Differential Vulnerability to Environmental Contaminants and Adverse Health Outcomes During Early Childhood

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LTG 3 Poster 07

Science Questions

What are the joint effects of social stressors and environmental exposures on disparities in children's health outcomes?

What are best approaches to investigating disparities in children's environmental health outcomes?

What are the opportunities for effective interventions to eliminate disparities and achieve better health for all children?

Research Goals

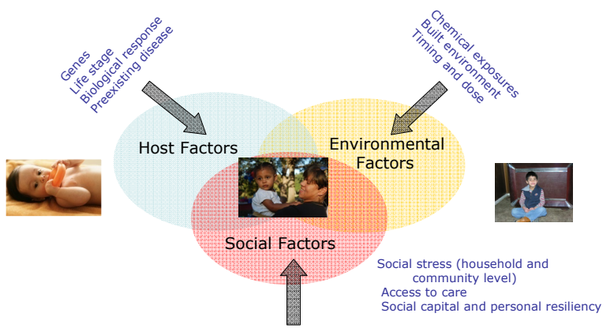
To address the key research questions and to understand how genetic, social and environmental factors jointly influence differential health outcomes, the ORD-supported Centers for Children's Environmental Health Research have developed the following:
(1) biological tools and models to characterize and evaluate gene-environment interactions which elucidate variations in response and metabolic processes due to chemical exposure;
(2) systematic methods for inventorying household- and community-level characteristics (particularly the built environment) and then relating these to children's exposures and childhood health outcomes;
(3) cumulative models to consider the various outcomes from multiple chemical exposures on multiple target organs in a human system.; and
(4) novel statistical methods for addressing health disparities related to the environment.
In addition, the Children's Centers have created research environments where environmental scientists readily collaborate with sociologists, psychologists, and social epidemiologists to examine the joint effects of social and environmental stressors.

Highlights of Findings and Conclusions

- Developed a systematic data collection approach to estimate children's aggregate and cumulative exposures to environmental contaminants.
- Innovative methods using spatial Bayesian hierarchical modeling and data missingness techniques are providing new insights into the etiology of health disparities.
- Demonstrated that children's exposures to certain classes of chemicals do have an effect on weight, birth outcomes, mental development, and memory.
- Demonstrated that disparities in access to health care can result in significant differences in environmentally related childhood disease outcomes such as asthma.
- Demonstrated that socioeconomic status and residential environments do influence exposures to various environmental contaminants.
- Demonstrated that certain groups of children may be more than 65 times more genetically vulnerable to the effects of organophosphate pesticides than other children.
- Showed that housing characteristics related to poverty, combined with behavioral and genetic differences, can significantly increase the extent of exposure to indoor air toxics such as PM and NO_2.
- Demonstrated that social factors such as behavior, psychosocial stress and cultural differences can interact with differences in genetics and environmental exposures, resulting in significant disparities in birth outcomes among urban populations.

Methods/Approach

Establishing A Conceptual Framework for Disparities in Birth and Early Childhood Health Outcomes

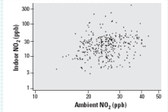


Although it is widely agreed that maternal and child health and well-being are influenced by host, social, and environmental factors, little is known about the interactions of these forces, particularly on early life development. For example, elevated environmental exposures often occur in communities facing multiple social stressors like deteriorating housing, inadequate access to health care, poor schools, high unemployment, high crime, and high poverty – all of which may compound the effects of environmental exposures. Research currently supported by ORD/NCER incorporates all three types of factors in an integrated framework.

Urban Air Pollutants, Housing and Health Care

Researchers at the **Johns Hopkins University Center for Childhood Asthma in the Urban Environment** have characterized the households and asthma care of 150 asthmatic cases and 150 controls in Inner-city East Baltimore, predominately African American, ages 2-6. They have recently found:

- Significant fluctuations in asthma control after initial assessment, with poor control predicting future medical care (Sharma et al, 2007)
- Inner city homes showed PM levels twice as high indoors than outdoors. Common household activities predicted higher PM concentrations. Indoor PM concentrations can decrease with modified behavior (McCormack et al, 2008)



- High levels of indoor NO_2 were independently associated with health care utilization and asthma symptoms. A significant source of indoor NO_2 in some urban populations includes gas heaters, ovens and ovens used as heaters during the winter. (Hansel et al, 2008)

Table 3. Risk of asthma symptoms per 20-ppb increase in NO_2 exposure.

