

NIEHS and EPA Children's Environmental Health and Disease Prevention Research Centers: *Strengthening the Network*

March 6–7, 2012 • NIH Campus, Bethesda, Md.



Developing a Pilot Study to Study the Determinants of Vitamin D Status in Adult Asthmatics in Barbados

Presenting Author: Sonali Bose, Johns Hopkins University

Contributing Authors: Smith-Waters, L. (Johns Hopkins University); Jeyaseelan, S. (The University of the West Indies); Watson, H. (Queen Elizabeth Hospital); Roach, T. (Queen Elizabeth Hospital); Diette, G. (Johns Hopkins University); McCormack, M. (Johns Hopkins University)

Abstract:

Background: Barbados has one of the highest rates of asthma in the world and prevalence is increasing. Of the many environmental exposures and host susceptibility factors that contribute to disease burden, vitamin D deficiency has recently been linked to greater asthma morbidity. Despite the abundance of sun that is needed for vitamin D synthesis, vitamin D deficiency has been demonstrated even in equatorial regions. This finding may reflect urban lifestyle changes where increasingly more time is spent indoors. Barbados is a high-income developed country, with universally accessible health care services; however, the infrastructure for clinical research is still developing. To study the role of vitamin D in asthma in this population, we aimed to build capacity and develop collaborative relationships between Johns Hopkins and Barbados.

Methods: Fifty adults with asthma were proposed to be studied for one week. Funding was obtained from the Center for Global Health at Johns Hopkins. Collaborators from local clinics and the University of West Indies (UWI) were identified and contacted. Interval meetings on the island as well as regular correspondence via email and telephone were used to develop study protocols. Research instruments were developed by adapting tools previously used in published and unpublished studies to urban Barbadian lifestyle and conditions.

Results: Collaborations were formed with UWI investigators and ED and community physicians in Barbados through organized symposia, meetings, and correspondence. With their input, a recruitment strategy capturing adults with asthma from local ED and clinics was developed. Study forms and data collection sheets, including consent forms, screening tools, asthma questionnaires, pulmonary function data, symptom and activity diaries, and surveys to assess sun-related habits and dietary intake, were iteratively refined to be appropriate for a Barbadian population. All finalized study protocols and materials were subject to the approval of the Hopkins IRB, UWI IRB, and UWI Ethics Committee prior to recruitment in February 2012.

Conclusion: Through our funded pilot study, we have solidified collaborative relationships in Barbados to enable successful completion of our ongoing study. These efforts have led to the creation of a Barbados Hopkins Respiratory Research Group that can provide the infrastructure needed in future studies to assess risk factors in patients with respiratory disease within this community.



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Relationships between Lead Exposure and Maternal Cortisol Concentrations during Pregnancy

Presenting Author: Joe Braun, Harvard University School of Public Health

Contributing Authors: Tellez-Rojo, M (National Institute of Perinatology); Mercado-Garcia, A (National Institute of Perinatology); Schnaas, L (National Institute of Perinatology); Hu, H (University of Michigan); Wright, R (Harvard School of Public Health)

Abstract:

Introduction: Gestational lead (Pb) exposure and stress may increase the risk of adverse neonatal and childhood health outcomes. Pb may interfere with hypothalamic-pituitary-adrenal (HPA)-axis function, but no studies have examined this relationship during pregnancy when the fetus may be susceptible to environmentally mediated hormonal dysregulation.

Methods: Low to moderate-income women were recruited from hospitals and clinics affiliated with the Mexican Social Security System. Concurrent Pb exposure was estimated using blood Pb concentrations measured during the 2nd trimester of pregnancy. Tibia Pb concentrations, measured using K-shell X-ray fluorescence 1-month postpartum, were used to estimate cumulative Pb exposure. We characterized diurnal HPA-axis function using salivary cortisol concentrations from 10-timed saliva samples collected over 2-days in the 2nd trimester. We used linear mixed-effect models to examine the relationship between blood and bone Pb biomarkers and changes in the slope of cortisol concentrations during the morning and afternoon, as well as individual cortisol measurements.

Results: Median blood and tibia Pb concentrations were 3.3 $\mu\text{g}/\text{dL}$ and 3.1 $\mu\text{g}/\text{g}$, respectively. Salivary cortisol concentrations exhibited a diurnal pattern, rising in the 1st hour after waking and decreasing across the rest of the morning and afternoon. After adjustment for confounders a 3.3 $\mu\text{g}/\text{dL}$ (Interquartile Range) increase in blood Pb concentrations was associated with a 7% decrease (95% confidence interval [CI]: -11, -2%) in the morning rise slope and an 8% increase (95% CI: 0, 17%) in the afternoon slope. The increase in the morning slope was due to decreased salivary cortisol concentrations 1 hour after waking (19.3 vs. 18.4 nmol/L; % difference: -5%, 95% CI: -7, -2%). Tibia Pb concentrations were not associated with alterations in cortisol concentrations or slopes.

Conclusions: These results suggest that concurrent Pb exposures may alter HPA-axis function during pregnancy while cumulative and past Pb exposures do not. Given the important role of cortisol on multiple health outcomes, including neurodevelopment, further studies need to determine if lead-induced changes in maternal cortisol concentrations during pregnancy are associated with or mediate changes in infant and child health.



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Analysis of Thirdhand Smoke Exposure Using Dust Nicotine

Presenting Author: Patrick Breyse, Johns Hopkins University

Contributing Authors: Torrey, C (John Hopkins School of Public Health); Youngblom, E (John Hopkins School of Public Health); Williams, D (John Hopkins School of Public Health); Massie, A (Johns Hopkins Medical Institute); Cato, A (John Hopkins School of Public Health); Campbell, K (John Hopkins School of Public Health); Butz, A (Johns Hopkins Medical Institute)

Abstract:

Thirdhand smoke (THS) refers to residual tobacco smoke pollutants that remain on surfaces after the cigarettes have been extinguished. Because surface contamination persists long after active smoking has ceased, there is concern about the potential health effects of exposure to THS, especially to children. The contribution to children's exposure to smoking-related contaminants through the THS pathway is poorly understood and it has been suggested that house dust nicotine may be a useful marker of THS exposure. As part of a larger study we analyzed dust nicotine (N=23 homes) to evaluate the range of concentrations and correlated them with previously measured airborne nicotine and urinary cotinine. All homes participating in this had at least one active smoker. Airborne nicotine samples were collected using passive samplers and analyzed using gas chromatography with nitrogen detection. Urinary cotinine samples were analyzed by Center for Disease Control and Prevention (CDC) by liquid chromatography/atmospheric-pressure ionization, tandem mass spectrometry (LC API MS/MS). House dust, collected using vacuum samplers, were analyzed using gas chromatography with mass spectrometry in selected ion mode. Twenty-three dust samples from inner city homes were analyzed. Dust nicotine concentrations ranged from 0.68 to 360 ng/mg with a mean of 86 ± 96 ng/mg (median = 45 ng/mg). Log dust nicotine was strongly correlated with log air nicotine ($r=0.75$). In contrast, log dust nicotine was only moderately correlated with log urinary cotinine ($r=0.39$). These results suggest that nicotine can be detected in the dust from homes of smokers. While dust nicotine is highly correlated with airborne nicotine it is only moderately correlated with cotinine in children's urine. While the sample size is small these results suggest dust nicotine may be a valuable marker for THS exposure pathway in children. More research is needed to assess the relative importance of THS and SHS pathways of exposure.



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Children's Environmental Health Initiatives in Providence, RI

Presenting Author: Phil Brown, Brown University

Contributing Author: Panikkar, B. (Brown University)

Abstract:

Brown University's CEHC Community Outreach and Translation Core (COTC) plays a vital role in the CEHC's work, serving as a public interface between the CEHC's research projects and the Rhode Island community. We provide educational and consultation services on children's environmental Health to the broader RI community. The poster will feature all the community outreach activities we do in RI for the Children's Center.



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Hospitals for a Healthy Environment in Rhode Island

Presenting Author: Phil Brown, Brown University

Contributing Author: Panikkar, B (Brown University)

Abstract:

Hospitals for a Healthy Environment in RI is a coalition of hospitals, hospital associations, professional associations, nursing schools, unions, academic institutions, government agencies, local food groups, and environmental organizations. We promote cost effective, efficient, healthy and sustainable green care practice in health care institutions. The poster will feature all the activities we have done in RI to promote environmental sustainability in healthcare.



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Flame Retardant Chemical Exposure and Health Impacts

Presenting Author: Jonathon Chevrier, University of California, Berkeley

Contributing Authors: Bradman, A (UC Berkeley School of Public Health); Castorina, R (UC Berkeley School of Public Health); Fenster, L (California Department of Public Health); Harley, KG (UC Berkeley School of Public Health); Holland, N (UC Berkeley School of Public Health); Quiros-Alcala, L (UC Berkeley School of Public Health); Rosas, LG (UC Berkeley School of Public Health); Sjodin, A (Centers for Disease Control and Prevention); Eskenazi, B (UC Berkeley School of Public Health)

Abstract:

Polybrominated diphenyl ethers (PBDEs) are flame retardants that were commonly used in polyurethane foam, carpet, textiles, construction materials and electronics. PBDEs are persistent and highly lipophilic chemicals with properties similar to polychlorinated biphenyls (PCBs). Evidence suggests that PBDEs may affect thyroid hormones which play an essential role in female fertility, fetal growth and fetal and neonatal neurobehavioral development. Our objectives were therefore to examine whether exposure to PBDEs during pregnancy is related to maternal and neonatal thyroid hormone, time to pregnancy, birth weight, gestation duration, and child neurobehavioral development at ages 5 and 7 years. Women enrolled in the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) were included in the present study (n=601). Women who were \geq 18 years of age, $<$ 20 weeks gestation, English or Spanish speaking, Medi-Cal eligible (state-sponsored health care) and planning to deliver at Natividad Medical Center, the county hospital, were eligible for inclusion in the CHAMACOS study. We measured the concentration of 7 PBDE congeners (IUPAC Nos 47, 85, 99, 100, 153, 154 and 183) using high resolution gas chromatography/high resolution mass spectrometry with isotope dilution quantification (HRGC/HRMS) in serum samples collected at 26 weeks gestation. We concomitantly measured total T4 and TSH using immunochemiluminometric assays and free T4 using direct equilibrium dialysis followed by ultrasensitive radioimmunoassay. Data on time to pregnancy was obtained from questionnaires, birth weight and gestation duration was abstracted from medical records, and neurodevelopment was assessed by trained psychometricians. We found that increasing maternal PBDE serum concentration was related to a reduction in maternal TSH, but not with maternal free or total T4 or neonatal TSH; longer time to pregnancy, reduced birth weight and altered neurobehavioral development on several scales. Results suggest that maternal exposure to PBDEs may be related to impairments in reproductive function and child development.



