variants in antioxidant genes HMOX-1 and CAT modify risk of new onset asthma and have ethnic-specific effects.
- Community-level monitoring of PM2.5, PM10, NO, NO2, ozone, acid vapor, and meteorology
- Outdoor residential measures for traffic-related pollutants
- Genetic analysis
- Traffic proximity analysis and regional air pollution analysis
- Anthropometric measures of lung function
- Field measurements of exhaled nitric oxide



Respiratory Health Outcomes

Children exposed to elevated levels of ambient air pollutants including ozone, PM, NO2 and fresh traffic-related emissions show adverse effects on asthma pathogenesis, lung function development, respiratory symptoms and infections

- Residential distance from traffic sources was associated with deficits in lung function and prevalent asthma.
- Markers of traffic-related pollution were associated with new onset asthma. (McConnell, 2006; Gauderman, 2007 and Jerrett, 2008)

- 2005 "Clearing the Air Campaign"
- 2005 Diesel Emissions Reduction Act
- Emissions Reduction Plan for Ports (2006)

Through the Community Outreach and Translation Core, USC Children's Center researchers have directly influenced policy and decisions related to the Los Angeles/Long Beach Ports, a major source of criteria air pollutants.

- Their work has been cited in landmark state and federal documents on air quality and emissions reduction plans.
- Recent findings linking traffic-related air pollution to childhood respiratory illness are expected to directly influence transportation and land use planning across the entire Los Angeles region.

Evaluation of Risk Management Decisions