Symptom	Unadjusted IRR	Unadjusted 95% CI	Adjusted[a] IRR	Adjusted[a] 95% CI	Adjusted[b] IRR	Adjusted[b] 95% CI
Daytime wheezing, coughing, or chest tightness	1.05	0.99–1.12	1.03	0.96–1.11	1.04	0.97–1.12
Slowing activity due to asthma, wheeze, chest tightness, or cough	1.07	1.00–1.14*	1.06	0.99–1.14	1.08	0.94–1.15
Limited speech due to wheeze	1.12	1.04–1.21**	1.15	1.05–1.25**	1.17	1.08–1.27**
Wheeze, cough, or chest tightness while running	1.08	1.01–1.15*	1.07	0.99–1.14	1.09	1.01–1.17*
Coughing without a cold	1.13	1.06–1.20[c]	1.10	1.02–1.18**	1.15	1.07–1.23[c]
Nocturnal awakenings due to cough, wheeze, shortness of breath, or chest tightness	1.11	1.04–1.18[c]	1.09	1.02–1.16*	1.12	1.04–1.19**

[a]Models are adjusted for $PM_{2.5}$; SHS; season of sampling; age, sex, and race of the child; and mother's education level. [b]Models are adjusted for $PM_{2.5}$; SHS; distance from the curb, type of street in front of home, season of sampling; age, sex, and race of the child; and mother's education level. *$p < 0.05$. **$p < 0.01$. [c]$p < 0.001$.

Pregnancy, PAHs and Differential Outcomes

Table 4. SGA, fetal growth ratio, ponderal index, and cephalization index with increasing PAH exposure concentration.

	Size for gestational age: AGA (reference)	Size for gestational age: SGA	Fetal growth ratio: ≥ 85% (reference)	Fetal growth ratio: < 85%	Ponderal index	Cephalization index
African American						
ΣB c-PAHs (ng/m³)						
≤ 1.55	37 (21.0)	3 (9.1)	41 (21.1)	4 (14.3)	2.48 ± 0.30	104.17 ± 22.52
1.56–2.30	47 (26.7)	4 (12.1)	49 (25.3)	4 (14.3)	2.63 ± 0.31	101.20 ± 10.95
2.31–3.66	50 (28.4)	12 (36.4)	59 (30.4)	6 (21.4)	2.52 ± 0.28	102.89 ± 13.04
≥ 3.67	42 (23.9)	14 (42.4)*	45 (23.2)	14 (50.0)*	2.44 ± 0.26	111.94 ± 17.64**
Dominican						
ΣB c-PAHs (ng/m³)						
≤ 1.55	94 (27.9)	4 (17.4)	98 (28.5)	8 (21.1)	2.54 ± 0.29	103.04 ± 11.14
1.56–2.30	85 (25.2)	8 (34.8)	85 (24.7)	13 (34.2)	2.68 ± 0.64	99.82 ± 10.19
2.31–3.66	74 (22.0)	8 (34.8)	76 (22.1)	10 (26.3)	2.63 ± 0.32	101.37 ± 11.72
≥ 3.67	84 (24.9)	3 (13.0)	85 (24.7)	7 (18.4)	2.61 ± 0.28	101.12 ± 12.12

Values are no. (%) or mean ± SD.
*$p < 0.05$ and **$p < 0.01$ for linear trend in outcome with increasing exposure.

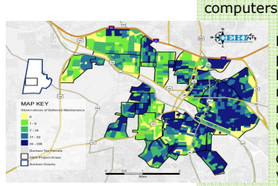
Results from the **Columbia Center for Children's Environmental Health** include:

- Preterm delivery risk was 5-fold greater among African Americans per ln-unit increase in prenatal PAH exposure. The same unit increase in exposure significantly increased the ratio of head circumference to birth weight by 0.04% in African Americans. These effects were not observed in Dominicans. Prenatal PAH exposure is likely to contribute to the occurrence of SGA as well as preterm births among African Americans. (Choi et al, 2008)
- In a group of 806 mothers, PAHs were measured by personal air monitoring during pregnancy and maternal blood samples were obtained. The cohort was comprised of three different self-described ethnic groups: African Americans, Dominicans, and Caucasians. Significant interactions ($p < 0.05$) were observed between certain genetic polymorphisms and CYP1A1 haplotype and PAHs in mothers and their newborns in the three ethnic groups (Wang et al., 2008).
- Prenatal residential environmental tobacco smoke (ETS) exposure exhibited synergistic effects with the level of material hardship on 2-year cognitive development. Children with both ETS exposure and material hardship exhibited the greatest cognitive deficit (Rauh et al., 2004).