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Clean Air Projects (CAP) - Educational Resources Linking Air Quality and Health

Presenting Author: Lisa Cicutto, National Jewish Health

Contributing Authors: Crews, K. (National Jewish Health)

Abstract:

Introduction: Air quality is connected to our health, ecosystems, energy consumption, economy and quality of life. It is essential that youth understand interrelationships between our environment and human health. The priority of our Community Advisory Board is to target youth through schools by integrating air quality and health within the state's curriculum. The overall goal is to prepare Colorado youth to become critical thinkers capable of making informed decisions and taking actions about their environment and health. To assist educators a resource of "best" lesson plans and supports was developed.

Methods: Several steps were completed to develop a resource of best materials based on solid evidence and current pedagogical principles. Since several resources exist, an additional purpose was to avoid duplication and reinvention of resources while simultaneously creating an accessible resource. Developmental steps included: performing a needs assessment and environmental scan, retrieving and reviewing existing resources to identify "best" lesson plans, blueprinting lesson plans to Colorado curriculum frameworks, and teacher reviewing and rating of the best available lesson plans.

Results: The initial search identified thousands of resources related to air, air quality/pollution and/or health. After additional refinement of search terms and initial review of identified resources, 21 programs consisting of 192 resources underwent a second level review. This second level review was completed against identified criteria for a "best" resource as defined through the needs assessment and environmental scan. Examples of criteria used included: inquiry based, critical thinking development, easy to use, accuracy, and links air quality and health. Following the second level of review, 17 lesson plans were identified as ready to use, 39 resources identified as needing additional work and 136 resources were identified as not useful. Of the 17 ready to use lesson plans, 8 were suitable for 6th to 8th grades, 5 were suitable for K-5th grades and 4 were suitable for 9th-12th grades. The most common areas of foci for resources were air pollution in general and the Air Quality Index. The most common reasons for resources being identified as not useful were the lack of a link between air quality and health and the lack of an inquiry based framework.

Conclusion: Several ready to use lesson plans exist for educators of grades K-12 to prepare future generations to make informed decisions and serve as environmental stewards related to air quality and health. A website was developed to make these resources available as a one stop place for educators.

Next steps include assessing the usability of the website, working with local partners to provide continuing professional development opportunities related to teaching within an inquiry based and critical thinking paradigm, and collaborating with educators for implementation of resources.



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Food Borne Exposure to Arsenic During the First Year of Life

Presenting Author: Kathryn Cottingham, Dartmouth College

Contributing Authors: Karagas, M.R. (Dartmouth Medical School); Punshon, T. (Dartmouth College); Folt, C.L. (Dartmouth College); Gilbert-Diamond, D. (Dartmouth Medical School); Jackson, B.J. (Dartmouth College); Taylor, V.F. (Dartmouth College); Sayarath, V. (Dartmouth Medical School); Davis, M.A. (Dartmouth Medical School); Bannon, D.M. (Dartmouth College); Webb, L.M. (Dartmouth College)

Abstract:

Exposure to environmental toxicants during fetal development and early infancy can increase disease risk both during childhood and later in life. We are studying the influence of diet on exposure to arsenic during the first year of life, focusing on babies born into the New Hampshire Birth Cohort study. This study seeks to evaluate effects of exposure to elevated arsenic in drinking water and food on pregnancy outcomes and infant health. Connections between food borne arsenic and established biomarkers of exposure are not well studied in children, especially in the U.S., where nutritional status is markedly different than in acutely arsenic-impacted areas such as Bangladesh and the Andes.

We are determining what infants eat both before and during weaning, as well as the arsenic content of these foods. We will use these data to estimate actual exposure, then compare our estimates to short- and long-term biomarkers (urine and toenails, respectively). Our particular focus is on the period from birth through the transition to solid foods (~4-6 months of age), but we are also collecting pilot data on the period when solid foods increase in dietary importance (~6-12 months). In addition to quantifying general infant dietary patterns at 4, 8 and 12 months by telephone questionnaire, we have conducted extensive market basket studies of infant formulas and weaning foods. We are also finalizing protocols to collect detailed dietary records, infant urine, and (where possible) breast milk at each focal time point.

A particular emphasis of our study has been rice and rice-based products. When we began our studies in 2010, concerns were growing not only about arsenic in drinking water, but also the possible health effects of high concentrations of inorganic arsenic in US-grown rice and rice-based products, including baby cereal. Infants, with their low body mass and limited diet of water (via formula) and rice cereal, were thought to be at particular risk. Our findings suggest that there is indeed cause for concern: we have found that (1) rice consumption is positively associated with urinary arsenic biomarkers during both pregnancy and childhood, (2) infant formulas sweetened with organic brown rice syrup contain concentrations of inorganic arsenic that exceed current U.S. and W.H.O. drinking water standards (10 µg/L), and (3) weaning foods containing rice and rice products have elevated arsenic relative to foods that do not contain rice. Thus, arsenic in rice is a potential source of human exposure that could be reduced by regulatory limits on arsenic concentrations in rice and rice products.



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Maternal Arsenic Exposure in Relation to Infant Infection in a US Cohort

Presenting Author: Shohreh Farzan, Dartmouth Medical School, Section of Biostatistics and Epidemiology

Contributing Authors: Li, Z. (Dartmouth Medical School); Korrick, S. (Harvard Medical School); Enelow, R. (Dartmouth Medical School); Gandolfi, A. (University of Arizona); Madan, J. (Dartmouth Medical School); Karagas, M. (Dartmouth Medical School)

Abstract:

Arsenic is a ubiquitous environmental toxicant with a broad range of deleterious health effects. A potent carcinogen, arsenic more recently has been related to disrupted immune function and enhanced susceptibility to infections in highly exposed populations. Due to geologic formations, and reliance on private wells, naturally occurring arsenic levels above the US EPA maximum contaminant level (MCL) in drinking water can occur in our New Hampshire study area. Arsenic exposure is a particular health concern for vulnerable populations such as pregnant women and infants. Therefore, as part of the New Hampshire Birth Cohort Study, we investigated whether in utero exposure to arsenic affects risk of infant infections. We obtained postnatal follow-up information for approximately 150 infants using a telephone-administered infant health survey. Mothers were asked a series of questions about infections and common symptoms that their infant may have experienced in the first four months of life, such as upper and lower respiratory tract infections, fever, diarrhea and specific illnesses. The survey also asked mothers about the duration of any reported infections and their severity, based upon whether the infection warranted a doctor visit or required prescription medication. In a preliminary analysis of this group of infants, we found maternal urinary arsenic concentrations during pregnancy to be related to rate of infections ($p=0.08$). In particular, more severe infant infections were observed in relation to arsenic exposure, including higher urinary arsenic concentrations among mothers whose infant required prescription medication for bronchiolitis ($p=0.07$) and reported diarrhea lasting more than 2 days ($p=0.08$) in the first four months of life. These results provide initial evidence that in utero arsenic exposure may be related to impaired ability to effectively clear infections and provides insight into the early life impacts of fetal arsenic exposure.



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Center for Child Environmental Health Risks Research

Presenting Author: Elaine M. Faustman, University of Washington

Contributing Authors: Thompon, B. (Fred Hutchinson Cancer Research Center); Griffith, W.C. (University of Washington); Vigoren, E. (University of Washington)

Abstract:

The overall goal of the University of Washington's Center for Child Environmental Health Risks Research is to protect children's health, with specific objectives to: (1) identify cellular, biochemical and molecular mechanisms for the adverse developmental neurotoxicity of pesticides; (2) identify susceptibility factors for developmental neurotoxicity of pesticides; (3) improve our understanding of critical pathways of pesticide exposure for children; (4) intervene to reduce children's exposure to pesticides; and (5) provide core support for the development and application of risk assessment methods. This will enable basic research on pesticide toxicity and exposure to inform risk decisions to protect children's health from pesticides; and (6) foster partnerships between academic researchers and the community in which information requested by the community and basic research questions are translated into studies that address the needs of both.

The Center represents a multi-disciplinary research program including members from multiple institutions, schools, departments, and disciplines. Elaine M. Faustman, PhD, DABT, is the Center's Director. The Center is housed in the School of Public Health at the University of Washington. For the Center's Community Based Participatory Research Project (CBPR), we have partnered with the Fred Hutchinson Cancer Research Center to coordinate the study in Yakima Valley communities, located in the agricultural center of Washington State, to jointly sponsor a program aimed at reducing childhood pesticide exposure.

For over a decade the CBPR has worked with community groups and individuals in the Yakima Valley to examine the potential for farmworkers to inadvertently take home pesticide residues on their cloths and skin, potentially leading to pesticide exposure in their children. The Center has recruited over 800 households (700 farmworker households; 100 non-farmworker households) and has retained this cohort (77.8%) for over 10 years. We have used a community-based participatory approach because of the potential to facilitate a two-way community dialogue affecting research design and implementation. The findings of the CBPR study have important public health significance and have shown that children living in agricultural communities have higher exposures than the general population, and that the take-home exposure pathway contributes to residential pesticide contamination in agricultural homes where young children are present. The Center's facility cores support this research program. In 2009 the Center entered the field again to launch an aggressive campaign to evaluate two different types of pesticide applications and community impacts.



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Identification of Novel Biomarkers for Low-Level Arsenic Exposure in Human Placenta

Presenting Author: Dennis Liang Fei, Miller School of Medicine, University of Miami

Contributing Authors: Koestler, D.C. (Dartmouth Medical School); Giambelli, C. (University of Miami); Sanchez-Mejias, A. (University of Miami); Karagas, M.R. (Dartmouth Medical School); Robbins, D.J. (University of Miami)

Abstract:

Background: Emerging evidence suggests that arsenic exposure in utero affects fetal health. However, such results are based largely on data from animal models treated with very high doses of arsenic or from individuals who reside in areas of the world highly contaminated with arsenic. In the present study, we aim to increase our understanding of the impact of low-dose arsenic exposure on fetal health by identifying arsenic-associated placental biomarkers in a cohort of pregnant women who are exposed to arsenic at or below the current drinking water standard (10 µg/L).

Methods: Arsenic concentrations for urine and home tap-water samples were collected from 89 pregnant women from New Hampshire. Placental tissue samples collected from enrollees were homogenized and profiled for gene expression across a panel of candidate genes, including known arsenic regulated targets, and genes involved in arsenic transport, metabolism, or disease susceptibility. Multivariable adjusted linear regression was used to examine the relationship between arsenic exposure and the expression of various candidate genes.

