ehp CHILDREN'S HEALTH COLLECTION 2012

OCTOBER **2011**–SEPTEMBER **2012**
www.ehponline.org

Disease Outcomes

- Asthma/Respiratory Disease, Lung Development, Allergy
- Neurodevelopmental/Neurobehavioral Disorders
- Autism
- Cancers
- Birth Defects
- Pregnancy Outcomes: Preterm Birth/Small for Gestational Age/Fetal Development
- Infections
- Fetal or Early-life Exposures Contributing to Adult Disease
- Obesity
- Stress and Health

Exposures

- Heavy metals (e.g., lead, mercury)
- Pesticides and Other Chemicals/Compounds (e.g., BPA, PCBs, PBDEs, PFCs, phthalates, endocrine disruptors)
- Air Pollution: Particulate Matter/Smoke/Indoor Air
- Endotoxins and Water Toxins
- Built Environment
- Climate Change
- Natural Disasters
- Food Safety/Insecurity/Nutrition

Methodologies and Populations

- Biomarkers and Biomonitoring
- Community-based Participatory Research and Translation
- Epigenetics
- Methodologies

PREFACE

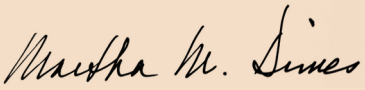
As with the previous collections, *Children's Health Collection 2012* comprises all relevant articles published in *EHP* from the October 2011 issue (devoted mostly to Children's Health) through September 2012: peer-reviewed research articles (including reviews and commentaries), news articles, Science Selections, editorials, and podcasts. Each abstract contains a hyperlink to take readers directly to the full article on our website (http://www.ehponline.org). Each article can be searched by author, key word, or phrase, and additional research previously published can also be easily accessed.

The collection includes not only research that has appeared in the Children's Health section of *EHP,* but also articles concerning adult–child cohorts, early origins of adult disease, experimental studies with direct application to children's health, and related topics of interest (e.g., regulatory standards, food safety).

This collection contains some changes from previous years: Instead of summaries, full abstracts of the research articles are provided. And a new main category—Methodologies and Populations—has been added. With new cohort descriptions, tools for understanding biomarkers and epigenetics, and community and translational studies, the new category adds another dimension to the literature on outcomes and exposures.

One new topic—obesity—reflects an unfortunate trend, as does the growth in research on natural disasters and their health effects, locally and globally. On the other hand, research on biomarkers, mechanisms, and epigenetics is increasingly able to identify critical windows of developmental vulnerability, responses to early-life exposures, and possible mediations. Greater understanding of the specifics of timing and type of exposure and multiple epigenetic characteristics and responses should, we hope, increase our ability to protect our children's health.

As *EHP* moves to an online-only format in January 2013, we will continue to provide full coverage of news and research in all areas of children's environmental health.



Martha M. Dimes, PhD

Children's Health Editor

dimes@niehs.nih.gov

TABLE *of* CONTENTS

ehp CHILDREN'S HEALTH COLLECTION 2012
OCTOBER 2011–SEPTEMBER 2012
www.ehponline.org

Disease Outcomes

Exposures

Methodologies and Populations

Disease Outcomes

ASTHMA/RESPIRATORY DISEASE, LUNG DEVELOPMENT, ALLERGY

Acute Respiratory Inflammation in Children and Black Carbon in Ambient Air before and during the 2008 Beijing Olympics

Weiwei Lin, Wei Huang, Tong Zhu, Min Hu, Bert Brunekreef, Yuanhang Zhang, Xingang Liu, Hong Cheng, Ulrike Gehring, Chengcai Li, and Xiaoyan Tang

119:1507–1512 (2011) | http://dx.doi.org/10.1289/ehp.1103461

Background: Epidemiologic evidence for a causative association between black carbon (BC) and health outcomes is limited.

Objectives: We estimated associations and exposure–response relationships between acute respiratory inflammation in schoolchildren and concentrations of BC and particulate matter with an aerodynamic diameter of ≤ 2.5 μm ($PM_{2.5}$) in ambient air before and during the air pollution intervention for the 2008 Beijing Olympics.

Methods: We measured exhaled nitric oxide (eNO) as an acute respiratory inflammation biomarker and hourly mean air pollutant concentrations to estimate BC and $PM_{2.5}$ exposure. We used 1,581 valid observations of 36 subjects over five visits in 2 years to estimate associations of eNO with BC and $PM_{2.5}$ according to generalized estimating equations with polynomial distributed-lag models, controlling for body mass index, asthma, temperature, and relative humidity. We also assessed the relative importance of BC and $PM_{2.5}$ with two-pollutant models.

Results: Air pollution concentrations and eNO were clearly lower during the 2008 Olympics. BC and $PM_{2.5}$ concentrations averaged over 0–24 hr were strongly associated with eNO, which increased by 16.6% [95% confidence interval (CI), 14.1–19.2%] and 18.7% (95% CI, 15.0–22.5%) per interquartile range (IQR) increase in BC (4.0 μg/m^3) and $PM_{2.5}$ (149 μg/m^3), respectively. In the two-pollutant model, estimated effects of BC were robust, but associations between $PM_{2.5}$ and eNO decreased with adjustment for BC. We found that eNO was associated with IQR increases in hourly BC concentrations up to 10 hr after exposure, consistent with effects primarily in the first hours after exposure.

Conclusions: Recent exposure to BC was associated with acute respiratory inflammation in schoolchildren in Beijing. Lower air pollution levels during the 2008 Olympics also were associated with reduced eNO.

Formaldehyde Exposure and Lower Respiratory Infections in Infants: Findings from the PARIS Cohort Study

Célina Roda, Isabelle Kousignian, Chantal Guihenneuc-Jouyaux, Claire Dassonville, Ioannis Nicolis, Jocelyne Just, and Isabelle Momas

119:1653–1658 (2011) | http://dx.doi.org/10.1289/ehp.1003222

Background: Certain chemical pollutants can exacerbate lower respiratory tract infections (LRIs), a common childhood ailment. Although formaldehyde (FA) is one of the most common air pollutants found in indoor environments, its impact on infant health is uncertain.

Objective: Our aim was to determine the impact of FA exposure on the LRI incidence during the first year of life of infants from the Pollution and Asthma Risk: an Infant Study (PARIS) birth cohort.

Methods: FA was measured in a random sample of 196 infants' dwellings, and exposure to this pollutant was estimated for 2,940 infants using predictive models based on measurements and data about potential determinants of FA levels. Health data were collected from parents by regular self-administered questionnaires. We used multivariate logistic regressions to estimate associations between FA exposure and the occurrence of LRI and wheezy LRI (wLRI), adjusting for potential confounders/risk factors.

Results: During the first year of life, 45.8% of infants had at least one LRI, and LRI occurred simultaneously with wheezing in 48.7% of cases. The FA predictive models correctly classified 70% of dwellings as having high or low exposure, and we estimated that 43.3% of infants were exposed throughout the first year to levels of FA > 19.5 μg/m^3. FA exposure was significantly associated with LRI and wLRI before and after adjustment for known LRI risk factors/confounders. For an interquartile increase in FA levels (12.4 μg/m^3), we estimated a 32% [95% confidence interval (CI): 11, 55] and 41% (95% CI: 14, 74) increase in the incidence of LRI and wLRI, respectively.

Conclusion: The findings of this study suggest that infants exposed to FA at an early age have an increased incidence of LRI.

▾ NEWS | SCIENCE SELECTION

Formaldehyde Connection: Modeled Exposure Linked to Lower Respiratory Infections in Infants

Julia R. Barrett | 119:A489

http://dx.doi.org/10.1289/ehp.119-a489a

Disease Outcomes

Air Pollution and Acute Respiratory Response in a Panel of Asthmatic Children along the U.S.–Mexico Border

Stefanie Ebelt Sarnat, Amit U. Raysoni, Wen-Whai Li, Fernando Holguin, Brent A. Johnson, Silvia Flores Luevano, Jose Humberto Garcia, and Jeremy A. Sarnat

120:437–444 (2012) | http://dx.doi.org/10.1289/ehp.1003169

Background: Concerns regarding the health impact of urban air pollution on asthmatic children are pronounced along the U.S.–Mexico border because of rapid population growth near busy border highways and roads.

Objectives: We conducted the first binational study of the impacts of air pollution on asthmatic children in Ciudad Juarez, Mexico, and El Paso, Texas, USA, and compared different exposure metrics to assess acute respiratory response.

Methods: We recruited 58 asthmatic children from two schools in Ciudad Juarez and two schools in El Paso. A marker of airway inflammation [exhaled nitric oxide (eNO)], respiratory symptom surveys, and pollutant measurements (indoor and outdoor 48-hr size-fractionated particulate matter, 48-hr black carbon, and 96-hr nitrogen dioxide) were collected at each school for 16 weeks. We examined associations between the pollutants and respiratory response using generalized linear mixed models.

Results: We observed small but consistent associations between eNO and numerous pollutant metrics, with estimated increases in eNO ranging from 1% to 3% per interquartile range increase in pollutant concentrations. Effect estimates from models using school-based concentrations were generally stronger than corresponding estimates based on concentrations from ambient air monitors. Both traffic-related and non–traffic-related particles were typically more robust predictors of eNO than was nitrogen dioxide, for which associations were highly sensitive to model specification. Associations differed significantly across the four school-based cohorts, consistent with heterogeneity in pollutant concentrations and cohort characteristics. Models examining respiratory symptoms were consistent with the null.

Conclusions: The results indicate adverse effects of air pollution on the subclinical respiratory health of asthmatic children in this region and provide preliminary support for the use of air pollution monitors close to schools to track exposure and potential health risk in this population.

Association between Residential Proximity to Fuel-Fired Power Plants and Hospitalization Rate for Respiratory Diseases

Xiaopeng Liu, Lawrence Lessner, and David O. Carpenter

120:807–810 (2012) | http://dx.doi.org/10.1289/ehp.1104146

Background: Air pollution is known to cause respiratory disease. Unlike motor vehicle sources, fuel-fired power plants are stationary.

Objective: Using hospitalization data, we examined whether living near a fuel-fired power plant increases the likelihood of hospitalization for respiratory disease.

Methods: Rates of hospitalization for asthma, acute respiratory infection (ARI), and chronic obstructive pulmonary disease (COPD) were estimated using hospitalization data for 1993–2008 from New York State in relation to data for residences near fuel-fired power plants. We also explored data for residential proximity to hazardous waste sites.

Results: After adjusting for age, sex, race, median household income, and rural/urban residence, there were significant 11%, 15%, and 17% increases in estimated rates of hospitalization for asthma, ARI, and COPD, respectively, among individuals > 10 years of age living in a ZIP code containing a fuel-fired power plant compared with one that had no power plant. Living in a ZIP code with a fuel-fired power plant was not significantly associated with hospitalization for asthma or ARI among children < 10 years of age. Living in a ZIP code with a hazardous waste site was associated with hospitalization for all outcomes in both age groups, and joint effect estimates were approximately additive for living in a ZIP code that contained a fuel-fired power plant and a hazardous waste site.