Southern Center on Environmentally Driven Disparities in Birth Outcomes
Duke University's Emphasis on Novel Methods

Assessing the Built Environment

Motivated by increasing evidence regarding the relationship between public health and the built environment, the Community Assessment Project was conceived with two key goals: 1) provide community residents with maps of the built environment to support residents' efforts to improve quality of life; and 2) elucidate the relationship between the built environment and health. The Duke children's center built a custom application, launched off handheld computers equipped with GPS technology, to assess the built environment.



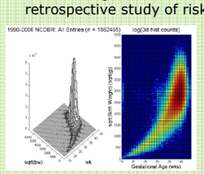
From May to August 2008, data collectors canvassed over 17,000 parcels in Durham using a standardized visual assessment of building exteriors. The map at right shows total counts of deferred maintenance, including broken or boarded windows, holes in walls, roof damage, chimney damage, foundation damage, front entry damage, peeling paint, fire damage, condemnation notices, standing water, excess litter, garbage, broken glass, discarded furniture, discarded appliances, discarded tires, inoperable vehicles in the yard, high weeds or grass, graffiti, and fence damage, for each Census 2000 block.

Dealing with Data Missingness

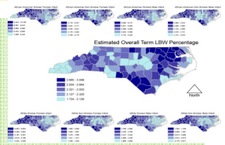
The Duke children's center includes a clinical obstetrics project, which like most studies, suffers from missing data problems. With relatively few women and hundreds of predictors, imputation strategies must not disguise complex (non-linear and interactive) relationships. We have developed imputation techniques based on chained regression trees: 1) we fill in the missing data with plausible starting values; 2) for each variable, we estimate a large regression tree using that variable as the outcome and all other variables as predictors; 3) we impute missing values by sampling from the leaves of the tree, conditional on the values of other variables; 4) we repeat steps 2-3 for each variable, using previously imputed values for the predictors; 5) we repeat this process many times, ultimately using the last set of imputed values as a completed dataset; and 6) we repeat steps 1-5 multiple times to create multiple completed datasets used for analysis.

Innovations in Spatial Statistics

We have developed a modeling approach that substantially extends the inferential possibilities available using standard disease mapping models. For each areal unit, we assume a multi-way contingency table for outcomes and risk factors, explained with a loglinear model, and connect these loglinear models through spatial random effects. Flexible aggregation allows us to investigate groups of interest; flexible conditioning enables not only study of outcomes given risk factors but also retrospective study of risk factors given outcomes.



Customary modeling for birthweight is conditional on gestational age. In other work, we use **joint** modeling to increase flexibility and interpretation. We have developed a hierarchical finite mixture of bivariate regressions model which enables us to capture non-Gaussian distributional shapes of joint birthweight and gestational age and to incorporate well-established risk factors (e.g., sex, maternal age, race, and tobacco use).



Impact and Outcomes

ORD-supported research is having direct impact on policy outcomes across the United States. Here are some examples:

- Columbia Children's Center investigators, in conjunction with community environmental justice and public interest groups, convinced New York City officials to convert the City's bus fleet to use clean diesel fuel, and also to install permanent EPA air monitors in Harlem.
- The Duke Children's Center implemented a detailed community assessment project, the data from which are now available to government agencies and community groups and allow for data-based decisions on allocating scarce neighborhood rehabilitation funds. The technology development has widespread replicability for assessing the built environment and is available for use by other communities.
- In other work not featured on this poster, intervention studies have demonstrated low-cost methods of reducing take-home exposure of pesticides to children of farmworkers. These methods are now being considered for implementation by state farm bureaus and grower organizations.

Future Directions

There is an emerging trend in environmental health research to consider the broader social context in which individuals live and experience exposures to environmental contaminants and hazards. This trend is responsive to community demands for EPA and other regulatory agencies to view the "environment" more holistically and builds on the wealth of existing evidence of the interplay among biological and social determinants of health in social epidemiology, medical anthropology and health disparities research.

Multilevel approaches that include ecological perspective are more likely to provide a better understanding of susceptibilities, vulnerabilities that contribute to health (like asthma) disparities at different stages in the life course.

We envision more emphasis on this type of interdisciplinary research, which will lead to improved approaches for risk assessment by considering social factors and non-chemical stressors, as recently recommended by the National Research Council, and enhance EPA's ability to conduct cumulative risk assessments and design policies and programs that meet the needs of disadvantaged, underserved, and environmentally-overburdened communities.

Additional Contributors

Nigel Fields, Richard Callan (NCER); Patrick Breysse, (Johns Hopkins University), Frederica Perera, Virginia Rauh (Columbia University)

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Susceptible Populations