Results: We have identified significant associations between low-level arsenic exposure and the expression of two known arsenic targets, *ARK1C3* and *ENPP2*, and the arsenic transporter *AQP9*. In particular, the enhanced expression of *AQP9* by arsenic exposure is the most significant association among all genes examined. This association between arsenic exposure and *AQP9* expression is more significant in individuals expressing low-level *GSTM1*, a phase II enzyme involved in arsenic metabolism. Moreover, *AQP9* levels are associated with the expression of many of the other arsenic targets we tested in our study cohort. Multivariable adjusted analyses suggest that *AQP9* expression primarily affects the expression of *HMOX1*, while *AQP9* expression and arsenic exposure both influence the expression of *AKR1C3*, *ENPP2*, *HMOX1*, *NFE2L2*, and *TYMS*.

Conclusion: Our results suggest that arsenic exposure at levels similar to or below the current WHO drinking water standard can impact the expression of a subset of target genes in human placenta. Among all the gene candidates tested, the significant induction by arsenic, and its function as an arsenic transporter, combine to make *AQP9* an intriguing novel biomarker for low-dose arsenic exposure during human fetal development.



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Local Neighborhood Deprivation: New Methods to Define Neighborhoods and Measure Determinates of Poverty

Presenting Author: Sara Gale, University of California, Berkeley

Contributing Authors: Padula, A (University of California, Berkeley); Tager, I (University of California, Berkeley)

Abstract:

Background and Aims: Previous studies have demonstrated an association between neighborhood deprivation, exposure to air pollution and asthma outcomes. However, what constitutes a neighborhood and how best to characterize local environments is subjective and constantly evolving. A neighborhood is defined by a geographic boundary and thus, the appropriate scale and aggregation units must be considered in epidemiologic analyses. We aim to create individual neighborhoods based on walking distances from children's residences and to describe quantitatively neighborhood deprivation.

Methods: This study uses a geographic information system (GIS) to create neighborhoods and measure local, area-level deprivation in Fresno, CA. Markers of deprivation include low grocery store availability, alcohol outlets, cigarette sales permits, lack of schools and parks, no public transit, lack of daycares, and eight census-derived variables. We use item response theory (IRT) with maximum likelihood estimation to develop a deprivation scale for study subjects' neighborhoods (n=518) where geographic attributes are converted to positive and negative neighborhood influences.

Results: The median IRT score for participants is 0.16 (where scores range from -5 to 5 for low to high deprivation). The scores are correlated positively with census defined poverty (Spearman correlation $\rho=0.2$).

Conclusions: The IRT scores help summarize multiple GIS inputs and describe more precisely local deprivation with a composite score. The advantage of using individual neighborhoods defined by walking distances versus census defined boundaries is that the individual neighborhoods partly solves the problem of non-identifiability, an issue that plagues neighborhood research. Our future research will employ the IRT scores to determine if there is a relation between neighborhood deprivation and exposure to traffic and lung function among asthmatic children.



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Perinatal Lead Exposure, Epigenetics, and Growth: Combined Experimental and Epidemiological Approaches

Presenting Author: Jaclyn Goodrich, University of Michigan

Contributing Authors: Faulk, C. (University of Michigan); Peterson, K. (University of Michigan); Meeker J. (University of Michigan); Sanchez, B. (University of Michigan); Barks, A. (University of Michigan); Tellez-Rojo, M. (National Institute of Public Health, Mexico); Lee, J. (University of Michigan); Howard, H. (University of Michigan); Dolinoy, D. (University of Michigan)

Abstract:

The overall goal of our research is to elucidate the impact of perinatal lead exposure on childhood growth, DNA methylation, and the interplay between the two. Lead is hypothesized to associate with childhood obesity along with other related parameters (e.g., weight gain, hormonal biomarker levels) and hypomethylation of epigenetically labile genes in mice and humans at various time points during development. We utilize a two-pronged approach to test our hypothesis experimentally (with mice) and in an epidemiological cohort (the Early Life Exposures in Mexico to Environmental Toxicants, ELEMENT, Cohort). Viable yellow agouti mice (Avy/a) were exposed in utero to leaded water (dose groups: control- 0 ppm, 3.7 ppm, 27 ppm, 55 ppm). This gestational lead exposure paradigm results in a range of human-relevant maternal blood lead levels (peak BLL 0, 3, 10, and 25 ug/dL, respectively). Throughout the life course, physiological parameters (e.g., body composition, activity levels, hormone status) are characterized in these mice. Pyrosequencing is used to quantify DNA methylation levels at loci known to be epigenetically labile and/or important for growth (e.g. Avy, Cabp, Igf2). Initial screening of epigenetic marks using DNA purified from post-natal day 21 tail tips suggests lead is associated with hypomethylation of Cabp and Avy, and this effect appears to be dose-dependent. Near statistically significant decreases in methylation were observed at two Cabp CpG sites (ANOVA linear trend test p-values for sites 7 and 9 = 0.07 and 0.06). Furthermore, the two highest lead doses were associated with significant shifts in the coat color distribution towards yellow, a phenotype indicative of decreased Avy methylation (Chi-square goodness of fit test, p-value= 0.009 and 0.006, respectively). Epigenetic analyses in the ELEMENT Cohort are ongoing and include relating lead biomarker levels to growth parameters (e.g., childhood weight gain, hormone levels) and DNA methylation of genes crucial to growth and development (IGF2, H19, HSD11B2). Biomarkers and anthropometry measures are available from various time points ranging prenatally through adolescence, allowing for a longitudinal assessment of the impact of lead on childhood development and the epigenome. By studying perinatal lead exposure in an animal model and an epidemiological cohort, we aim to significantly increase current understanding of lead exposure and adverse growth outcomes and the contribution of epigenetic modification to these outcomes.



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Combined Use of Research-Based Methods and Community Outreach Approaches to Improve Respiratory Health of Preschool Children

Presenting Author: Diane Heck, Children's Environmental Health Center of the Hudson Valley

Contributing Authors: Shakarjian MP (NYMC School of Health Sciences and Practice & Institute of Public Health); Ansehl A (NYMC School of Health Sciences and Practice & Institute of Public Health); Fan Z-H (Environmental and Occupational Health Science Institute); Kim HD (NYMC School of Health Sciences and Practice & Institute of Public Health); Dozor A (New York Medical College); Amler R (NYMC School of Health Sciences and Practice & Institute of Public Health); Hudson J (Orange County NY Department of Health); Laskin JD (Environmental and Occupational Health Science Institute)

Abstract:

Vehicle exhaust is the leading source of toxic air pollution for most communities in the Lower Hudson Valley (LHV) of New York State, and a single vehicle used to commute children to school contributes 3 pounds of air pollution monthly. Studies demonstrate that initial incidents of asthma develop before age 5, suggesting that preschool years mark the critical period for development of the disease and that prevention be focused at this age group.

Furthermore, analysis of SPARCS data demonstrated high asthma hospitalization rates for children in the LHV. Interestingly, for preschoolers, these rates are higher in some counties (ex. 40.1/10,000 for Orange County) than they are in NYC, and for the region early childhood asthma rates are higher than Healthy People 2020 goals (25/10,000).

These criteria prompted us to hypothesize that that automobile exhausts from delivering and retrieving children have a significant impact on the quality of outdoor and indoor ambient air at school facilities. To test this hypothesis we initiated a study analyzing the baseline levels of asthma triggering contaminants of automobile and bus exhaust (nitrogen dioxide, VOCs, and particulates) at three preschool facilities in Orange County, NY. The objectives of this study are to document automobile and bus traffic and determine the levels of asthma-triggering contaminants of exhaust at three preschools. Results from this study will be used to develop a community-based effort to incorporate a 'no idling' policy as part of their environmental program. We have completed studies at the first site in Orange County. Our results clearly indicated that increases in airborne toxicants correlate with traffic levels, and that large vehicles including buses and trucks are major contributors. Importantly the levels of traffic-related air pollutants were markedly higher inside of the preschool than those outside, reflecting accumulation within the enclosed environment. The results of these studies will be presented to the local town boards and a steering committee of school representatives and community leaders are relying upon well-established local social networks, in support of community regulation of the locations of preschools and vehicular no-idling policies. It is our goal to raise awareness of the effects of preschool location and car idling through advocacy using the framework for action and change is based on theory developed by Everett M. Rogers that diffusion of innovations spreads via channels of communication developed by social members.



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Urinary Concentrations of Bisphenol-A in an Urban Minority Birth Cohort in New York City, Prenatal Through Age 7 Years

Presenting Author: Lori Hoepner, Columbia University Center for Children's Environmental Health

Contributing Authors: Whyatt, R. (Columbia University); Just, A. (Columbia University); Calafat, A. (Centers for Disease Control and Prevention); Perera, R. (Columbia University); Rundle, A. (Columbia University)

Abstract:

Objective: Describe bisphenol-A (BPA) concentrations and correlated factors in a birth cohort through age 7 years.

Background: There is growing epidemiologic evidence that prenatal and early childhood exposures to ubiquitous endocrine disruptors such as BPA can result in adverse disease outcomes. Insufficient information is available on determinants of BPA concentrations among minority populations in the US.

Methods: As part of the Columbia Center for Children's Environmental Health (CCCEH) birth cohort of African American and Dominican children living in the South Bronx and Upper Manhattan, 568 mother-child dyads were analyzed for total BPA in spot urines. Mothers were selected if they had a sample analyzed prenatally and their children were selected if they had at least one sample analyzed at age three, five or seven years. All analyses used log-transformed BPA and adjusted for specific gravity.

Results: BPA was analyzed in 377 prenatal samples (94% above limit of detection (LOD)), 419 age three year samples (98% above LOD), 401 age five year samples (98% above LOD), and 318 age seven year samples (96% above LOD). BPA concentration geometric means were higher among African Americans compared to Dominicans in prenatal ($p=0.007$), five year ($p=0.001$) and seven year ($p=0.001$) samples. Geometric means for the five and seven year samples were higher ($p=0.002$, $p=0.015$ respectively) for children of mothers never married at baseline compared to mothers ever married at baseline. BPA concentrations were significantly correlated with eight phthalate metabolite concentrations prenatally and at three and five years (r values from 0.12 to 0.35, all p -values <0.05). Calendar season predicted BPA concentrations in children ages three, five and seven years (summer=reference, Beta estimates -0.26 to -0.12 ng/ml, all p -values <0.05).

Conclusions: The CCCEH is uniquely poised to evaluate early life exposures to BPA in urban minority children. This study shows widespread BPA exposure in an inner-city minority population. BPA concentration variations were associated with socio-demographic characteristics.