Conclusions: Our results are consistent with the hypothesis that exposure to air pollution from fuel-fired power plants and volatile compounds coming from hazardous waste sites increases the risk of hospitalization for respiratory diseases.

Satellite-based Estimates of Ambient Air Pollution and Global Variations in Childhood Asthma Prevalence

H. Ross Anderson, Barbara K. Butland, Aaron van Donkelaar, Michael Brauer, David P. Strachan, Tadd Clayton, Rita van Dingenen, Marcus Amann, Bert Brunekreef, Aaron Cohen, Frank Dentener, Christopher Lai, Lok N. Lamsal, Randall V. Martin, and the ISAAC Phase One and Phase Three study groups

120:1333–1339 (2012) | http://dx.doi.org/10.1289/ehp.1104724

Background: The effect of ambient air pollution on global variations and trends in asthma prevalence is unclear.

Objectives: Our goal was to investigate community-level associations between asthma prevalence data from the International Study of Asthma and Allergies in Childhood (ISAAC) and satellite-based estimates of particulate matter with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) and nitrogen dioxide (NO_2), and modelled estimates of ozone.

Methods: We assigned satellite-based estimates of $PM_{2.5}$ and NO_2 at a spatial resolution of 0.1° × 0.1° and modeled estimates of ozone at a resolution of 1° × 1° to 183 ISAAC centers. We used center-level prevalence of severe asthma as the outcome and multilevel models to adjust for gross national income (GNI) and center- and country-level sex, climate, and population density. We examined associations (adjusting for GNI) between air pollution and asthma prevalence over time in centers with data from ISAAC Phase One (mid-1900s) and Phase Three (2001–2003).

Results: For the 13- to 14-year age group (128 centers in 28 countries), the estimated average within-country change in center-level asthma prevalence per 100 children per 10% increase in center-level $PM_{2.5}$ and NO_2 was −0.043 [95% confidence interval (CI): −0.139, 0.053] and 0.017 (95% CI: −0.030, 0.064) respectively. For ozone the estimated change in prevalence per parts per billion by volume was −0.116 (95% CI: −0.234, 0.001). Equivalent results for the 6- to 7-year age group (83 centers in 20 countries), though slightly different, were not significantly positive. For the 13- to 14-year age group, change in center-level asthma prevalence over time per 100 children per 10% increase in $PM_{2.5}$ from Phase One to Phase Three was −0.139 (95% CI: −0.347, 0.068). The corresponding association with ozone (per ppbV) was −0.171 (95% CI: −0.275, −0.067).

Conclusion: In contrast to reports from within-community studies of individuals exposed to traffic pollution, we did not find evidence of a positive association between ambient air pollution and asthma prevalence as measured at the community level.

NEURODEVELOPMENTAL/NEUROBEHAVIORAL DISORDERS

Thyroid Dysfunction as a Mediator of Organochlorine Neurotoxicity in Preschool Children

Jordi Julvez, Frodi Debes, Pal Weihe, Anna L. Choi, and Philippe Grandjean

119:1429–1435 (2011) | http://dx.doi.org/10.1289/ehp.1003172

Background: Exposure to organochlorine compounds (OCs) can alter thyroid function in humans, and hypothyroidism during early life can adversely affect a child's neurodevelopment.

Objectives: In this study we aimed to assess the relationship between developmental organochlorine exposures and thyroid function and the relationship between thyroid function and subsequent neurodevelopment.

Methods: A population-based birth cohort of 182 children was followed annually up to 5.5 years of age. The assessments included OC concentrations in maternal pregnancy serum and milk, clinical thyroid parameters in maternal and cord serum, and subsequent neuropsychological outcomes of the child, along with sociodemographic cofactors. Resin triiodothyronine uptake ratio (T3RU) was also assessed as an estimate of the amount of thyroxine-binding globulin (TBG) sites unsaturated by thyroxine. The T3RU is high in hyperthyroidism and low in hypothyroidism.

Results: The findings showed consistent inverse and monotonic associations between organochlorine exposure and T3RU after covariate adjustments. We observed no associations with other thyroid parameters. T3RU was positively associated with improved performance on most of the neuropsychological tests. For other thyroid parameters, the findings were less consistent.

Conclusions: The results suggest that OC exposures may decrease the T3RU during early life, which is a proxy measure of the binding capacity of TBG. In addition, minor decreases of the thyroid function may be inversely associated with a child's neurodevelopment.

Serum Perfluorinated Compound Concentration and Attention Deficit/ Hyperactivity Disorder in Children 5–18 Years of Age

Cheryl R. Stein and David A. Savitz

119:1466–1471 (2011) | http://dx.doi.org/10.1289/ehp.1003538

Background: Perfluorinated compounds (PFCs) are persistent environmental pollutants. Toxicology studies demonstrate the potential for perfluorooctanoic acid (PFOA) and other PFCs to affect human growth and development. Attention deficit/ hyperactivity disorder (ADHD) is a developmental disorder with suspected environmental and genetic etiology.

Objectives: We examined the cross-sectional association between serum PFC concentration and parent or self-report of doctor-diagnosed ADHD with and without current ADHD medication.

Methods: We used data from the C8 Health Project, a 2005–2006 survey in a Mid-Ohio Valley community highly exposed to PFOA through contaminated drinking water, to study non-Hispanic white children 5–18 years of age. Logistic regression models were adjusted for age and sex.

Results: Of the 10,546 eligible children, 12.4% reported ADHD and 5.1% reported ADHD plus ADHD medication use. We observed an inverted J-shaped association between PFOA and ADHD, with a small increase in prevalence for the second quartile of exposure compared with the lowest, and a decrease for the highest versus lowest quartile. The prevalence of ADHD plus medication increased with perfluorohexane sulfonate (PFHxS) levels, with an adjusted odds ratio of 1.59 (95% confidence interval, 1.21–2.08) comparing the highest quartile of exposure to the lowest. We observed a modest association between perfluorooctane sulfonate and ADHD with medication.

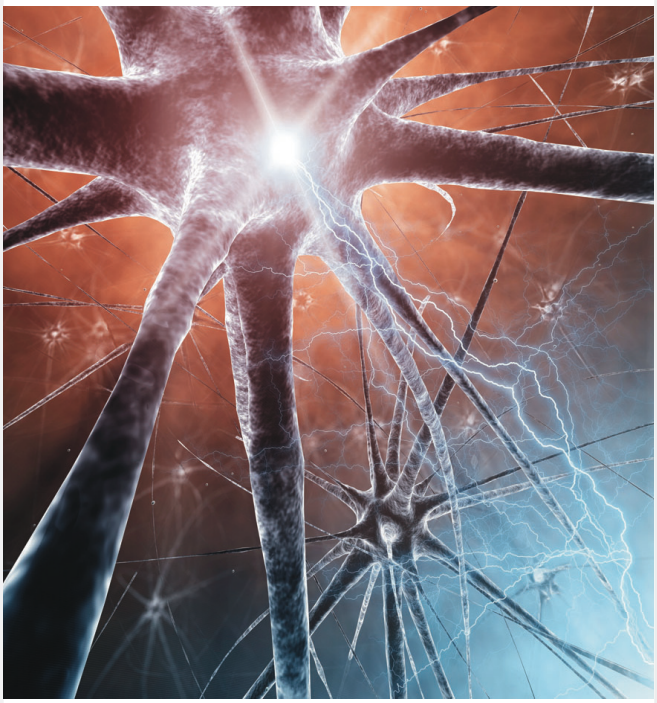
Conclusions: The most notable finding for PFOA and ADHD, a reduction in prevalence at the highest exposure level, is unlikely to be causal, perhaps reflecting a spurious finding related to the geographic determination of PFOA exposure in this population or to unmeasured behavioral or physiologic correlates of exposure and outcome. Possible positive associations between other PFCs and ADHD, particularly PFHxS, warrant continued investigation.

RELATED ARTICLES

NEWS | Reduced Bacterial Biodiversity Is Associated with Increased Allergy
Sharon Levy | 120:A304
http://dx.doi.org/10.1289/ehp.120-a304

NEWS | Decoding Neurodevelopment: Findings on Environmental Exposures and Synaptic Plasticity
Angela Spivey | 120:A70–A75
http://dx.doi.org/10.1289/ehp.120-a70

NEWS | Newly Discovered Mechanism for Chlorpyrifos Effects on Neurodevelopment
Carol Potera | 120:A270–A271
http://dx.doi.org/10.1289/ehp.120-a270a



Disease Outcomes

Early-Life Soy Exposure and Gender-Role Play Behavior in Children

Margaret A. Adgent, Julie L. Daniels, Lloyd J. Edwards, Anna Maria Siega-Riz, and Walter J. Rogan

119:1811–1816 (2011) | http://dx.doi.org/10.1289/ehp.1103579

Background: Soy-based infant formula contains high levels of isoflavones. These estrogen-like compounds have been shown to induce changes in sexually dimorphic behaviors in animals exposed in early development.

Objective: We examined gender-role play behavior in relation to soy-based and non-soy-based infant feeding methods among children in the Avon Longitudinal Study of Parents and Children.

Methods: We studied 3,664 boys and 3,412 girls. Four exposure categories were created using data from questionnaires administered at 6 and 15 months postpartum: primarily breast, early formula (referent), early soy, and late soy. Gender-role play behavior was assessed using the Pre-School Activities Inventory (PSAI). Associations between infant feeding and PSAI scores at 42 months of age were assessed using linear regression. Post hoc analyses of PSAI scores at 30 and 57 months were also conducted.

Results: Early-infancy soy use was reported for approximately 2% of participants. Mean [95% confidence interval (CI)] PSAI scores at 42 months were 62.3 (62.0, 62.6) and 36.9 (36.6, 37.2) for boys and girls, respectively. After adjustment, early soy (vs. early formula) feeding was associated with higher (less feminine) PSAI scores in girls (β = 2.66; 95% CI: 0.19, 5.12) but was not significantly associated with PSAI scores in boys. The association between soy exposure and PSAI scores in girls was substantially attenuated at 30 and 57 months.

Conclusions: Although not consistent throughout childhood, early-life soy exposure was associated with less female-typical play behavior in girls at 42 months of age. Soy exposure was not significantly associated with play behavior in boys.