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Epigenetic Effects of Environmental Toxicants in Minority Children

Presenting Author : Nina Holland, CERCH, SPH, University of California, Berkeley, CA

Contributing Authors: Yousefi, P (University of California, Berkeley); Aguilar, R (University of California, Berkeley); Quach, H (University of California, Berkeley); Volberg, V (University of California, Berkeley); Bradman, A (University of California, Berkeley); Barcellos, L (University of California, Berkeley); Eskenazi, B (University of California, Berkeley)

Abstract:

The CHAMACOS longitudinal birth cohort study investigates exposure to pesticides and other environmental pollutants and their effects on growth and neurodevelopment of children from low-income Mexican-American farmworker families in California who were followed from birth to 9 years of age. We have found that pre-natal exposures to several of these pollutants are associated with shortened gestation and decreased IQ at age 7. Epigenetic changes, particularly DNA methylation, may play a significant role in mediating the effects of environmental exposure on human health and development. Global and site-specific DNA methylation was assessed in 254 newborn- and 9-year-old CHAMACOS children by Illumina Infinium HumanMethylation450K BeadChips to simultaneously interrogate methylation at 485,577 CpG sites, and by pyrosequencing of Alu and LINE-1 repeats. We found that global DNA methylation increased with age and differ by sex but the measures were not correlated across the three assays. Analysis of Illumina data presents an opportunity to assess different parts of 24,275 genes across methylome. After adjusting for multiple testing by controlling for the False Discovery Rate, we observed that approximately 15.5% of all investigated CpG sites, representing >15,000 genes, were differentially methylated between children at birth and 9 years of age. More than 2% of CpG sites investigated in >1,900 genes showed significant differences in methylation by sex. As expected, most were located in sex chromosomes; however, some 731 CpG sites with significant differences between girls and boys were found in autosomes. Markers of DNA methylation were also associated with prenatal exposure to persistent organic pollutants. Different patterns of methylation change were observed between shores, shelves, and CpG island regions. Candidate genes and pathways involved in age and sex differentiation, and in response to early life exposures, have been identified for future analyses of their effects on obesity and puberty.



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Genetic and Epigenetic Biomarkers of Susceptibility to OP Pesticides and Obesity in Children

Presenting Author: Nina Holland, CERCH, SPH, University of California, Berkeley

Contributing Authors: Huen, K (University of California, Berkeley); Harley, K (University of California, Berkeley); Bradman, A (University of California, Berkeley); Barcellos, L (University of California, Berkeley); Pratt, K (University of California, Berkeley)

Abstract:

Children's susceptibility to environmental toxicants may depend on their genotype, levels of exposure and their interactions. In the longitudinal birth cohort study of low-income Mexican-American farmworker families in California (CHAMACOS) we found that in utero exposures to pesticides were associated with abnormal birth and neurodevelopmental outcomes at different ages (Eskenazi et al, 2004, 2007, 2010; Young et al, 2005; Bouchard et al, 2011). We also demonstrated that these health effects depend on phenotype and genotype of paraoxonase (PON1), a multifunctional enzyme involved in detoxification of organophosphate (OP) pesticides and oxidative stress (Holland et al, 2006; Huen et al, 2009; 2010; Eskenazi et al, 2010; Harley et al, 2011). CHAMACOS population has a high prevalence of obesity in mothers and children that exceeds national averages for Mexican-Americans. In this study of 383 CHAMACOS children, we observed significant associations of child PON1 genotypes and PON1 status (PON1192 genotype and PON1 enzyme levels) with both body mass index (BMI) Z-score and obesity status at age 2. Compared to children with the PON1192RR genotype, the odds of obesity were 5.2 and 9.6 fold higher in PON1192QR and PON1192QQ children, respectively. Additionally, we genotyped ancestry informative markers (AIMs) to estimate proportional ancestry for each individual and found little evidence of genetic confounding among two year old CHAMACOS children. In addition to genetic polymorphisms, epigenetic mechanisms such as DNA methylation in PON promoter region (assessed by Illumina 450K Methylation BeadChip), were also associated with PON1 expression in an allele-specific manner. Epigenetic and genetic influences on PON1 may affect susceptibility to OP pesticides and conditions related to oxidative stress including obesity. Possible contribution of environmental exposures such as prenatal pesticide exposures, to the genetic, epigenetic and behavioral mechanisms of obesity warrants additional attention.



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Immune Function and Ambient Air Pollution Exposure in Asthmatic Children

Presenting Author: Dr. Olivier Humblet, Stanford University and University of California, Berkeley

Contributing Authors: Noth, E (University of California, Berkeley); Lurmann, F (Sonoma Technology, Inc.); Pratt, B (University of California, Berkeley); Hammond, K (University of California, Berkeley); Balmes, J (University of California, Berkeley); Tager, I (University of California, Berkeley); Nadeau, K (Stanford University)

Abstract:

Introduction: Asthma is the most frequent chronic disease in children. Both its severity and incidence are associated with exposure to ambient air pollution (AAP). Studies have demonstrated that short-term and long-term exposure to AAP leads to changes in inflammatory mediators in the lung and blood. However there is a research gap on the link between AAP and changes in Foxp3+ regulatory T cells (Tregs). Tregs are a newly-identified class of CD4+ cell which play an essential role in the regulation of immune function, including the inhibition of allergic sensitization.

Methods: Immune function was assessed in blood collected from 71 asthmatic children enrolled in the Children's Health and Air Pollution Study in the San Joaquin Valley (CHAPS-SJV), a prospective cohort study in Fresno, CA. Asthma severity (e.g. FEV1 and GINA score) was assessed at each participant's baseline visit (between 2000 and 2005).

Individual daily exposure to ozone (O3), nitrogen dioxide (NO2), carbon monoxide (CO), particulate matter (PM10) and fine PM (PM2.5) for each child using integrated spatial data from multiple air monitoring sites. The most recent available annual mean and most recent summer mean were calculated.

Multiple immune assays were conducted, including cell proliferation assays to assess the capacity of each person's Tregs to suppress proliferation by conventional CD4+ T cells in vitro (i.e. Treg % suppression); flow cytometry to assess the percentage of conventional CD4+ T cells expressing IL-4 and IL-13, and the percentage of CD4+ CD25^{HI}CD127⁻ Tregs expressing Foxp3; real-time PCR to measure Foxp3 expression in Tregs; methylation of the Foxp3 promoter in Tregs, and in vitro migration of purified Treg.

Results: Treg % suppression was associated with higher lung function at baseline (FEV1). A measure of recent sub-acute exposure to fine particulate matter (i.e. mean summer PM2.5) was associated with decreased Treg function and increased inflammation. No associations were seen for the other pollutants. Weaker or nonexistent associations with the immune markers were seen for the annual mean AAP measures.

Conclusions: The preliminary data obtained from samples of asthmatic children with high levels of ambient air exposure demonstrate that:

- A measure of recent exposure to ambient fine particulate matter (i.e. mean summer PM2.5), was associated with decreased Treg function and increased inflammation measured in 2009.
- Recent exposures to ambient O3, NO2, CO, and PM10 were not associated with any differences in immune function, nor were annual mean measures of ambient O3, NO2, CO, PM10 or PM2.5.



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Future work: Recruitment of over 300 new participants continues with the NIEHS- and EPA-funded Children's Health and Air Pollution Study in California's San Joaquin Valley (CHAPS-SJV). Future work will seek to replicate and extend the present findings with other pollutants, including PAHs.



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ASD Prevalence Studies: Stepping Stones to Understanding GEX in Developmental Psychopathology

Presenting Author: Young Shin Kim, Child Study Center, Yale University School of Medicine

Contributing Authors: Bennett Leventhal; Matthew State

Abstract:

Identifying the etiology of ASD is challenging due to methodological shortcoming including phenotypic heterogeneity and the use of mainly clinical samples that may reflect biased selection. Using total population approach in a two-stage prevalence study, we will 1) Examine a comprehensive prevalence of ASD; 2) Describe entire distribution of ASD phenotype including clinical and non-clinical populations; and 3) Establish an epidemiologically-ascertained population-based cohort of ASD to examine the roles of GEX in the risks for ASD.

Target Population (N=55,266) included all 7-12 year-old children attending elementary schools in Goyang City, South Korea, between years 2005 and 2006. 1st Screening Stage (N=23,337) was performed with Parent/teacher Autism Spectrum Screening Questionnaires. In 2nd stage, Confirmative Diagnoses (N=286) were made by clinical best estimate diagnoses utilizing Autism Diagnostic Observation Scale, Autism Diagnostic Interview-Revised and cognitive tests.

ASD prevalence estimate was 2.64% (clinical sample 0.8%, comparable; 1.8% prevalence in the non-clinical sample.) The majority of children in the clinical sample had autistic disorder with more severe symptoms, male:female=5:1, and mean IQ 75. For the non-clinical sample, most children were diagnosed with other types of ASD with lesser severity, male:female=2.5:1, and mean IQ 98.

Comprehensive ASD phenotype represents less male dominance and average IQ without seeking clinical services. Etiological research requires un-biased, population-based, epidemiologically ascertained study subjects. For the future study, we will: 1) develop an independent community sample with dimensional phenotype measures (N=10,000); 2) acquire blood markers for ASD biological markers; and 3) conduct whole genome genotyping to examine the roles of GEX in the risks for ASD.



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Community Outreach and Engagement Addressing Environmental Health in a Multi-Faceted Agricultural Community

Presenting Author: Daniel Madrigal, UC Berkeley, Center for Environmental Research and Children's Health

Contributing Authors: Camacho, J (Clinica de Salud Valle de Salinas); Trujillo, C (UC Berkeley); Casillas, G (UC Berkeley); Parra, K (Clinica de Salud Valle de Salinas); Rosas, L (Stanford Prevention Research Center); Salvatore, A (Stanford Prevention Research Center); Minkler, M (UC Berkeley); Bradman, A (UC Berkeley); Eskenazi, B (UC Berkeley)

Abstract:

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) is a community/university partnership examining environmental exposures and children's health and development in the Salinas Valley, CA. To complement the research aims, the CHAMACOS community outreach and translation core (COTC) is engaged in extensive translational activities in this low-income, agricultural area, including: (1) timely dissemination of study findings to individuals, key stakeholders, and the general community, (2) providing a mechanism for community members to contribute to the research process and also help set priorities for future directions, (3) increasing awareness about children's environmental health, (4) targeted outreach to prevent toxicant exposures, (5) developing an environmental health leadership program for local adolescents, and, (6), when requested, educating policy makers about the implications of our research findings. Our central mechanism involves a Community Advisory Board (CAB) consisting of farmworkers, county health and agricultural officials, community groups, elected officials, and agricultural industry representatives. To complement the CAB, we convened a Grower Council consisting of major industry groups and growers and a Farmworker Council, a forum conducted solely in Spanish to enhance ease of communication. Members of each council participate on the CAB. Research findings are disseminated to study participants through community fora (attended by hundreds of people each year), newsletters, and a website. Environmental education and exposure-prevention activities are conducted at several levels, including education to farmworkers and their families, training of service providers such as schools, child care centers, and housing managers, delivery of continuing medical education (CME) approved presentations, and working with growers to implement field-based pesticide exposure-prevention work practices. Each of the community-engagement activities are targeted to populations with different education levels and personal and economic interests and thus require population-specific framing strategies to ensure effective, two-way, communication. In this presentation, the overall outreach program and the essential components of our framing strategy for each population will be described. We will also discuss future directions for the CHAMACOS COTC activities.