▾NEWS | SCIENCE SELECTION

Full of Beans? Early Soy Exposure Associated with Less Feminine Play in Girls

Tanya Tillett | 119:A525

http://dx.doi.org/10.1289/ehp.119-a525b

Synthetic Food Colors and Neurobehavioral Hazards: The View from Environmental Health Research

Bernard Weiss

120:1–5 (2012) | http://dx.doi.org/10.1289/ehp.1103827

Background: The proposition that synthetic food colors can induce adverse behavioral effects in children was first enunciated in 1975 by Feingold [*Why Your Child Is Hyperactive*. New York:Random House (1975)], who asserted that elevated sensitivity to food additives underlies the signs of hyperactivity observed in some children. Although the evidence suggested that some unknown proportion of children did respond to synthetic food colors, the U.S. Food and Drug Administration (FDA) interpreted the evidence as inconclusive. A study published in 2007 [McCann et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial. Lancet 370:1560–1567 (2007)] drew renewed attention to the hypothesis because of the study's size and scope. It led the FDA to review the evidence, hold a public hearing, and seek the advice of its Food Advisory Committee. In preparation for the hearing, the FDA reviewed the available evidence and concluded that it did not warrant further agency action.

Objectives: In this commentary I examine the basis of the FDA's position, the elements of the review that led to its decision and that of the Food Advisory Committee, and the reasons that this is an environmental health issue.

Discussion: The FDA review confined itself, in essence, to the clinical diagnosis of hyperactivity, as did the charge to the committee, rather than asking the broader environmental question of behavioral effects in the general population; it failed to recognize the significance of vulnerable subpopulations; and it misinterpreted the meaning of effect size as a criterion of risk. The FDA's response would have benefited from adopting the viewpoints and perspectives common to environmental health research. At the same time, the food color debate offers a lesson to environmental health researchers; namely, too narrow a focus on a single outcome or criterion can be misleading.

Prenatal Exposure to Residential Air Pollution and Infant Mental Development: Modulation by Antioxidants and Detoxification Factors

Mònica Guxens, Inmaculada Aguilera, Ferran Ballester, Marisa Estarlich, Ana Fernández-Somoano, Aitana Lertxundi, Nerea Lertxundi, Michelle A. Mendez, Adonina Tardón, Martine Vrijheid, and Jordi Sunyer, on behalf of the INMA (INfancia y Medio Ambiente) Project

120:144–149 (2012) | http://dx.doi.org/10.1289/ehp.1103469

Background: Air pollution effects on children's neurodevelopment have recently been suggested to occur most likely through the oxidative stress pathway.

Objective: We aimed to assess whether prenatal exposure to residential air pollution is associated with impaired infant mental development, and whether antioxidant/detoxification factors modulate this association.

Methods: In the Spanish INfancia y Medio Ambiente (INMA; Environment and Childhood) Project, 2,644 pregnant women were recruited during their first trimester. Nitrogen dioxide (NO_2) and benzene were measured with passive samplers covering the study areas. Land use regression models were developed for each pollutant to predict average outdoor air pollution levels for the entire pregnancy at each residential address. Maternal diet was obtained at first trimester through a validated food frequency questionnaire. Around 14 months, infant mental development was assessed using Bayley Scales of Infant Development.

Results: Among the 1,889 children included in the analysis, mean exposure during pregnancy was 29.0 μg/m^3 for NO_2 and 1.5 μg/m^3 for benzene. Exposure to NO_2 and benzene showed an inverse association with mental development, although not statistically significant, after adjusting for potential confounders [β (95% confidence interval) = −0.95 (−3.90, 1.89) and −1.57 (−3.69, 0.56), respectively, for a doubling of each compound]. Stronger inverse associations were estimated for both pollutants among infants whose mothers reported low intakes of fruits/vegetables during pregnancy [−4.13 (−7.06, −1.21) and −4.37 (−6.89, −1.86) for NO_2 and benzene, respectively], with little evidence of associations in the high-intake group (interaction *p*-values of 0.073 and 0.047). Inverse associations were also stronger in non-breast-fed infants and infants with low maternal vitamin D, but effect estimates and interactions were not significant.

Conclusions: Our findings suggest that prenatal exposure to residential air pollutants may adversely affect infant mental development, but potential effects may be limited to infants whose mothers report low antioxidant intakes.

Maternal Prenatal Urinary Phthalate Metabolite Concentrations and Child Mental, Psychomotor, and Behavioral Development at 3 Years of Age

Robin M. Whyatt, Xinhua Liu, Virginia A. Rauh, Antonia M. Calafat, Allan C. Just, Lori Hoepner, Diurka Diaz, James Quinn, Jennifer Adibi, Frederica P. Perera, and Pam Factor-Litvak

120:290–295 (2012) | http://dx.doi.org/10.1289/ehp.1103705

Background: Research suggests that prenatal phthalate exposures affect child executive function and behavior.

Objective: We evaluated associations between phthalate metabolite concentrations in maternal prenatal urine and mental, motor, and behavioral development in children at 3 years of age.

Methods: Mono-*n*-butyl phthalate (MnBP), monobenzyl phthalate (MBzP), monoisobutyl phthalate (MiBP), and four di-2-ethylhexyl phthalate metabolites were measured in a spot urine sample collected from 319 women during the third trimester. When children were 3 years of age, the Mental Development Index (MDI) and Psychomotor Development Index (PDI) were measured using the Bayley Scales of Infant Development II, and behavior problems were assessed by maternal report on the Child Behavior Checklist.

Results: Child PDI scores decreased with increasing $\log_e$ MnBP [estimated adjusted β-coefficient = −2.81; 95% confidence interval (CI): −4.63, −1.0] and $\log_e$ MiBP (β = −2.28; 95% CI: −3.90, −0.67); odds of motor delay increased significantly [per $\log_e$ MnBP: estimated adjusted odds ratio (OR) = 1.64; 95% CI: 1.10, 2.44; per $\log_e$ MiBP: adjusted OR =1.82; 95% CI: 1.24, 2.66]. In girls, MDI scores decreased with increasing $\log_e$ MnBP (β = −2.67; 95% CI: −4.70, −0.65); the child sex difference in odds of mental delay was significant ($p = 0.037$). The ORs for clinically withdrawn behavior were 2.23 (95% CI: 1.27, 3.92) and 1.57 (95% CI: 1.07, 2.31) per $\log_e$ unit increase in MnBP and MBzP, respectively; for clinically internalizing behaviors, the OR was 1.43 (95% CI: 1.01, 1.90) per $\log_e$ unit increase in MBzP. Significant child sex differences were seen in associations between MnBP and MBzP and behaviors in internalizing domains ($p < 0.05$).

Conclusion: Certain prenatal phthalate exposures may decrease child mental and motor development and increase internalizing behaviors.

Disease Outcomes

A Strategy for Comparing the Contributions of Environmental Chemicals and Other Risk Factors to Neurodevelopment of Children

David C. Bellinger

120:501–507 (2012) | http://dx.doi.org/10.1289/ehp.1104170

Background: The impact of environmental chemicals on children's neurodevelopment is sometimes dismissed as unimportant because the magnitude of the impairments are considered to be clinically insignificant. Such a judgment reflects a failure to distinguish between individual and population risk. The population impact of a risk factor depends on both its effect size and its distribution (or incidence/prevalence).

Objective: The objective was to develop a strategy for taking into account the distribution (or incidence/prevalence) of a risk factor, as well as its effect size, in order to estimate its population impact on neurodevelopment of children.

Methods: The total numbers of Full-Scale IQ points lost among U.S. children 0–5 years of age were estimated for chemicals (methylmercury, organophosphate pesticides, lead) and a variety of medical conditions and events (e.g., preterm birth, traumatic brain injury, brain tumors, congenital heart disease).

Discussion: Although the data required for the analysis were available for only three environmental chemicals (methylmercury, organophosphate pesticides, lead), the results suggest that their contributions to neurodevelopmental morbidity are substantial, exceeding those of many nonchemical risk factors.

Conclusion: A method for comparing the relative contributions of different risk factors provides a rational basis for establishing priorities for reducing neurodevelopmental morbidity in children.

▾ NEWS | SCIENCE SELECTION

Brain Tax: Estimating the Population-Level Impact of Environmental Chemicals on IQ Scores

Wendee Holtcamp | 120:A165

http://dx.doi.org/10.1289/ehp.120-a165b

Response Inhibition and Error Monitoring during a Visual Go/No-Go Task in Inuit Children Exposed to Lead, Polychlorinated Biphenyls, and Methylmercury

Olivier Boucher, Matthew J. Burden, Gina Muckle, Dave Saint-Amour, Pierre Ayotte, Éric Dewailly, Charles A. Nelson, Sandra W. Jacobson, and Joseph L. Jacobson

120:608–615 (2012) | http://dx.doi.org/10.1289/ehp.1103828

Background: Lead (Pb) and polychlorinated biphenyls (PCBs) are neurotoxic contaminants that have been related to impairment in response inhibition.

Objectives: In this study we examined the neurophysiological correlates of the response inhibition deficits associated with these exposures, using event-related potentials (ERPs) in a sample of school-age Inuit children from Arctic Québec exposed through their traditional diet.

Methods: In a prospective longitudinal study, we assessed 196 children (mean age, 11.3 years) on a visual go/no-go response inhibition paradigm. Pb, PCB, and mercury (Hg) concentrations were analyzed in cord and current blood samples. Hierarchical multiple regression analyses were conducted to examine the associations of contaminant levels to go/no-go performance (mean reaction time, percent correct go, percent correct no-go) and five ERPs [N2, P3, error-related negativity, error positivity (Pe), and correct response positivity (Pc)] after control for confounding variables.

Results: Current blood Pb concentrations were associated with higher rates of false alarms and with decreased P3 amplitudes to go and no-go trials. Current plasma PCB-153 concentrations were associated with slower reaction times and with reduced amplitudes of the Pe and Pc response-related potentials. Hg concentrations were not related to any outcome on this task but showed significant interactions with other contaminants on certain outcomes.

Conclusions: These results suggest that Pb exposure during childhood impairs the child's ability to allocate the cognitive resources needed to correctly inhibit a prepotent response, resulting in increased impulsivity. By contrast, postnatal PCB exposure appears to affect processes associated with error monitoring, an aspect of behavioral regulation required to adequately adapt to the changing demands of the environment, which results in reduced task efficiency.

Cadmium Exposure and Neurodevelopmental Outcomes in U.S. Children

Timothy Ciesielski, Jennifer Weuve, David C. Bellinger, Joel Schwartz, Bruce Lanphear, and Robert O. Wright

120:758–763 (2012) | http://dx.doi.org/10.1289/ehp.1104152

Background: Low-level environmental cadmium exposure in children may be associated with adverse neurodevelopmental outcomes.

Objective: Our aim was to evaluate associations between urinary cadmium concentration and reported learning disability (LD), special education utilization, and attention deficit hyperactivity disorder (ADHD) in U.S. children using National Health and Nutrition Examination Survey (NHANES) data.

Methods: We analyzed data from a subset of participants in NHANES (1999–2004) who were 6–15 years of age and had spot urine samples analyzed for cadmium. Outcomes were assessed by parent or proxy-respondent report. We fit multivariable-adjusted logistic regression models to estimate associations between urinary cadmium and the outcomes.

Results: When we compared children in the highest quartile of urinary cadmium with those in the lowest quartile, odds ratios adjusted for several potential confounders were 3.21 [95% confidence interval (CI): 1.43, 7.17] for LD, 3.00 (95% CI: 1.12, 8.01) for special education, and 0.67 (95% CI: 0.28, 1.61) for ADHD. There were no significant interactions with sex, but associations with LD and special education were somewhat stronger in males, and the trend in the ADHD analysis was only evident among those with blood lead levels above the median.

Conclusions: These findings suggest that children who have higher urinary cadmium concentrations may have increased risk of both LD and special education. Importantly, we observed these associations at exposure levels that were previously considered to be without adverse effects, and these levels are common among U.S. children.

Neuropsychological Measures of Attention and Impulse Control among 8-Year-Old Children Exposed Prenatally to Organochlorines

Sharon K. Sagiv, Sally W. Thurston, David C. Bellinger, Larisa M. Altshul, and Susan A. Korrick

120:904–909 (2012) | http://dx.doi.org/10.1289/ehp.1104372

Background: We previously reported associations between organochlorines and behaviors related to attention deficit hyperactivity disorder among boys and girls at 8 years of age using a teacher's rating scale for a birth cohort in New Bedford, Massachusetts (USA).

Objectives: Our goal was to corroborate these findings using neuropsychological measures of inattentive and impulsive behaviors.

Methods: We investigated the association between cord serum polychlorinated biphenyls (PCBs) and *p,p´*-dichlorodiphenyl-dichloroethylene (*p,p´*-DDE) and attention and impulse control using a Continuous Performance Test (CPT) and components of the Wechsler Intelligence Scale for Children, 3rd edition (WISC-III). Participants came from a prospective cohort of children born during 1993–1998 to mothers residing near a PCB-contaminated harbor in New Bedford. Median (range) cord serum levels for the sum of four prevalent PCBs [congeners 118, 138, 153, and 180 (∑PCB4)] and *p,p´*-DDE were 0.19 (0.01–2.59) and 0.31 (0–14.93) ng/g serum, respectively.

Results: We detected associations between PCBs and neuropsychological deficits for 578 and 584 children with CPT and WISC-III measures, respectively, but only among boys. For example, boys with higher exposure to ∑PCB4 had a higher rate of CPT errors of omission [rate ratio for the exposure interquartile range (IQR) = 1.12; 95% confidence interval (CI): 0.98, 1.27] and slower WISC-III Processing Speed (change in score for the IQR = –2.0; 95% CI: –3.5, –0.4). Weaker associations were found for *p,p´*-DDE. For girls, associations were in the opposite direction for the CPT and null for the WISC-III.

Conclusions: These results support an association between organochlorines (mainly PCBs) and neuropsychological measures of attention among boys only. Sex-specific effects should be considered in studies of organochlorines and neurodevelopment.

Disease Outcomes

Prenatal Polycyclic Aromatic Hydrocarbon (PAH) Exposure and Child Behavior at Age 6–7 Years

Frederica P. Perera, Deliang Tang, Shuang Wang, Julia Vishnevetsky, Bingzhi Zhang, Diurka Diaz, David Camann, and Virginia Rauh

120:921–926 (2012) | http://dx.doi.org/10.1289/ehp.1104315

Background: Airborne polycyclic aromatic hydrocarbons (PAH) are widespread urban air pollutants from fossil fuel burning and other combustion sources. We previously reported that a broad spectrum of combustion-related DNA adducts in cord blood was associated with attention problems at 6–7 years of age in the Columbia Center for Children's Environmental Health (CCCEH) longitudinal cohort study.

Objectives: We evaluated the relationship between behavioral problems and two different measures of prenatal exposure—both specific to PAH—in the same cohort.

Methods: Children of nonsmoking African-American and Dominican women in New York City (NYC) were followed from *in utero* to 6–7 years. Prenatal PAH exposure was estimated by personal air monitoring of the mothers during pregnancy as well as by the measurement of DNA adducts specific to benzo[*a*]pyrene (BaP), a representative PAH, in maternal and cord blood. At 6–7 years of age, child behavior was assessed using the Child Behavior Checklist (CBCL) ($n = 253$). Generalized linear models were used to test the association between prenatal PAH exposure and behavioral outcomes.

Results: In multivariate analyses, high prenatal PAH exposure, whether characterized by personal air monitoring (greater than the median of 2.27 ng/m^3) or maternal and cord adducts (detectable or higher), was positively associated with symptoms of Anxious/Depressed and Attention Problems ($p \le 0.05$).

Conclusion: These results provide additional evidence that environmental levels of PAH encountered in NYC air can adversely affect child behavior.

Prenatal Bisphenol A Exposure and Child Behavior in an Inner-City Cohort

Frederica Perera, Julia Vishnevetsky, Julie B. Herbstman, Antonia M. Calafat, Wei Xiong, Virginia Rauh, and Shuang Wang

120:1190–1194 (2012) | http://dx.doi.org/10.1289/ehp.1104492

Background: Experimental laboratory evidence suggests that bisphenol A (BPA), an endocrine disruptor, is a neurodevelopmental toxicant. However, there have been limited and inconclusive results with respect to sex-specific BPA effects on child behavior.

Objective: We examined the association between prenatal BPA exposure and child behavior, adjusting for postnatal BPA exposure and hypothesizing sex-specific effects.

Methods: We followed African-American and Dominican women and their children from pregnancy to child's age 5 years, collecting spot urine samples from the mothers during pregnancy (34 weeks on average) and from children between 3 and 4 years of age to estimate BPA exposure. We assessed child behavior between 3 and 5 years of age using the Child Behavior Checklist (CBCL) and used generalized linear models to test the association between BPA exposure and child behavior, adjusting for potential confounders.

Results: The analysis was conducted on 198 children (87 boys and 111 girls). Among boys, high prenatal BPA exposure (highest quartile vs. the lowest three quartiles) was associated with significantly higher CBCL scores (more problems) on Emotionally Reactive [1.62 times greater; 95% confidence interval (CI): 1.13, 2.32] and Aggressive Behavior syndromes (1.29 times greater; 95% CI: 1.09, 1.53). Among girls, higher exposure was associated with lower scores on all syndromes, reaching statistical significance for Anxious/Depressed (0.75 times as high; 95% CI: 0.57, 0.99) and Aggressive Behavior (0.82 times as high; 95% CI: 0.70, 0.97).

Conclusion: These results suggest that prenatal exposure to BPA may affect child behavior, and differently among boys and girls.

AUTISM

Tipping the Balance of Autism Risk: Potential Mechanisms Linking Pesticides and Autism

Janie F. Shelton, Irva Hertz-Picciotto, and Isaac N. Pessah

120:944–951 (2012) | http://dx.doi.org/10.1289/ehp.1104553

Background: Autism spectrum disorders (ASDs) have been increasing in many parts of the world and a portion of cases are attributable to environmental exposures. Conclusive replicated findings have yet to appear on any specific exposure; however, mounting evidence suggests gestational pesticides exposures are strong candidates. Because multiple developmental processes are implicated in ASDs during gestation and early life, biological plausibility is more likely if these agents can be shown to affect core pathophysiological features.

Objectives: Our objectives were to examine shared mechanisms between autism pathophysiology and the effects of pesticide exposures, focusing on neuroexcitability, oxidative stress, and immune functions and to outline the biological correlates between pesticide exposure and autism risk.

Methods: We review and discuss previous research related to autism risk, developmental effects of early pesticide exposure, and basic biological mechanisms by which pesticides may induce or exacerbate pathophysiological features of autism.

Discussion: On the basis of experimental and observational research, certain pesticides may be capable of inducing core features of autism, but little is known about the timing or dose, or which of various mechanisms is sufficient to induce this condition.

Conclusions: In animal studies, we encourage more research on gene × environment interactions, as well as experimental exposure to mixtures of compounds. Similarly, epidemiologic studies in humans with exceptionally high exposures can identify which pesticide classes are of greatest concern, and studies focused on gene × environment are needed to determine if there are susceptible subpopulations at greater risk from pesticide exposures.

RELATED ARTICLES

NEWS | UV Radiation and Skin Cancer: The Science Behind Age Restrictions for Tanning Beds

Charles W. Schmidt | 120:A308–A313
http://dx.doi.org/10.1289/ehp.120-a308

EDITORIAL | A Research Strategy to Discover the Environmental Causes of Autism and Neurodevelopmental Disabilities

Philip J. Landrigan, Luca Lambertini, and Linda S. Birnbaum | 120:A258–A260
http://dx.doi.org/10.1289/ehp.1104285

EDITORIAL | Environment and Reproductive Health in China: Challenges and Opportunities

Weihua Li, Bo Chen, and Xuncheng Ding | 120:A184–A185
http://dx.doi.org/10.1289/ehp.1205117

Disease Outcomes

Maternal Smoking during Pregnancy and the Prevalence of Autism Spectrum Disorders, Using Data from the Autism and Developmental Disabilities Monitoring Network

Amy E. Kalkbrenner, Joe M. Braun, Maureen S. Durkin, Matthew J. Maenner, Christopher Cunniff, Li-Ching Lee, Sydney Pettygrove, Joyce S. Nicholas, and Julie L. Daniels

120:1042–1048 (2012) | http://dx.doi.org/10.1289/ehp.1104556

Background: Reported associations between gestational tobacco exposure and autism spectrum disorders (ASDs) have been inconsistent.

Objective: We estimated the association between maternal smoking during pregnancy and ASDs among children 8 years of age.

Methods: This population-based case–cohort study included 633,989 children, identified using publicly available birth certificate data, born in 1992, 1994, 1996, and 1998 from parts of 11 U.S. states subsequently under ASD surveillance. Of these children, 3,315 were identified as having an ASD by the active, records-based surveillance of the Autism and Developmental Disabilities Monitoring Network. We estimated prevalence ratios (PRs) of maternal smoking from birth certificate report and ASDs using logistic regression, adjusting for maternal education, race/ethnicity, marital status, and maternal age; separately examining higher- and lower-functioning case subgroups; and correcting for assumed under-ascertainment of autism by level of maternal education.

Results: About 13% of the source population and 11% of children with an ASD had a report of maternal smoking in pregnancy: adjusted PR (95% confidence interval) of 0.90 (0.80, 1.01). The association for the case subgroup autistic disorder (1,310 cases) was similar: 0.88 (0.72, 1.08), whereas that for ASD not otherwise specified (ASD-NOS) (375 cases) was positive, albeit including the null: 1.26 (0.91, 1.75). Unadjusted associations corrected for assumed under-ascertainment were 1.06 (0.98, 1.14) for all ASDs, 1.12 (0.97, 1.30) for autistic disorder, and 1.63 (1.30, 2.04) for ASD-NOS.