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Daily Changes in Air Pollution and Lung Function: Use of Modeled Daily Personal Exposures

Presenting Author: Jennifer Mann, University of California, Berkeley, Sonoma Technology, Inc.

Contributing Authors: Lurmann, F.(Sonoma Technology, Inc.); Noth, E (University of California, Berkeley); Balmes, J (University of California, Berkeley); Hammond, K (University of California, Berkeley); Alcorn, S (Sonoma Technology, Inc.); Reid, C (University of California, Berkeley); Pratt, B (University of California, Berkeley); Tager, I (University of California, Berkeley)

Abstract:

Background/Aims: Exposure measurement error should be reduced when estimates of ambient air pollutant exposures account for spatiotemporal variations in concentrations and time/location/activity. We investigated the relationship of daily concentrations of nitrogen dioxide (NO₂), aerosol nitrate (NO₃), ozone, elemental carbon, PM_{2.5}, coarse fraction of PM₁₀, endotoxin and both FEV₁ and FEF₂₅₋₇₅, in a cohort of 315 asthmatic children in Fresno, CA, followed from 2000 to 2008

Methods: Pollutants were estimated using measurements at a USEPA supersite (SS) within 20 kilometers of all households. Modeled daily personal exposure estimates (MDPE) were developed for child-day, based on concentrations at the supersite, measurements at schools and homes (spatial component), and exposures to ambient pollutants when indoors (a time/location/activity sub-study, diary reports, penetration coefficients and loss rates) (indoor component). Pulmonary function was measured each morning with a programmable spirometer (EasyOne®, ndd, Zurich, Switzerland) for 14 days, up to 3 times a year. Effects of 0- to 7-day lags and 2- to 7 day moving averages for a change in interquartile range were investigated. MDPE concentrations were re-estimated with the spatial component only ("Spatial Only") and the spatial component removed ("No Spatial").

Results: After adjustment for height cubed, African American race and asthma diagnosis before the age of 2 and a fitted ARIMA term, NO₂ was the only pollutant associated with declines in pulmonary function (both FEV₁ and FEF₂₅₋₇₅), when SS were used to estimate exposure. However, with MDPE, both NO₂ and NO₃ were associated with decrements in FEF₂₅₋₇₅. NO₂ lag 1 was associated with a 26.4 ml/s decline in FEF₂₅₋₇₅ (95 CI=2.37-50.4 ml/s decline for a 9.4 ppb increase) with SS and a 26.9 ml/s decline in FEF₂₅₋₇₅ (95 CI=2.37-50.4 ml/s decline for a 9.4 ppb increase) with SS and a 26.9 ml/s decline in FEF₂₅₋₇₅ MDPE (95% CI= 4.30 to 49.5 ml/s decline, 3.8 ppb increase). For NO₃ lag 1, declines increased from 10.9 to 26.6 ml/s with use of MDPE (95% CI=-9.7 to 43.5, for a 3.9 µg/m³ increase in SS and -14.3 to 125 ml/s for a 0.99 µg/m³ increase in MDPE respectively. In general, the MDPE and "No Spatial" estimates were associated with a greater impact on FEF₂₅₋₇₅ than the "Spatial Only" or SS estimates, although the differences were not always statistically significant.

Conclusion: MDPE were associated with greater impacts on pulmonary function in asthmatic children, possibly due to reduction of exposure measurement error. For the deconstructed estimates, the "Spatial Only" and supersite estimates were associated with lower magnitude effect estimates and associations were less often significant.



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Childhood Tobacco Smoke and Air Pollution Exposure in a Longitudinal Cohort Study of Body Mass Index

Presenting Authors: Rob McConnell and Kiros Berhane, Keck School of Medicine, University of Southern California

Contributing Authors: Shen, E. (University of Southern California); Gilliland, G. (University of Southern California); Jerrett, M. (University of California, Berkeley); Wolch, J. (University of California, Berkeley); Chang, C. (University of Southern California); Lurmann, F. (Sonoma Technology, Inc., Petaluma, California)

Abstract:

Background: Secondhand tobacco smoke exposure (SHS) has been associated with increased childhood body mass index (BMI), but there have been few longitudinal studies or evaluations of the joint effects of SHS and other combustion products such as ambient air pollution.

Methods: Information on history of exposure to SHS was collected from parents at the time of enrollment of a cohort of 3318 participants (mean age 10.1) in the southern California Children's Health Study. Information on personal smoking and SHS during the 8 year follow-up period was collected yearly from each child at the time that height and weight were measured. Near-roadway traffic-related pollution (TRP) exposure at each child's residence was modeled from a line source dispersion model previously associated with asthma and other respiratory outcomes in this cohort. The growth trajectory and level of BMI and the association with exposure to SHS and TRP were assessed using a hierarchical statistical modeling framework.

Results: SHS exposure was positively associated with the 8-year growth of BMI (0.81 units; 95% confidence interval (0.35,1.26) and with BMI at age 18 (1.23 units; 0.85,1.60) compared to children without SHS exposure. Children with both SHS and TRP exposure above the median were more than 2 BMI units heavier than children with no SHS exposure living in low traffic residences.

Conclusion: BMI growth during the childhood period and level in young adulthood were associated with SHS exposure and effects were larger among children also exposed to higher levels of TRP.



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Using Quality Improvement Methods to Enhance Recruitment: The National Children's Study in Ramsey County, Minnesota

Presenting Author: Pat McGovern, University of Minnesota

Contributing Authors: Nancy Nachreiner, Bonika Steward, Deb Hendricks, Mindy Geisser, Gavin Watt, Wendy Hellerstedt, Deb Engelhard, Jill Cordes, Tim Church (University of Minnesota); National Opinion Research Center: John Sokolowski

Abstract:

Introduction: Participant recruitment is a critical factor in any longitudinal study. Identifying the most effective toolkit of approaches, tailored to the target population, is key to optimizing response.

Methods: Quality improvement principles guided testing of recruitment methods to inform design of for the Main Study. Our objective was to identify factors that increase response rates for Ramsey County. Study mailings were sent weekly to a random sample of over 30,000 dwelling units, beginning with Low Intensity (LoI) segments. Two adjacent LoI segments were selected for every High Intensity (HiI) segment.

Data collection mode. The original contact procedures included an advance letter mailed to the dwelling unit in LoI segments, followed by an invitation. Residents were instructed to call a toll-free number to participate. Subsequently, mailings began to HiI segments. Next Pregnancy Screeners were mailed, providing a second response mode. After all dwelling units were sent advance and invitation letters, mailings began for non-responders.

Results: Initial response rates varied from 1% to 15% by segment, with an overall response of 5% for LoI segments, and 9% for HiI segments. Response more than tripled for the HiI segments after introducing the mail response option. Non-responder mailings that included response options of calling or returning a mailed questionnaire also showed a strong effect---nearly the same level of response to the initial mailing.

Conclusions: Findings suggest multiple response modes and repeat mailings increase response. Multivariate analyses of response rates by county characteristics may provide additional insights into the most effective strategies.



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Health Examination System of Chemicals to Decrease the Health Risk on Future Generations

Presenting Author: Chisato Mori, Center for Preventive Medical Science, Chiba University, Japan

Contributing Authors: Todaka, E. (Chiba University, Japan)

Abstract:

Blood concentration levels of total polychlorinated biphenyls (PCBs) were measured from 526 Japanese people, including infants and children, by using a gas chromatograph equipped with a packed column and electron capture detector (packed column GC/ECD) (Mori, 2004; Fukata et al, 2005). The detection rate of total PCB was 100%. The total PCB is correlated with many other persistent organic pollutants (POPs), and it could represent contamination of POPs in human such as dioxins, hexachlorocyclohexane, and hexachlorobenzene (Mori and Todaka, 2011). In this study, the current exposure level to PCBs of modern Japanese people from prenatal period to 80 years old was examined. In general, blood PCB level increased with age. Also, adult males and females without pregnant experience showed similar tendency of increase with age. However, blood PCB levels of females who have given birth(s) to child(ren) was lower than those of males and females without pregnant experience probably because they transferred their PCBs to fetuses during pregnancy and to babies through lactation after giving births.

Fetal exposure level of total PCBs was estimated as 0.04 ± 0.02 ng/g-wet (average \pm S.D.) from the analysis of cord blood level. However, in the case of the infants lactated for more than 3 months, average value of total PCBs was 0.58 ± 0.27 ng/g-wet under 2 years old. The blood PCB levels of infants varied according to the length of the lactation period, while they decreased rapidly after the lactation period; the rapid decrease was probably due to the change of diet from breast milk to less-contaminated diet and dilution of the contaminants due to the rapid increase of body weight.

These results show the importance of decreasing the contaminant level before pregnancy. Contaminants in women are transferred to their children through umbilical cord and lactation, which means that if the contaminant level is decreased before pregnancy, the amount of contaminants that their children receive will be decreased. It was reported that if the cord blood PCB level was over 0.09ng/g-wet, there was higher possibility that the children have attention deficit / hyperactivity disorder (ADHD) (Stewart, et al., 2005). Therefore, we suggested establishing the health examination system for women at reproductive age by using the blood PCB level (Mori and Todaka, 2009). If women who accumulate PCBs at higher level are found by the health examination, then life intervention or medication is taken to decrease the level, then future children can reduce the risk on health. It is possible to promote health of future generation by applying this health examination system. We published a book, "Environmental Contaminants and Children's Health –Sustainable Health Science for Future Generations" in 2010, and it will be distributed at the poster presentation.



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Phenanthrene Linked to AhR-Mediated Treg Instability and Th2 Conversion

Presenting Author: Kari Nadeau, Stanford University and University of California, Berkeley

Contributing Authors: Liu, J (Stanford University); Winterroth, L (Stanford University); Zhang, L (Stanford University); Sunwoo, J (Stanford University); Hammond, K (University of California, Berkeley); Tager, I (University of California, Berkeley); Balmes, J (University of California, Berkeley)

Abstract:

Exposure to polycyclic aromatic hydrocarbons (PAHs), a major constituent of urban air pollution, is associated with impaired CD4⁺CD25^{hi}CD127^{lo} regulatory T cell (Treg) function and increased CpG island methylation of Foxp3, a gene essential for normal Treg development and function.