Conclusions: After accounting for the potential of under-ascertainment bias, we found a null association between maternal smoking in pregnancy and ASDs, generally. The possibility of an association with a higher-functioning ASD subgroup was suggested, and warrants further study.

▾NEWS | SCIENCE SELECTION

A Sensitive Approach to Studying ASDs: Teasing Out Relationships between Autism and Maternal Smoking

Tanya Tillett | 120:A285

http://dx.doi.org/10.1289/ehp.120-a285b

CANCERS

Solar UV Doses of Young Americans and Vitamin D_3 Production

Dianne Eyvonn Godar, Stanley James Pope, William Burgess Grant, and Michael Francis Holick

120:139–143 (2012) | http://dx.doi.org/10.1289/ehp.1003195

Background: Sunlight contains ultraviolet B (UVB) radiation (290–315 nm) that affects human health in both detrimental (skin cancers) and beneficial (vitamin D_3) ways. Serum 25-hydroxyvitamin D concentrations from young Americans (≤ 19 years) show that many have deficient (< 50 nmol/L, 20 ng/mL) or insufficient (< 75 nmol/L, 30 ng/mL) vitamin D levels, indicating that they are not getting enough sun exposure. Those findings are in conflict with some calculated, published values that suggest people make "ample" vitamin D_3 (~ 1,000 IU/day) from their "casual," or everyday, outdoor exposures even if they diligently use sunscreens with sun protection factor (SPF) 15.

Objective: We estimated how much vitamin D_3 young Americans (n = ~ 2,000) produce from their everyday outdoor ultraviolet doses in the North (45°N) and South (35°N) each season of the year with and without vacationing.

Methods: For these vitamin D_3 calculations, we used geometric conversion factors that change planar to whole-body doses, which previous calculations did not incorporate.

Results: Our estimates suggest that American children may not be getting adequate outdoor UVB exposures to satisfy their vitamin D_3 needs all year, except some Caucasians during the summer if they do not diligently wear sunscreens except during beach vacations.

Conclusion: These estimates suggest that most American children may not be going outside enough to meet their minimal (~ 600 IU/day) or optimal (≥ 1,200 IU/day) vitamin D requirements.

Disease Outcomes

BIRTH DEFECTS

Maternal Pregnancy Levels of *trans*-Nonachlor and Oxychlordane and Prevalence of Cryptorchidism and Hypospadias in Boys

Britton Trabert, Matthew P. Longnecker, John W. Brock, Mark A. Klebanoff, and Katherine A. McGlynn

120:478–482 (2012) | http://dx.doi.org/10.1289/ehp.1103936

Background: The etiologies of the male urogenital anomalies—cryptorchidism and hypospadias—are poorly understood. Given positive associations between chlordane isomers and testicular germ cell tumors, it is reasonable to assume that chlordanes might also be associated with other testicular dysgenesis syndrome disorders, namely cryptorchidism and hypospadias.

Objective: To examine whether exposure to *in utero* chlordane is related to cryptorchidism and hypospadias, we evaluated levels of chlordane derivatives, *trans*-nonachlor and oxychlordane, among pregnant women enrolled in the Collaborative Perinatal Project (CPP).

Methods: From 1959 to 1965, the CPP enrolled pregnant women at 12 U.S. medical centers. We analyzed serum *trans*-nonachlor and oxychlordane levels measured in third-trimester serum from the mothers of 217 sons with cryptorchidism, 197 sons with hypospadias, and 557 sons with neither condition. Adjusted odds ratios (ORs) and 95% confidence intervals were calculated using conditional logistic regression.

Results: The quartile-specific ORs for cryptorchidism or hypospadias show no notable associations with *trans*-nonachlor or oxychlordane. Further, there were no significant trends with increasing quartile of maternal *trans*-nonachlor or oxychlordane level in either cryptorchidism or hypospadias (p-trend all > 0.45).

Conclusions: The results do not support an association between chlordane levels and cryptorchidism or hypospadias. It is unlikely that current chlordane exposure is related to the development of either anomaly, given that serum chlordane levels at the time of sample collection, the early 1960s, were considerably higher than levels at present.

Maternal Occupational Exposure to Polycyclic Aromatic Hydrocarbons: Effects on Gastroschisis among Offspring in the National Birth Defects Prevention Study

Philip J. Lupo, Peter H. Langlois, Jennita Reefhuis, Christina C. Lawson, Elaine Symanski, Tania A. Desrosiers, Zeina G. Khodr, A.J. Agopian, Martha A. Waters, Kara N. Duwe, Richard H. Finnell, Laura E. Mitchell, Cynthia A. Moore, Paul A. Romitti, and Gary M. Shaw, for the National Birth Defects Prevention Study

120:910–915 (2012) | http://dx.doi.org/10.1289/ehp.1104305

Background: Exposure to polycyclic aromatic hydrocarbons (PAHs) occurs in many occupational settings. There is evidence in animal models that maternal exposure to PAHs during pregnancy is associated with gastroschisis in offspring; however, to our knowledge, no human studies examining this association have been conducted.

Objective: Our goal was to conduct a case–control study assessing the association between estimated maternal occupational exposure to PAHs and gastroschisis in offspring.

Methods: Data from gastroschisis cases and control infants were obtained from the population-based National Birth Defects Prevention Study for the period 1997–2002. Exposure to PAHs was assigned by industrial hygienist consensus, based on self-reported maternal occupational histories from 1 month before conception through the third month of pregnancy. Logistic regression was used to determine the association between estimated occupational PAH exposure and gastroschisis among children whose mothers were employed for at least 1 month during the month before conception through the third month of pregnancy.

Results: The prevalence of estimated occupational PAH exposure was 9.0% in case mothers (27 of 299) and 3.6% in control mothers (107 of 2,993). Logistic regression analyses indicated a significant association between occupational PAHs and gastroschisis among mothers ≥ 20 years of age [odds ratio (OR) = 2.53; 95% confidence interval (CI): 1.27, 5.04] after adjusting for maternal body mass index, education, gestational diabetes, and smoking. This association was not seen in mothers < 20 years (OR = 1.14; 95% CI: 0.55, 2.33), which is notable because although young maternal age is the strongest known risk factor for gastroschisis, most cases are born to mothers ≥ 20 years.

Conclusion: Our findings indicate an association between occupational exposure to PAHs among mothers who are ≥ 20 years and gastroschisis. These results contribute to a body of evidence that PAHs may be teratogenic.

PREGNANCY OUTCOMES:
PRETERM BIRTH/SMALL FOR GESTATIONAL AGE/FETAL DEVELOPMENT

Exposure to Trihalomethanes through Different Water Uses and Birth Weight, Small for Gestational Age, and Preterm Delivery in Spain

Cristina M. Villanueva, Esther Gracia-Lavedán, Jesús Ibarluzea, Loreto Santa Marina, Ferran Ballester, Sabrina Llop, Adonina Tardón, Mariana F. Fernández, Carmen Freire, Fernando Goñi, Xavier Basagaña, Manolis Kogevinas, Joan O. Grimalt, and Jordi Sunyer, on behalf of the INMA (Infancia y Medio Ambiente) Project

119:1824–1830 (2011) | http://dx.doi.org/10.1289/ehp.1002425

Background: Evidence associating exposure to water disinfection by-products with reduced birth weight and altered duration of gestation remains inconclusive.

Objective: We assessed exposure to trihalomethanes (THMs) during pregnancy through different water uses and evaluated the association with birth weight, small for gestational age (SGA), low birth weight (LBW), and preterm delivery.

Methods: Mother–child cohorts set up in five Spanish areas during the years 2000–2008 contributed data on water ingestion, showering, bathing, and swimming in pools. We ascertained residential THM levels during pregnancy periods through ad hoc sampling campaigns (828 measurements) and regulatory data (264 measurements), which were modeled and combined with personal water use and uptake factors to estimate personal uptake. We defined outcomes following standard definitions and included 2,158 newborns in the analysis.

Results: Median residential THM ranged from 5.9 µg/L (Valencia) to 114.7 µg/L (Sabadell), and speciation differed across areas. We estimated that 89% of residential chloroform and 96% of brominated THM uptakes were from showering/bathing. The estimated change of birth weight for a 10% increase in residential uptake was –0.45 g (95% confidence interval: –1.36, 0.45 g) for chloroform and 0.16 g (–1.38, 1.70 g) for brominated THMs. Overall, THMs were not associated with SGA, LBW, or preterm delivery.

Conclusions: Despite the high THM levels in some areas and the extensive exposure assessment, results suggest that residential THM exposure during pregnancy driven by inhalation and dermal contact routes is not associated with birth weight, SGA, LBW, or preterm delivery in Spain.

Traffic-Related Air Toxics and Term Low Birth Weight in Los Angeles County, California

Michelle Wilhelm, Jo Kay Ghosh, Jason Su, Myles Cockburn, Michael Jerrett, and Beate Ritz

120:132–138 (2012) | http://dx.doi.org/10.1289/ehp.1103408

Background: Numerous studies have linked criteria air pollutants with adverse birth outcomes, but there is less information on the importance of specific emission sources, such as traffic, and air toxics.

Objectives: We used three exposure data sources to examine odds of term low birth weight (LBW) in Los Angeles, California, women when exposed to high levels of traffic-related air pollutants during pregnancy.

Methods: We identified term births during 1 June 2004 to 30 March 2006 to women residing within 5 miles of a South Coast Air Quality Management District (SCAQMD) Multiple Air Toxics Exposure Study (MATES III) monitoring station. Pregnancy period average exposures were estimated for air toxics, including polycyclic aromatic hydrocarbons (PAHs), source-specific particulate matter < 2.5 µm in aerodynamic diameter ($PM_{2.5}$) based on a chemical mass balance model, criteria air pollutants from government monitoring data, and land use regression (LUR) model estimates of nitric oxide (NO), nitrogen dioxide (NO_2) and nitrogen oxides (NO_x). Associations between these metrics and odds of term LBW (< 2,500 g) were examined using logistic regression.

Results: Odds of term LBW increased approximately 5% per interquartile range increase in entire pregnancy exposures to several correlated traffic pollutants: LUR measures of NO, NO_2, and NO_x, elemental carbon, and $PM_{2.5}$ from diesel and gasoline combustion and paved road dust (geological $PM_{2.5}$).

Conclusions: These analyses provide additional evidence of the potential impact of traffic-related air pollution on fetal growth. Particles from traffic sources should be a focus of future studies.