Data presented here demonstrate a causative mechanism for PAH-induced Treg impairment using ex-vivo studies of Treg isolated from healthy human controls. We found that phenanthrene exposure induced aryl hydrocarbon receptor (AhR) activation, which in conjunction with Sp1, upregulated DNA methyltransferases (DNMT) 1 and 3b. Subsequent Foxp3 CpG island methylation destabilized Foxp3 expression, leading to impaired Treg function and conversion of Treg into a CD4⁺CD25^{lo} T effector cell phenotype consistent with a Th2 subset.

Taken together, our findings present a mechanism by which exposure to PAHs could impact the regulatory arm of the immune system, skewing immune response towards atopy with implications for asthma and allergic inflammation.

HIGHLIGHTS

- PAH exposure impairs Treg function, induces T_{eff} conversion in ex-vivo human studies
- Novel molecular mechanism for Treg to Th2 conversion via AhR, Sp1 and DNMT pathways
- Phenanthrene destabilizes Treg Foxp3 expression via DNMT1,3b mediated methylation
- Specificity of AhR activation by PAH exposure determines T cell fate



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Spatio-Temporal Modeling for Individual Exposure to PAHs for Preterm Birth

Presenting Author: Dr. Elizabeth Noth, University of California, Berkeley

Contributing Authors: Padula, A (University of California, Berkeley); Lurmann, F (Sonoma Technology, Inc.); Tager, I (University of California, Berkeley); Hammond, K (University of California, Berkeley)

Abstract:

Preterm birth is an important marker of health both in the neonatal period, through childhood and possibly into adulthood. In the U.S., 12-13% of births are preterm— a public health problem that costs society at least \$26 billion a year. Polycyclic aromatic hydrocarbons (PAHs) are a group of organic contaminants that form from the incomplete combustion of hydrocarbons, such as coal and gasoline. Studies suggest that exposure to PAHs during pregnancy is related to adverse birth outcomes including low birth weight, preterm birth, small for gestational age and intrauterine growth retardation. Exposure to PAHs during the last 6 weeks of pregnancy was modeled for a cohort of pregnant women in Fresno County, CA, 2000-2006 for an epidemiology study of preterm delivery and low birth weight.

Data collected in the Fresno Asthmatic Children's Environment Study (FACES) was used with mixed models to build a spatio-temporal regression model of exposure to the sum of PAHs with 4-, 5- or 6-rings (PAH456). PAH data were collected daily at the US EPA Supersite in Fresno, CA from 10/2000 through 12/2006. From 2/2002-2/2003, we conducted intensive air pollution sampling at 83 homes with 5-10 24-hr PAH measurements per home. However, since the measurements were not made contemporaneously, the between- and within-in home variability had to be accounted for using mixed modeling. The PAH456 concentrations at participant homes were the dependent variables for each model; the candidate independent covariates in the model included the particle-bound PAH concentrations at the US EPA Supersite, meteorological data, source data, and other temporal and spatial variables. For each pregnancy, the daily mean exposure and 6-week cumulative exposure were calculated for the last 6 weeks of the pregnancy.

Mixed effects regression modeling with home as a random variable found that both temporal and spatial variables were important for estimation of PAH456 in Fresno, CA. The model for daily, outdoor PAH456 concentrations calculated daily mean and total cumulative PAH456 for the last 6 weeks of pregnancy for 44,927 pregnancies. The mean of the daily 6-week mean PAH456 exposure was 3.6 ng/m³ and the mean of the 6-week cumulative exposure was 154.25 ng/m³. The ratio of the 90th :10th percentiles for average individual temporal variability from entry to study through 2/2007 for estimated PAH456 was 3.2, and the ratio of the 90th :10th percentiles of the average daily spatial range was 1.7.

By using a mixed modeling regression approach, we were able to use all the observed data available from a longitudinal panel-based research project to create a model for PAH exposure in the last 6-weeks of pregnancy. We found that PAH concentrations within Fresno fluctuate significantly over both time and space. This indicates that it is necessary to account for the variability in both time and space when modeling the class of PAHs.



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Partnerships for Environmental Public Health

Presenting Author: Liam O'Fallon, National Institute of Environmental Health Sciences (NIEHS)

Contributing Authors: Anderson, B (NIEHS); Beard, S; Dilworth, C; Gray, K; Lawler, C; Eckert-Tilotta, S; Phelps, J; Pettibone, K; Drew, C; Hughes, C; Thompson, C; Davis, H; Humble, M; Balbus, J; Crane, J

Abstract:

The National Institute of Environmental Health Sciences (NIEHS) has promoted and developed community engaged programs since 1994. Over the years, NIEHS established grant programs to address environmental public health issues of greatest concern to community groups. These individual programs focused on community engagement, capacity building, research, education, and communication. A key challenge for these successful programs has been 'programmatic silos' that hinder interactions among different grantees. In 2008, NIEHS initiated a 're-visioning' process, which led to the design and implementation of the Partnerships for Environmental Public Health Program (PEPH). PEPH serves as a coordinating body that integrates the various new and existing initiatives that involve communities and scientists working together on contemporary issues in environmental public health; in effect, PEPH breaks down the 'programmatic silos' and promotes a virtual network among the projects. Through PEPH, NIEHS seeks to stimulate both scientific advances and development of practical tools, materials, and resources that can be used by a variety of audiences to improve environmental public health.

We believe that PEPH is an useful model for bringing together individuals, project teams, and partners to discuss, learn from, and advance their common experiences, approaches, and materials regardless of which program they receive their funding. This poster highlights the overall structure, function and benefits of the PEPH program. The poster describes the key tenets of PEPH, the methods employed to integrate activities, and the challenges we face in coordinating new and existing initiatives in an effort to have a greater positive impact on the environmental public health of communities.



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Levels of Metabolites of Naphthalene in Urine Predict Translocations in Peripheral Blood Lymphocytes in Children

Presenting Author: Manuela Orjuela, Columbia University, Department of EHS, Columbia Center for Children's Environmental Health

Contributing Authors: Liu, X. (Columbia University); Warburton, D. (Columbia University); Miller, R. (Columbia University); Tang, D. (Columbia University); Cujar, C. (Columbia University); Suen, I. (Columbia University); Hoepner, L. (Columbia University); Perera, F. (Columbia University)

Abstract:

Chromosomal aberrations (CAs) and translocations (TRNS) (subtype of CAs) are a validated biomarker of increased cancer risk in adults. Prenatal exposure to semi-volatile air PAH predicts levels of stable CAs in neonatal (cord) blood. Urinary levels of 1- and 2-naphthol, metabolites of naphthalene and an IARC class 2b possible carcinogen, appear elevated in the Columbia Center for Children's Environmental Health (CCCEH) birth cohort. We hypothesize that concurrent exposure to naphthalene is associated with development of CAs and TRNS in children. Whole blood from 113 five year old children (68 girls) participating in the CCCEH birth cohort composed of Dominican (DomAm) (N=66) and African-Americans (AfrAm) (N=47) was processed fresh for Whole Chromosome Paint (WCP)- Fluorescent *In Situ* Hybridization using WCP for chromosomes 1-6. 400 Cell Equivalents (CE) were scored for each child. TRNS were scored in accordance with the PAINT convention and frequencies were expressed per 100 CE. Levels of PAH metabolites were measured using MS-GC in spot urine samples (Sjodin laboratory, CDC) collected concurrently and adjusted for urine specific gravity (SG). We examined predictors of presence of CAs or TRNS. For predicting frequency of CA and TRNS, mean ratios were derived for doubling of naphthol levels using negative binomial models. Results: 35 children had CAs and 20 had TRNS. Geometric means among AfrAm were 3490.2 for 1-naphthol, and 3005.1 for 2-naphthol, and 3336.4 and 5256.6 for 1- & 2-naphthol in DomAm children, respectively. 2-naphthol was higher in girls ($p=0.08$) and in DomAm ($p=0.01$). After adjusting for gender and ethnicity, presence of both CAs and TRNS was predicted by increasing levels of 1- and 2-naphthol, but the effect was significantly higher in DomAms for both 1- and 2-naphthols. To examine possible dose-response, levels of 2-naphthol were grouped into tertiles using the lowest tertile as the referent group. After adjusting for gender/ethnicity, the proportion with TRNS present increased with increasing 2-naphthol (though trend $p=0.09$). Children with 2-naphthol in the highest tertile were significantly more likely to have translocations (**OR 4.29; 95% CI: 1.11-16.55**) when compared with children in the lowest tertile. The effect of increasing naphthol on aberrations or translocations was not dominated by any one chromosome, in contrast to our findings in newborns and prenatal air-PAH. Together these findings support our earlier findings that PAH exposure is associated with formation of TRNS, and suggests a dose response pattern with exposure to naphthalene, and an ethnic difference in susceptibility to formation of CAs.



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The Population-Level Estimate of the Effect of Prenatal Exposure to Traffic on Preterm Birth

Presenting Author: Amy Padula, University of California, Berkeley

Contributing Authors: Mortimer, K (University of California, Berkeley); Tager, I (University of California, Berkeley)

Abstract:

Background and Aims: Preterm birth is an important marker of health both in the neonatal period, through childhood and possibly into adulthood. In the U.S., 12-13% of births are preterm (Goldenberg 2008) and preterm constitutes a public health problem that costs society at least \$26 billion a year (Behrman 2007). Associations between prenatal exposure to traffic and a variety of adverse birth outcomes including preterm birth have been reported, (Shah 2011). but a causal relationship has not been established (HEI 2010). The aim of this study is to use causal inference estimators to evaluate the marginal (population-level) effect of traffic density on preterm birth in a cohort of over 300,000 births in four counties in the Central Valley of California during years 2000-2006.

Methods: Preterm birth was defined as less than 37 weeks gestation as reported on the birth certificate. Traffic density was based on distance-decayed annual average daily traffic volumes. Targeted maximum likelihood estimation (TMLE) was applied to estimate the counterfactual probability of preterm birth had everyone been exposed to each quartile of traffic density. In addition, a population intervention model (PIM) was applied to estimate the potential change in preterm birth given a hypothetical intervention in which traffic density in the population was fixed at each quartile.

Results: The estimated probability of preterm birth is 11.9% had everyone been exposed to the highest quartile of traffic density, compared to 10.8% had everyone been exposed to the lowest quartile of traffic density. The PIM showed that if a hypothetical intervention could reduce the entire population's exposure to that of the lowest quartile, the population would have a reduction in preterm birth of 0.45% compared to what is observed.

Conclusion: Semi-parametric causal inference methods applied to these data support findings from previous studies that prenatal exposure to traffic adversely affects birth outcomes.

Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *The Lancet* 2008;371 (9606):75–84.

Behrman RE, Butler AS, eds. *Preterm Birth: Causes, Consequences and Prevention*. Washington, D.C., Institute of Medicine, Committee on Understanding Premature Birth and Assuring Healthy Outcomes: National Academies Press 2007.

Shah PS, Balkhair T. Knowledge Synthesis Group on Determinants of Preterm/LBW births. Air pollution and birth outcomes: a systematic review. *Environ Int* 2011;Feb 37(2):498-516.