Disease Outcomes

Air Pollution Exposure During Pregnancy, Ultrasound Measures of Fetal Growth, and Adverse Birth Outcomes: A Prospective Cohort Study

Edith H. van den Hooven, Frank H. Pierik, Yvonne de Kluizenaar, Sten P. Willemsen, Albert Hofman, Sjoerd W. van Ratingen, Peter Y.J. Zandveld, Johan P. Mackenbach, Eric A.P. Steegers, Henk M.E. Miedema, and Vincent W.V. Jaddoe

120:150–156 (2012) | http://dx.doi.org/10.1289/ehp.1003316

Background: Air pollution exposure during pregnancy might have trimester-specific effects on fetal growth.

Objective: We prospectively evaluated the associations of maternal air pollution exposure with fetal growth characteristics and adverse birth outcomes in 7,772 subjects in the Netherlands.

Methods: Particulate matter with an aerodynamic diameter < 10 μm (PM_{10}) and nitrogen dioxide (NO_2) levels were estimated using dispersion modeling at the home address. Fetal head circumference, length, and weight were estimated in each trimester by ultrasound. Information on birth outcomes was obtained from medical records.

Results: In cross-sectional analyses, NO_2 levels were inversely associated with fetal femur length in the second and third trimester, and PM_{10} and NO_2 levels both were associated with smaller fetal head circumference in the third trimester [–0.18 mm, 95% confidence interval (CI): –0.24, –0.12 mm; and –0.12 mm, 95% CI: –0.17, –0.06 mm per 1-μg/m^3 increase in PM_{10} and NO_2, respectively]. Average PM_{10} and NO_2 levels during pregnancy were not associated with head circumference and length at birth or neonatally, but were inversely associated with birth weight (–3.6 g, 95% CI: –6.7, –0.4 g; and –3.4 g, 95% CI: –6.2, –0.6 g, respectively). Longitudinal analyses showed similar patterns for head circumference and weight, but no associations with length. The third and fourth quartiles of PM_{10} exposure were associated with preterm birth [odds ratio (OR) = 1.40, 95% CI: 1.03, 1.89; and OR = 1.32; 95% CI: 0.96, 1.79, relative to the first quartile]. The third quartile of PM_{10} exposure, but not the fourth, was associated with small size for gestational age at birth (SGA) (OR = 1.38; 95% CI: 1.00, 1.90). No consistent associations were observed for NO_2 levels and adverse birth outcomes.

Conclusions: Results suggest that maternal air pollution exposure is inversely associated with fetal growth during the second and third trimester and with weight at birth. PM_{10} exposure was positively associated with preterm birth and SGA.

Maternal Cadmium Exposure during Pregnancy and Size at Birth: A Prospective Cohort Study

Maria Kippler, Fahmida Tofail, Renee Gardner, Anisur Rahman, Jena D. Hamadani, Matteo Bottai, and Marie Vahter

120:284–289 (2012) | http://dx.doi.org/10.1289/ehp.1103711

Background: Cadmium (Cd) is an embryotoxic and teratogenic metal in a variety of animal species, but data from humans are limited.

Objectives: The aim of the present study was to assess the effects of maternal Cd exposure in pregnancy on size at birth.

Methods: This prospective cohort study was nested in a population-based nutritional supplementation trial in pregnancy conducted in rural Bangladesh. We selected women recruited from February 2002 through January 2003 who had a singleton birth with measurements of size at birth and had donated a urine sample in early pregnancy for Cd analyses (n = 1,616). Urinary Cd was measured with inductively coupled plasma mass spectrometry and adjusted for specific gravity.

Results: Multiple linear regression analyses adjusted for sex and other potential confounders showed that maternal urinary Cd (median, 0.63 μg/L) was significantly negatively associated with birth weight [unstandardized regression coefficient B = –31.0; 95% confidence interval (CI): –59, –2.8] and head circumference (B = –0.15; 95% CI: –0.27, –0.026). However, associations appeared to be limited to girls, with little evidence of effects in boys. A 1-μg/L increase in Cd in maternal urine was associated with a 0.26-cm (95% CI: –0.43, –0.088 cm) and 0.24-cm (95% CI: –0.44, –0.030 cm) decrease in girls' head and chest circumferences, respectively, and a 45-g (95% CI: –82.5, 7.3 g) decrease in birth weight. Quantile regression analyses indicated that associations with maternal Cd were similar for girls of smaller (25th percentile) and larger (50th and 75th percentiles) sizes at birth.

Conclusion: We found evidence of a sex difference in the association between maternal Cd exposure and birth size, which was apparent only in girls. Results add support for the need to reduce Cd pollution to improve public health.

NEWS | SCIENCE SELECTION

Cadmium May Affect Newborn Girls More than Boys: Maternal Exposure Linked to Smaller Birth Size

Julia R. Barrett | 120:A76

http://dx.doi.org/10.1289/ehp.120-a76b

Disease Outcomes

Birth Weight and Prenatal Exposure to Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyldichloroethylene (DDE): A Meta-analysis within 12 European Birth Cohorts

Eva Govarts, Mark Nieuwenhuijsen, Greet Schoeters, Ferran Ballester, Karolien Bloemen, Michiel de Boer, Cécile Chevrier, Merete Eggesbø, Mònica Guxens, Ursula Krämer, Juliette Legler, David Martínez, Lubica Palkovicova, Evridiki Patelarou, Ulrich Ranft, Arja Rautio, Maria Skaalum Petersen, Rémy Slama, Hein Stigum, Gunnar Toft, Tomas Trnovec, Stéphanie Vandentorren, Pál Weihe, Nynke Weisglas Kuperus, Michael Wilhelm, Jürgen Wittsiepe, and Jens Peter Bonde, and OBELIX/ENRIECO

120:162–170 (2012) | http://dx.doi.org/10.1289/ehp.1103767

Objectives: Exposure to high concentrations of persistent organochlorines may cause fetal toxicity, but the evidence at low exposure levels is limited. Large studies with substantial exposure contrasts and appropriate exposure assessment are warranted. Within the framework of the EU (European Union) ENRIECO (ENvironmental Health RIsks in European Birth Cohorts) and EU OBELIX (OBesogenic Endocrine disrupting chemicals: LInking prenatal eXposure to the development of obesity later in life) projects, we examined the hypothesis that the combination of polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE) adversely affects birth weight.

Methods: We used maternal and cord blood and breast milk samples of 7,990 women enrolled in 15 study populations from 12 European birth cohorts from 1990 through 2008. Using identical variable definitions, we performed for each cohort linear regression of birth weight on estimates of cord serum concentration of PCB-153 and *p,p´*-DDE adjusted for gestational age and *a priori* selected covariates. We obtained summary estimates by meta-analysis and performed analyses of interactions.

Results: The median concentration of cord serum PCB-153 was 140 ng/L (range of cohort medians 20–484 ng/L) and that of *p,p´*-DDE was 528 ng/L (range of cohort medians 50–1,208 ng/L). Birth weight decreased with increasing cord serum concentration of PCB-153 after adjustment for potential confounders in 12 of 15 study populations. The meta-analysis including all cohorts indicated a birth weight decline of 150 g [95% confidence interval (CI): –250, –50 g] per 1-µg/L increase in PCB-153, an exposure contrast that is close to the range of exposures across the cohorts. A 1-µg/L increase in *p,p´*-DDE was associated with a 7-g decrease in birth weight (95% CI: –18, 4 g).

Conclusions: The findings suggest that low-level exposure to PCB (or correlated exposures) impairs fetal growth, but that exposure to *p,p´*-DDE does not. The study adds to mounting evidence that low-level exposure to PCBs is inversely associated with fetal growth.

Association between Pregnancy Loss and Urinary Phthalate Levels around the Time of Conception

Gunnar Toft, Bo A.G. Jönsson, Christian H. Lindh, Tina Kold Jensen, Niels H. Hjollund, Anne Vested, and Jens Peter Bonde

120:458–463 (2012) | http://dx.doi.org/10.1289/ehp.1103552

Background: Animal studies indicate that some phthalate metabolites may harm female reproductive function.

Objectives: We assessed the associations between exposure to phthalate metabolites and pregnancy loss.

Methods: Using a previously established cohort of couples planning their first pregnancy, we analyzed four primary and two oxidized secondary phthalate metabolites in urine samples collected on day 10 after the first day of the last menstrual period before conception occurred ($n = 128$) and during the previous cycle (if any, $n = 111$). Subclinical embryonal loss was identified by repeated measurement of urinary human chorionic gonadotropin, and information on clinical spontaneous abortions was obtained by telephone interview with the mother.

Results: Pregnancy loss ($n = 48$) was increased among women with urinary concentration of monoethylhexyl phthalate (MEHP) in the upper tertile in the conception sample compared with women in the lowest tertile [adjusted odds ratio (OR) = 2.9; 95% confidence interval (CI): 1.1, 7.6]. The corresponding OR for subclinical embryonal loss ($n = 32$) was 40.7 (95% CI: 4.5, 369.5).

Conclusions: The phthalate metabolite MEHP was associated with higher occurrence of pregnancy loss. Because this is the first human study to show this association and the sample size is small, the findings need to be corroborated in independent studies.

Exposure to Phthalates and Phenols during Pregnancy and Offspring Size at Birth

Claire Philippat, Marion Mortamais, Cécile Chevrier, Claire Petit, Antonia M. Calafat, Xiaoyun Ye, Manori J. Silva, Christian Brambilla, Isabelle Pin, Marie-Aline Charles, Sylvaine Cordier, and Rémy Slama

120:464–470 (2012) | http://dx.doi.org/10.1289/ehp.1103634

Background: Data concerning the effects of prenatal exposures to phthalates and phenols on fetal growth are limited in humans. Previous findings suggest possible effects of some phenols on male birth weight.

Objective: Our aim was to assess the relationships between prenatal exposures to phthalates and phenols and fetal growth among male newborns.

Methods: We conducted a case–control study on male malformations of the genitalia nested in two French mother–child cohorts with recruitment between 2002 and 2006. We measured, in maternal urinary samples collected between 6 and 30 gestational weeks, the concentrations (micrograms per liter) of 9 phenol (n = 191 pregnant women) and 11 phthalate metabolites (n = 287). Weight, length, and head circumference at birth were collected from maternity records. Statistical analyses were corrected for the oversampling of malformation cases.

Results: Adjusted birth weight decreased by 77 g [95% confidence interval (CI): –129, –25] and by 49 g (95% CI: –86, –13) in association with a 1-unit increase in ln-transformed 2,4-dichlorophenol (DCP) and 2,5-DCP urinary concentrations, respectively. Benzophenone-3 (BP3) ln-transformed concentrations were positively associated with weight (26 g; 95% CI: –2, 54) and head circumference at birth (0.1 cm; 95% CI: 0.0, 0.2). Head circumference increased by 0.3 cm (95% CI: 0.0, 0.7) in association with a 1-unit increase in ln-transformed BPA concentration. For phthalate metabolites there was no evidence of monotonic associations with birth weight.

Conclusions: Consistent with findings of a previous study, we observed evidence of an inverse association of 2,5-DCP and a positive association of BP3 with male birth weight.