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HEI. Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. Boston, MA, Health Effects Institute 2010.



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Feasibility of Indoor Air Sampling in Homes Impacted by Biomass Use in Rural Appalachia

Presenting Author: Laura Paulin, Johns Hopkins School of Medicine Division of Pulmonary/Critical Care

Contributing Authors: Williams, DL (Johns Hopkins Bloomberg School of Public Health); Oberwieser, C (Appalachia Service Project); Diette, GB (Johns Hopkins School of Medicine); Breyse, PN (Johns Hopkins Bloomberg School of Public Health); McCormack, MC (Johns Hopkins School of Medicine); Matsui, EC (Johns Hopkins School of Medicine); Peng, R (Johns Hopkins Bloomberg School of Public Health); Metts, TA (East Tennessee State University); Hansel, NN (Johns Hopkins School of Medicine)

Abstract:

Rationale: Though the high prevalence of biomass fuel use in the developing world is widely known, the use of burning biomass for cooking and heating in the developed world is under-recognized. By partnering with the Appalachia Service Project (ASP), a faith-based non-profit Christian organization that provides free home repair to central Appalachia families, and East Tennessee State University (ETSU), we conducted a pilot study to assess the feasibility of conducting indoor environmental monitoring in rural Appalachia. We sought to explore the type of biomass being used for home heating and its impact upon indoor air quality in non-heating and heating seasons.

Methods: Residential indoor air monitoring was conducted in Lee County, Virginia in August and December 2011. English-speaking households that had received services from ASP and were willing to provide informed consent were eligible. Rental properties or homes with foster children were excluded. Monitors were placed in the main living area. Particulate matter (PM_{2.5}, PM₁₀), nitrogen dioxide, airborne nicotine, and settled dust were collected over a sampling period of 3-4 days. At each sampling visit, a home inspection was completed and participants filled out daily household activity diaries documenting pollutant-generating activities including heating, cooking, and smoking. Descriptive statistics were used to summarize pollutant concentrations by season and type of fuel.

Results: ASP identified 11 eligible homes in August 2011. Three additional homes were identified for sampling during the December 2011 heating season. Overall, participants were engaged in the sampling process and eager to participate in future studies. The majority of homes were smoking households and used wood or coal for heating. In general, PM concentrations were high: PM_{2.5} (mean±SD) during the heating season in homes using wood or coal for heating was 74±59ug/m³; homes with electric heat 9±3ug/m³; smoking homes 87±49ug/m³; non-smoking homes 15±11ug/m³.

Conclusions: Our collaboration with ASP and ETSU allowed for successful completion of a pilot study assessing common indoor air pollutants in rural Appalachia. Our results demonstrate high concentrations of indoor PM pollution and a large burden of cigarette smoking in an area impacted by biomass fuel use. Future studies are necessary to further characterize biomass use in this region and to determine the health impacts associated with such exposures.



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Bisphenol A and Children's Health: Results from the CHAMACOS Study

Presenting Author: Lesliam Quiros-Alcala, University of California, Berkeley

Contributing Authors: Harley, K. (UC Berkeley Children's Center); Chevrier, J. (UC Berkeley Children's Center); Gunier, R. (UC Berkeley Children's Center); Tyler, K. (UC Berkeley Children's Center); Vedar, M. (UC Berkeley Children's Center); Aguilar, R. (UC Berkeley Children's Center); Bradman, A. (UC Berkeley Children's Center); Calafat, A. (UC Berkeley Children's Center); Eskenazi, B. (UC Berkeley Children's Center)

Abstract:

Bisphenol-A (BPA), a chemical used in the production of polycarbonate plastics and epoxy resins, is an endocrine disrupter found in many consumer products, including in carbonless paper, children's toys and the lining of food cans. Animal evidence suggests that prenatal BPA exposure may alter neurodevelopment and lead to reproductive and metabolic problems. To characterize exposure to BPA during pregnancy and investigate the potential health consequences of this chemical, we evaluated the levels and predictors of BPA exposure during pregnancy at two time points (-14 and 26 weeks gestation), and assessed the association of prenatal BPA exposure with several health outcomes including: children's thyroid hormone levels, birth weight, cognitive functioning and behavior, and obesity in the ~HAMA~O~ longitudinal birth cohort. Data were collected on 507 pregnant women. Geometric mean (G~D) BPA concentrations were 0.97(2.7) j.Jg/L at 14 weeks and 1.03(2.6) j.Jg/L at 26 weeks. We observed poor reproducibility in urinary concentrations (1~~=0.27) and observed higher BPA concentrations in samples collected in the afternoon/evening hours. Significantly higher BPA concentrations were seen in women who had lived longer in the U.~. who consumed >3 sodas/day, or who consumed hamburgers >1 time/week. Prenatal BPA exposure was associated with decreased thyroid stimulating hormone (T~H) in boys. Prenatal BPA exposure was not associated with IQ at age 7, but was associated with increased odds of hyperactivity in boys, but not girls. Increasing BPA exposure was associated with decreased BMI at age 2, but increased weight gain in boys and girls between age 2 and 9.



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Identifying Perceptions, Attitudes and Health Behaviors Around Bisphenol-A Through Community

Presenting Author: Brennan Rhodes, Columbia Center for Children's Environmental Health

Contributing Authors: Evans, D (Columbia Center for Children's Environmental Health); Shepard, P (WE ACT for Environmental Justice); Dotson-Newman, O (WE ACT for Environmental Justice); Aguirre, A (Columbia Community Partnership for Health); Ansah-Samuels, E (Northern Manhattan Perinatal Partnership); Casado, J (The Bronx Health Link)

Abstract:

Background: Emerging evidence indicates that prenatal exposure to BPA interferes with normal growth and development. Recent findings from the Columbia Center for Children's Environmental Health (CCCEH) also suggest that BPA exposure is linked to anxiety/depressive mood, attention problems and obesity in children.

Objective: Based on this evidence, CCCEH's Community Outreach & Translation Core (COTC) developed an educational brochure outlining concerns and ways to reduce BPA exposure, using focus groups to ensure future materials are relevant and culturally tailored for low income, communities of color in Northern Manhattan (NM) and the South Bronx (SB).

Methods: Three focus groups with 24 women of childbearing age were conducted in English (n= 16) and Spanish (n= 8) using a discussion guide developed with the CCCEH Community Advisory and Stakeholders Board (CASB). Participants were recruited through community-based organizations that serve on CCCEH's CASB. Each focus group was conducted at the offices of the hosting community organization. We discussed participants' knowledge, perceptions, attitudes, beliefs, and health behaviors related to environmental health and BPA. The responses were tape-recorded, transcribed, and analyzed to determine key themes. These themes and high frequency responses shaped a brochure with advice for reducing BPA exposure that can be easily understood and used by NM and SB residents.

Results: Participants felt many harmful chemicals were in their homes, but didn't know what BPA was, nor how it harmed people, and wanted this information in materials. They knew microwaving food in plastic was harmful, as were the linings of canned goods. Many knew about recycling labels on plastic containers, but couldn't remember which numbers to avoid. Many were alarmed by learning receipts can contain BPA. They preferred cooking with fresh foods, but low quality produce at local stores, high prices for organic options, and the convenience of cooking with canned foods were reported barriers. To learn about BPA, participants preferred refrigerator magnets, wallet cards, subway ads, billboards, and workshops. The participants also made helpful stylistic suggestions.

Conclusion: These findings guided the design and content of the CCCEH brochure about BPA, highlighting the value of focus groups to obtain and incorporate community input into materials developed for their use and future direction of COTC activities.



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The Effects of Endocrine Disruption on the Developing Human Fetal Prostate

Presenting Author: Camelia Saffarini, Brown University

Contributing Authors: Hall, S. (Brown University); Boekelheide, K. (Brown University)

Abstract:

Prostate cancer is the most commonly diagnosed cancer and is the second highest cancer-related cause of death in men. This high incidence has led to speculation about the fetal origins of this adult disease and its etiology.

Exposure to exogenous estrogens in pregnant women has been postulated to disturb the normal development of the human fetal prostate by disrupting the natural hormonal balance. Previous studies demonstrate that early life exposure to estrogens in rats can cause some degree of epithelial and stromal hyperplasia, inflammation, and prostatic intraepithelial neoplasia (PIN) lesions. The present study used a xenograft model to characterize the differentiation of human fetal prostate implants (gestation 12-22 weeks) exposed to either corn oil (control) or 250 ug/kg/body weight of 17 β -estradiol 3-benzoate during an early acute exposure, as well as an additional later life exposure post-transplant. This xenograft model uses the renal subcapsular space as the site of implantation, thereby allowing for proper vascularization and growth of the implant. Characterization of the model included the expression of key immunohistochemical markers responsible for stromal and epithelial maturation, neuroendocrine cells, hormone receptors, cellular proliferation as well as apoptosis. As expected, the prostate implants grew and matured as seen in 7, 14, 30, 90, 200 and 400 day time-points following xenografting.

Interestingly, the human prostate xenografts exhibited marked differences in response to estrogen exposure compared to their endogenous rat prostate counterparts. Human prostate xenografts at 200 days post-transplant demonstrate basal cell hyperplasia shown by p63 staining, while the endogenous rat prostate exhibited atypical hyperplasia and the presence of cellular debris following estrogen exposure. This unique xenograft model provides insight on the growth and development of the human fetal prostate following developmental endocrine disruption.