Adverse Birth Outcomes and Maternal Exposure to Trichloroethylene and Tetrachloroethylene through Soil Vapor Intrusion in New York State

Steven P. Forand, Elizabeth L. Lewis-Michl, and Marta I. Gomez

120:616–621 (2012) | http://dx.doi.org/10.1289/ehp.1103884

Background: Industrial spills of volatile organic compounds (VOCs) in Endicott, New York (USA), have led to contamination of groundwater, soil, and soil gas. Previous studies have reported an increase in adverse birth outcomes among women exposed to VOCs in drinking water.

Objective: We investigated the prevalence of adverse birth outcomes among mothers exposed to trichloroethylene (TCE) and tetrachloroethylene [or perchloroethylene (PCE)] in indoor air contaminated through soil vapor intrusion.

Methods: We examined low birth weight (LBW), preterm birth, fetal growth restriction, and birth defects among births to women in Endicott who were exposed to VOCs, compared with births statewide. We used Poisson regression to analyze births and malformations to estimate the association between maternal exposure to VOCs adjusting for sex, mother's age, race, education, parity, and prenatal care. Two exposure areas were identified based on environmental sampling data: one area was primarily contaminated with TCE, and the other with PCE.

Results: In the TCE-contaminated area, adjusted rate ratios (RRs) were significantly elevated for LBW [RR = 1.36; 95% confidence interval (CI): 1.07, 1.73; n = 76], small for gestational age (RR = 1.23; 95% CI: 1.03, 1.48; n = 117), term LBW (RR = 1.68; 95% CI: 1.20, 2.34; n = 37), cardiac defects (RR = 2.15; 95% CI: 1.27, 3.62; n = 15), and conotruncal defects (RR = 4.91; 95% CI: 1.58, 15.24; n = 3). In the PCE-contaminated area, RRs for cardiac defects (five births) were elevated but not significantly. Residual socioeconomic confounding may have contributed to elevations of LBW outcomes.

Conclusions: Maternal residence in both areas was associated with cardiac defects. Residence in the TCE area, but not the PCE area, was associated with LBW and fetal growth restriction.

Disease Outcomes

Associations of Prenatal Exposure to Organophosphate Pesticide Metabolites with Gestational Age and Birth Weight

Stephen A. Rauch, Joe M. Braun, Dana Boyd Barr, Antonia M. Calafat, Jane Khoury, M. Angela Montesano, Kimberly Yolton, and Bruce P. Lanphear

120:1055–1060 (2012) | http://dx.doi.org/10.1289/ehp.1104615

Background: Prenatal exposure to organophosphate (OP) insecticides, a widely used class of pesticides, may be associated with decreased gestational age and lower birth weight. Single nucleotide polymorphisms in paroxanase (*PON1*) enzyme genotypes may modify the relationships between OP exposure and perinatal outcomes.

Objective: We examined the relationship of prenatal OP insecticide exposure, measured using urinary dialkyl phosphate (DAP) metabolite concentrations, with gestational age and birth weight.

Methods: We measured the concentrations of six nonspecific DAP metabolites of OP insecticides in two maternal spot urine samples collected in a prospective birth cohort. We performed multivariable regression to examine associations between the sum of six DAP concentrations (ΣDAP) with gestational age and birth weight. We also examined whether these associations differed according to infant $PON1_{192}$ and $PON1_{-108}$ genotypes.

Results: Among 306 mother–infant dyads, a 10-fold increase in ΣDAP concentrations was associated with a decrease in covariate-adjusted gestational age [–0.5 weeks; 95% confidence interval (CI): –0.8, –0.1] and birth weight (–151 g; CI: –287, –16); the decrements in birth weight were attenuated after adjusting for gestational age. The relationship between ΣDAP concentrations and gestational age was stronger for white (–0.7 weeks; CI: –1.1, –0.3) than for black (–0.1 weeks; 95% CI: –0.9, 0.6) newborns. In contrast, there was a greater decrease in birth weight with increasing urinary ΣDAP concentrations for black (–188 g; CI: –395, 19) than for white (–118 g; CI: –296, 60) newborns. Decrements in birth weight and gestational age associated with ΣDAP concentrations were greatest among infants with $PON1_{192QR}$ and PON_{-108CT} genotypes.

Conclusions: Prenatal urinary ΣDAP concentrations were associated with shortened gestation and reduced birth weight in this cohort, but the effects differed by race/ethnicity and $PON1_{192/108}$ genotypes.

INFECTIONS

Viruses in Nondisinfected Drinking Water from Municipal Wells and Community Incidence of Acute Gastrointestinal Illness

Mark A. Borchardt, Susan K. Spencer, Burney A. Kieke Jr., Elisabetta Lambertini, and Frank J. Loge

120:1272–1279 (2012) | http://dx.doi.org/10.1289/ehp.1104499

Background: Groundwater supplies for drinking water are frequently contaminated with low levels of human enteric virus genomes, yet evidence for waterborne disease transmission is lacking.

Objectives: We related quantitative polymerase chain reaction (qPCR)–measured enteric viruses in the tap water of 14 Wisconsin communities supplied by nondisinfected groundwater to acute gastrointestinal illness (AGI) incidence.

Methods: AGI incidence was estimated from health diaries completed weekly by households within each study community during four 12-week periods. Water samples were collected monthly from five to eight households per community. Viruses were measured by qPCR, and infectivity assessed by cell culture. AGI incidence was related to virus measures using Poisson regression with random effects.

Results: Communities and time periods with the highest virus measures had correspondingly high AGI incidence. This association was particularly strong for norovirus genogroup I (NoV-GI) and between adult AGI and enteroviruses when echovirus serotypes predominated. At mean concentrations of 1 and 0.8 genomic copies/L of NoV-GI and enteroviruses, respectively, the AGI incidence rate ratios (i.e., relative risk) increased by 30%. Adenoviruses were common, but tap-water concentrations were low and not positively associated with AGI. The estimated fraction of AGI attributable to tap-water–borne viruses was between 6% and 22%, depending on the virus exposure–AGI incidence model selected, and could have been as high as 63% among children < 5 years of age during the period when NoV-GI was abundant in drinking water.

Conclusions: The majority of groundwater-source public water systems in the United States produce water without disinfection, and our findings suggest that populations served by such systems may be exposed to waterborne viruses and consequent health risks.

FETAL OR EARLY-LIFE EXPOSURES CONTRIBUTING TO ADULT DISEASE

Dioxin Exposure and Cancer Risk in the Seveso Women's Health Study

Marcella Warner, Paolo Mocarelli, Steven Samuels, Larry Needham, Paolo Brambilla, and Brenda Eskenazi

119:1700–1705 (2011) | http://dx.doi.org/10.1289/ehp.1103720

Background: 2,3,7,8-Tetrachlorodibenzo-*para*-dioxin (TCDD), a widespread environmental contaminant, disrupts multiple endocrine pathways. The International Agency for Research on Cancer classified TCDD as a known human carcinogen, based on predominantly male occupational studies of increased mortality from all cancers combined.

Objectives: After a chemical explosion on 10 July 1976 in Seveso, Italy, residents experienced some of the highest levels of TCDD exposure in a human population. In 1996, we initiated the Seveso Women's Health Study (SWHS), a retrospective cohort study of the reproductive health of the women. We previously reported a significant increased risk for breast cancer and a nonsignificant increased risk for all cancers combined with individual serum TCDD, but the cohort averaged only 40 years of age in 1996. Herein we report results for risk of cancer from a subsequent follow-up of the cohort in 2008.

Methods: In 1996, we enrolled 981 women who were 0–40 years of age in 1976, lived in the most contaminated areas, and had archived sera collected near the explosion. Individual TCDD concentration was measured in archived serum by high-resolution mass spectrometry. A total of 833 women participated in the 2008 follow-up study. We examined the relation of serum TCDD with cancer incidence using Cox proportional hazards models.

Results: In total, 66 (6.7%) women had been diagnosed with cancer. The adjusted hazard ratio (HR) associated with a 10-fold increase in serum TCDD for all cancers combined was significantly increased [adjusted HR = 1.80; 95% confidence interval (CI): 1.29, 2.52]. For breast cancer, the HR was increased, but not significantly (adjusted HR = 1.44; 95% CI: 0.89, 2.33).

Conclusions: Individual serum TCDD is significantly positively related with all cancer incidence in the SWHS cohort, more than 30 years later. This all-female study adds to the epidemiologic evidence that TCDD is a multisite carcinogen.

In Utero Exposure to Maternal Tobacco Smoke and Subsequent Obesity, Hypertension, and Gestational Diabetes Among Women in the MoBa Cohort

Lea A. Cupul-Uicab, Rolv Skjaerven, Kjell Haug, Kari K. Melve, Stephanie M. Engel, and Matthew P. Longnecker

120:355–360 (2012) | http://dx.doi.org/10.1289/ehp.1103789

Background: Environmental factors influencing the developmental origins of health and disease need to be identified and investigated. *In utero* exposure to tobacco smoke has been associated with obesity and a small increase in blood pressure in children; however, whether there is a corresponding increased risk of conditions such as diabetes and hypertension during adulthood remains unclear.

Objective: Our goal was to assess the association of self-reported *in utero* exposure to tobacco smoke with the prevalence of obesity, hypertension, type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM) in women 14–47 years of age.

Methods: We conducted a cross-sectional analysis of the Norwegian Mother and Child Cohort Study, which enrolled pregnant women in Norway from 1999 thorough 2008. Exposure to tobacco smoke *in utero* (yes vs. no) was ascertained on the baseline questionnaire (obtained at ~ 17 weeks' gestation); the outcomes were ascertained from the Medical Birth Registry of Norway and the questionnaire. Our analysis included 74,023 women.

Results: Women exposed to tobacco smoke *in utero* had 1.53 times the odds of obesity [95% confidence interval (CI): 1.45, 1.61] relative to those unexposed, after adjusting for age, education, and personal smoking. After further adjustment for body mass index, the odds ratio for hypertension was 1.68 (95% CI: 1.19, 2.39); for T2DM 1.14 (95% CI: 0.79, 1.65); and for GDM 1.32 (95% CI: 1.10, 1.58) among exposed compared with unexposed.

Conclusions: Exposure to tobacco smoke *in utero* was associated with obesity, hypertension, and GDM in adult women. The possibility that the associations were attributable to unmeasured confounding cannot be excluded.

Disease Outcomes

Early-Life Exposures and Early-Onset Uterine Leiomyomata in Black Women in the Sister Study

Aimee A. D'Aloisio, Donna D. Baird, Lisa A. DeRoo, and Dale P. Sandler

120:406–412 (2012) | http://dx.doi.org/10.1289/ehp.1103620

Background: Uterine leiomyomata (fibroids) are hormonally responsive tumors, but little is known about risk factors. Early-life exposures may influence uterine development and subsequent response to hormones in adulthood. An earlier analysis of non-Hispanic white women who participated in the Sister Study found associations between several early-life factors and early-onset fibroids.