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Impact of Bisphenol A Exposure on Reproductive and Behavioral Development

Presenting Author: Susan Schantz, University of Illinois

Contributing Authors: Schantz, S. (University of Illinois at Urbana-Champaign); Flaws, J. (University of Illinois at Urbana-Champaign); Korrick, S. (Harvard Medical School); Juraska, J. (University of Illinois at Urbana-Champaign); Yao, H. (National Institute of Environmental Health Sciences); Aguiar, A. (University of Illinois at Urbana-Champaign); Baillargeon, R. (University of Illinois at Urbana-Champaign); Gardiner, J. (Michigan State University)

Abstract:

Current progress of pilot studies conducted at our Formative (P20) Children's Environmental Health and Disease Prevention Research Center is summarized. The primary goal of the Center is to address critical gaps in our knowledge of the risks to children from Bisphenol A (BPA) or phthalate exposure. Research in the Center focuses on endocrine mediated outcomes including gonadal development and sexually dimorphic aspects of brain development and behavior. Exposures during two developmental windows—prenatal and adolescent—are being assessed. At the heart of the research are two human cohort studies—a pilot birth cohort (Project 1) and a pilot adolescent cohort that is being studied in the context of an ongoing study (Project 2). These studies are assessing the relation of BPA or phthalate exposure with sexually dimorphic aspects of physical development and cognition in young infants and with cognition in adolescent children. These human cohort studies are still in the early stages. The poster summarizes progress to date and highlights the types of physical and cognitive assessments that are being conducted. The Center also includes animal studies that model the timing of exposure in the human cohorts. These studies are investigating mechanisms through which BPA disrupts male and female gonad development using transgenic and knockout mouse models (Project 3), and the impact of in utero or peripubertal BPA exposure on development of sexually dimorphic cortical brain regions and cognitive functions in a rat model (Project 4). Recently Project 3 investigated whether overexpression of ER α increases the susceptibility of the developing ovary to in utero exposure to BPA. Pregnant control and ER α overexpressing (EROE) dams (n=at least 4 dams per treatment group and genotype) were orally dosed with tocopherol-stripped corn oil (vehicle), 50 $\mu\text{g}/\text{kg}/\text{day}$ BPA or 0.5 $\mu\text{g}/\text{kg}/\text{day}$ BPA from embryonic day 10.5 to birth. On postnatal day 0, ovaries were removed from female pups and subjected to histological evaluation. Preliminary findings indicate that 0.5 $\mu\text{g}/\text{kg}/\text{day}$ BPA increased both germ cell number and primordial follicle number in control mice, but not in EROE mice. Additional studies assessing the impact of BPA on female and male gonad development are in progress. Project 4 has assessed maternal behavior in groups of Long Evans rats from Simonsen or Harlan exposed to 4, 40 or 400 $\mu\text{g}/\text{kg}/\text{day}$ BPA during the pre- and early postnatal period. Preliminary findings indicate that dams exposed to 4 or 40 $\mu\text{g}/\text{kg}/\text{day}$ BPA licked their pups more than control dams. Interestingly this effect was only present in the BPA-exposed rats from Harlan. The findings illustrate that animals of the same strain from different vendors can exhibit differential sensitivity to the effects of BPA. Additional studies assessing cognitive function and neuron number in rats exposed to BPA either perinatally or in adolescence are in progress. Supported by NIEHS P20 ES018163/USEPA RD 83459301.



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Interaction Effects between Maternal Prenatal Vitamin Intake and Pyrethroid Pesticide Exposure in Relation to Autism Spectrum Disorders in the CHARGE Case-Control Study

Presenting Author: Rebecca J. Schmidt, MIND Institute and the University of California Davis

Contributing Authors: Delwiche, L (University of California Davis); Hansen, R (University of California Davis); Hertz-Picciotto (University of California Davis)

Abstract:

Background and Aims: Autism spectrum disorder (ASD) is an increasingly prevalent neurodevelopmental disorder affecting 1:110 children in the United States (CDC, 2009). Evidence supports large heritable contributions to the etiology of ASD, though environmental factors are likely to modify both the development and the course of ASD. Prenatal nutrient-environment interactions are unstudied in relation to autism etiology and risk. The objective of this study is to examine interaction effects between maternal supplemental nutrient intake and pyrethroid pesticides in relation to ASD.

Methods: Northern California families were enrolled from 2003-2009 in the population-based case-control CHARGE (Childhood Autism Risks from Genetics and the Environment) Study. Children aged 24-60 months were evaluated and confirmed to have autism (n=288), autism spectrum disorder (n=141), or typical development (n=278) at the M.I.N.D. Institute using standardized clinical assessments. Maternal prenatal vitamin intake before and during pregnancy and use of products containing pyrethroid pesticides were retrospectively collected through telephone interviews. Adjusted odds ratios (OR) were estimated for associations between ASD and combinations of prenatal vitamin and pyrethroid pesticide exposure.

Results: Estimated risk for having a child with autism when mothers did not take a prenatal vitamin and were exposed to pyrethroid pesticides during pregnancy (OR=5.4, 95% CI: 2.4-11.9) was over twice what was expected for that combination by either an additive (OR=2.2) or multiplicative model (OR=2.6). Though still significantly elevated, the observed risk for having a child with ASD associated with pyrethroid exposure during pregnancy was much lower if the mother reported taking a prenatal vitamin during the period around conception (OR=1.7, 95% CI: 1.0-2.8).

Conclusions: These findings suggest that vitamin supplements taken before or early in pregnancy could potentially reduce the risk of ASD associated with pyrethroid pesticides. Further studies are warranted.



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An Integrated Geospatial and Epidemiological Study of Associations between Birth Problems and Arsenic Exposure

Presenting Author: Xun Shi, Dartmouth College

Contributing Authors: Miller, S (Dartmouth Medical School); Moeschler, J (Dartmouth Medical School); Gui, J (Dartmouth Medical School); Mwenda, K (Dartmouth College); Onda, A (Dartmouth College); Ayotte, J (USGS); Onega, T (Dartmouth Medical School); Rees, J (Dartmouth Medical School); Karagas, M (Dartmouth Medical School)

Abstract:

In this pilot project, we integrate geospatial and epidemiological analyses to quantitatively and geographically monitor, characterize, and evaluate the associations between birth problems (birth defects, low birth weight, and high birth weight) and arsenic exposure (i.e., inorganic arsenic) from drinking water in New Hampshire. Specifically, using the data of 2003-2009, we conducted sophisticated geocomputational and spatial statistical analyses to 1) characterize the spatial distribution of birth problems, and detect the presence of special patterns, particularly “hot spots”; and 2) evaluate spatial associations between birth problems and arsenic exposures from groundwater. The results from the geospatial analyses inform and assist the following case-control study that gives detailed investigation on the birth problem- arsenic exposure relationship in NH.



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From Advancing Science to Ensuring Prevention

Presenting Author: Jessica Trowbridge, University of California San Francisco, Program on Reproductive Health and the Environment

Contributing Authors: Sutton, P (University of California San Francisco); Stotland, N (University of California San Francisco); Charlesworth, A (University of California San Francisco); Atchley, D (University of California San Francisco); Woodruff, TJ (University of California San Francisco)

Abstract:

Virtually every pregnant woman in the United States has measurable levels of multiple chemicals in her body that can harm human reproduction and development. Chemical exposures during the prenatal period can have effects across the life span of individuals, ranging from short term effects such as birth defects to long term effects such as adult cancers. Thus, preventing harmful exposures incurred during the preconception and prenatal periods can have a lifetime of health benefits. Obstetricians and other reproductive health professionals are uniquely poised to intervene at key points of development for women's and children's health. To leverage this largely untapped opportunity to prevent developmental exposure to reproductive and developmental toxicants, in 2008 the University of California San Francisco's Program on Reproductive Health and the Environment (PRHE) formed the From Advancing Science to Ensuring Prevention (FASTEP) Alliance. The goal of FASTEP is to secure each and everyone's right to optimal reproductive health by fostering environments that prevent exposure to potential reproductive toxicants and provide the nutritive and social sustenance necessary for healthy pregnancies, children, adults, and future generations.

This poster will describe: (1) the results of FASTEP activities over the past 4 years to engage reproductive health professionals in the prevention of harmful environmental exposures in clinical and policy arenas; (2) preliminary data on the first empirical data gathered to assess obstetricians' beliefs, attitudes and practice about environmental health; and (3) limitations and strengths of this prevention strategy.



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Association of Preterm Birth with Weight Status and Waist Circumference in Mexico City Youth

Presenting Author: Tiffany Yang, University of Michigan

Contributing Authors: Peterson, K (University of Michigan); Sanchez, B (University of Michigan); Villamor, E (University of Michigan); Tellez-Rojo, M (Instituto Nacional de Salud Pública)

Abstract:

Background: Preterm birth has been associated with health profiles including as impaired insulin sensitivity and increased truncal fat patterning in adolescence. In developing countries such as Mexico, changing environments coupled with preterm birth may deleteriously impact the development of health risks. This study examines the association of preterm birth with adolescent obesity and markers of weight status and fat distribution among Mexico City adolescents.

Methods: Among 750 youths aged 7-15, we estimated differences in BMI and waist circumference by categories of premature birth (gestational age < 37 weeks; N = 61; 8.1%) using linear regression. In addition, we estimated odds ratios and 95% confidence intervals for obesity during adolescence according to preterm birth using logistic regression models adjusted for adolescent age, sex, and mother's age, education, marital status, and obesity.

Results: Premature birth was not associated with obesity in unadjusted (OR = 1.14; 95% CI: 0.49-2.64) or adjusted models (OR = 1.05; 95% CI: 0.43-2.55); it was associated with BMI and waist circumference in unadjusted ($p = 0.03$; $p = 0.67$) but not adjusted models ($p = 0.01$; $p = 0.93$). In the adjusted model, odds of obesity were greater with male sex (OR = 1.91; 95% CI: 1.24-2.96) and mother's obesity (OR = 3.84; 95% CI: 2.29-6.44) but odds were decreased with married mothers (OR = 0.56; 95% CI: 0.36-0.89).

Discussion: Preterm birth was not associated with adolescent BMI, waist circumference, or obesity in Mexico City youth. The direction of association suggests a need for further research in a larger sample size. Efforts to reduce obesity in this context should consider the child's sex, socioeconomic status, and weight status of the mother.



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Survey Results from a Questionnaire Designed to Characterize BPA Exposure Sources among Ethnically Diverse, Lower Income Pregnant Women

Presenting Author: Ami Zota, University of California San Francisco, Program on Reproductive Health and the Environment

Contributing Authors: Pan, J; Schwartz, J; Dickenson, C; Gerona, R; Woodruff, TJ

Abstract:

Bisphenol A (BPA) is a high production volume chemical used in a variety of applications, including food-can linings, polycarbonate plastics and paper production process. Low dose exposures to BPA can alter fetal development thus the fetus may be at increased risk. Over 90% of US pregnant women have measurable levels of BPA in their bodies. However, few studies have identified determinants of BPA exposure among pregnant women.

Our objective is to identify important sources of BPA exposure among a low income, ethnically diverse population of pregnant women during their second trimester of pregnancy, when many aspects of fetal development are vulnerable to disruption. As part of this study, we developed a comprehensive, original questionnaire to examine dietary, non-dietary, and sociodemographic determinants of BPA exposure including consumption of canned foods and drinks, consumption of paper packaged foods, and receipt contact. To date, we have examined data on 78 study participants. Our study population consists of 25% Latina, 39% African-America, 25% White, and 11% of mixed-ethnicity. Fifty percent reported using food-stamps, and 89% are on Medi-Cal. Common potential BPA exposure sources identified from the questionnaire include canned foods and beverages, paper-packaged foods, and occupational exposure to receipts. On average, study participants consumed 11 canned drinks items and 13 canned food items per week, and consume paper-packaged food once a day. This data helps fill the gap on food consumption patterns among ethnically diverse, lower income pregnant women, an understudied population that may face elevated BPA exposures. Future work will include examination of associations between questionnaire data and urinary BPA levels in this study population.



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