Objectives: We evaluated associations of early-life and childhood exposures with early-onset fibroids among black women and compared the results with those found among white women.

Methods: We analyzed baseline data from 3,534 black women, 35–59 years of age, in the Sister Study (a nationwide cohort of women who had a sister diagnosed with breast cancer) who self-reported information on early-life and childhood exposures. Early-onset fibroids were assessed based on self-report of a physician diagnosis of fibroids by the age of 30 years ($n = 561$). We estimated risk ratios (RR) and 95% confidence intervals (CI) from log-binomial regression models.

Results: Factors most strongly associated with early-onset fibroids were *in utero* diethylstilbestrol (DES; RR = 2.02; 95% CI: 1.28, 3.18), maternal prepregnancy diabetes or gestational diabetes (RR = 1.54; 95% CI: 0.95, 2.49), and monozygotic multiple birth (RR = 1.94; 95% CI: 1.26, 2.99). We also found positive associations with having been taller or thinner than peers at the age of 10 years and with early-life factors that included being the firstborn child of a teenage mother, maternal hypertensive disorder, preterm birth, and having been fed soy formula.

Conclusions: With the exception of monozygotic multiple birth and maternal hypertensive disorder, early-life risk factors for early-onset fibroids for black women were similar to those found for white women. However, in contrast to whites, childhood height and weight, but not low socioeconomic status indicators, were associated with early-onset fibroids in blacks. The general consistency of early-life findings for black and white women supports a possible role of early-life factors in fibroid development.

Prenatal Exposure to Perfluorooctanoate and Risk of Overweight at 20 Years of Age: A Prospective Cohort Study

Thorhallur I. Halldorsson, Dorte Rytter, Line Småstuen Haug, Bodil Hammer Bech, Inge Danielsen, Georg Becher, Tine Brink Henriksen, and Sjurdur F. Olsen

120:668–673 (2012) | http://dx.doi.org/10.1289/ehp.1104034

Background: Perfluoroalkyl acids are persistent compounds used in various industrial applications. Of these compounds, perfluorooctanoate (PFOA) is currently detected in humans worldwide. A recent study on low-dose developmental exposure to PFOA in mice reported increased weight and elevated biomarkers of adiposity in postpubertal female offspring.

Objective: We examined whether the findings of increased weight in postpubertal female mice could be replicated in humans.

Methods: A prospective cohort of 665 Danish pregnant women was recruited in 1988–1989 with offspring follow-up at 20 years. PFOA was measured in serum from gestational week 30. Offspring body mass index (BMI) and waist circumference were recorded at follow-up ($n = 665$), and biomarkers of adiposity were quantified in a subset ($n = 422$) of participants.

Results: After adjusting for covariates, including maternal pre-pregnancy BMI, smoking, education, and birth weight, *in utero* exposure to PFOA was positively associated with anthropometry at 20 years in female but not male offspring. Adjusted relative risks comparing the highest with lowest quartile (median: 5.8 vs. 2.3 ng/mL) of maternal PFOA concentration were 3.1 [95% confidence interval (CI): 1.4, 6.9] for overweight or obese (BMI ≥ 25 kg/m^2) and 3.0 (95% CI: 1.3, 6.8) for waist circumference > 88 cm among female offspring. This corresponded to estimated increases of 1.6 kg/m^2 (95% CI: 0.6, 2.6) and 4.3 cm (95% CI: 1.4, 7.3) in average BMI and waist circumference, respectively. In addition, maternal PFOA concentrations were positively associated with serum insulin and leptin levels and inversely associated with adiponectin levels in female offspring. Similar associations were observed for males, although point estimates were less precise because of fewer observations. Maternal perfluorooctane sulfonate (PFOS), perfluorooctane sulfonamide (PFOSA), and perfluorononanoate (PFNA) concentrations were not independently associated with offspring anthropometry at 20 years.

Conclusions: Our findings on the effects of low-dose developmental exposures to PFOA are in line with experimental results suggesting obesogenic effects in female offspring at 20 years of age.

Prenatal Lead Levels, Plasma Amyloid β Levels, and Gene Expression in Young Adulthood

Maitreyi Mazumdar, Weiming Xia, Oliver Hofmann, Matthew Gregas, Shannan Ho Sui, Winston Hide, Ting Yang, Herbert L. Needleman, and David C. Bellinger

120:702–707 (2012) | http://dx.doi.org/10.1289/ehp.1104474

Background: Animal studies suggest that early-life lead exposure influences gene expression and production of proteins associated with Alzheimer's disease (AD).

Objectives: We attempted to assess the relationship between early-life lead exposure and potential biomarkers for AD among young men and women. We also attempted to assess whether early-life lead exposure was associated with changes in expression of AD-related genes.

Methods: We used sandwich enzyme-linked immunosorbent assays (ELISA) to measure plasma concentrations of amyloid β proteins $A\beta_{40}$ and $A\beta_{42}$ among 55 adults who had participated as newborns and young children in a prospective cohort study of the effects of lead exposure on development. We used RNA microarray techniques to analyze gene expression.

Results: Mean plasma $A\beta_{42}$ concentrations were lower among 13 participants with high umbilical cord blood lead concentrations (≥ 10 μg/dL) than in 42 participants with lower cord blood lead concentrations ($p = 0.08$). Among 10 participants with high prenatal lead exposure, we found evidence of an inverse relationship between umbilical cord lead concentration and expression of ADAM metallopeptidase domain 9 (*ADAM9*), reticulon 4 (*RTN4*), and low-density lipoprotein receptor-related protein associated protein 1 (*LRPAP1*) genes, whose products are believed to affect Aβ production and deposition. Gene network analysis suggested enrichment in gene sets involved in nerve growth and general cell development.

Conclusions: Data from our exploratory study suggest that prenatal lead exposure may influence Aβ-related biological pathways that have been implicated in AD onset. Gene network analysis identified further candidates to study the mechanisms of developmental lead neurotoxicity.

RELATED ARTICLES

NEWS | Purifying Drinking Water with Sun, Salt, and Limes
Adrian Burton | 120:A305
http://dx.doi.org/10.1289/ehp.120-a305

NEWS | Perfluorinated Compounds May Lower Vaccine Protection in Children
Carol Potera | 120:A150–A151
http://dx.doi.org/10.1289/ehp.120-a150a

NEWS | Can Indoor Swimming Alter Hormones in Boys?
Bob Weinhold | 120:A18
http://dx.doi.org/10.1289/ehp.120-a18

PODCAST | Early Influences on Mammary Gland Development, with Suzanne Fenton
http://dx.doi.org/10.1289/ehp.trp100111

NEWS | Obesogens: An Environmental Link to Obesity
Wendee Holtcamp | 120:A62–A68
http://dx.doi.org/10.1289/ehp.120-a62

PODCAST | What Do We Know about Obesogens? with Bruce Blumberg
http://dx.doi.org/10.1289/ehp.trp070212

EDITORIAL | Is Supersize More than Just Too Much Food?
Linda S. Birnbaum | 120:A223–A224
http://dx.doi.org/10.1289/ehp.1205200

NEWS | Stress–Pollution Interactions: An Emerging Issue in Children's Health Research
Catherine M. Cooney | 119:A430–A435
http://dx.doi.org/10.1289/ehp.119-a430

Disease Outcomes

Prenatal and Early Childhood Exposure to Tetrachloroethylene and Adult Vision

Kelly D. Getz, Patricia A. Janulewicz, Susannah Rowe, Janice M. Weinberg, Michael R. Winter, Brett R. Martin, Veronica M. Vieira, Roberta F. White, and Ann Aschengrau

120:1327–1332 (2012) | http://dx.doi.org/10.1289/ehp.1103996

Background: Tetrachloroethylene (PCE; or perchloroethylene) has been implicated in visual impairments among adults with occupational and environmental exposures as well as children born to women with occupational exposure during pregnancy.

Objectives: Using a population-based retrospective cohort study, we examined the association between prenatal and early childhood exposure to PCE-contaminated drinking water on Cape Cod, Massachusetts, and deficits in adult color vision and contrast sensitivity.

Methods: We estimated the amount of PCE that was delivered to the family residence from participants' gestation through 5 years of age. We administered to this now adult study population vision tests to assess acuity, contrast sensitivity, and color discrimination.

Results: Participants exposed to higher PCE levels exhibited lower contrast sensitivity at intermediate and high spatial frequencies compared with unexposed participants, although the differences were generally not statistically significant. Exposed participants also exhibited poorer color discrimination than unexposed participants. The difference in mean color confusion indices (CCI) was statistically significant for the Farnsworth test but not Lanthony's D-15d test [Farnsworth CCI mean difference = 0.05, 95% confidence interval (CI): 0.003, 0.10; Lanthony CCI mean difference = 0.07, 95% CI: –0.02, 0.15].

Conclusions: Prenatal and early childhood exposure to PCE-contaminated drinking water may be associated with long-term subclinical visual dysfunction in adulthood, particularly with respect to color discrimination. Further investigation of this association in similarly exposed populations is necessary.

▾ NEWS | SCIENCE SELECTION

Subtle Shades of Impairment: Childhood Tetrachloroethylene Exposure May Cause Subclinical Deficits in Adult Vision

Wendee Holtcamp | 120:A362

http://dx.doi.org/10.1289/ehp.120-a362a

OBESITY

Prenatal Concentrations of Polychlorinated Biphenyls, DDE, and DDT and Overweight in Children: A Prospective Birth Cohort Study

Damaskini Valvi, Michelle A. Mendez, David Martinez, Joan O. Grimalt, Maties Torrent, Jordi Sunyer, and Martine Vrijheid

120:451–457 (2012) | http://dx.doi.org/10.1289/ehp.1103862

Background: Recent experimental evidence suggests that prenatal exposure to endocrine-disrupting chemicals (EDCs) may increase postnatal obesity risk and that these effects may be sex or diet dependent.

Objectives: We explored whether prenatal organochlorine compound (OC) concentrations [polychlorinated biphenyls (PCBs), dichlorodiphenyldichloroethylene (DDE), and dichlorodiphenyltrichloroethane (DDT)] were associated with overweight at 6.5 years of age and whether child sex or fat intakes modified these associations.

Methods: We studied 344 children from a Spanish birth cohort established in 1997–1998. Overweight at 6.5 years was defined as a body mass index (BMI) *z*-score ≥ 85th percentile of the World Health Organization reference. Cord blood OC concentrations were measured and treated as categorical variables (tertiles). Children's diet was assessed by food frequency questionnaire. Relative risks (RRs) were estimated using generalized linear models.

Results: After multivariable adjustment, we found an increased RR of overweight in the third tertile of PCB exposure [RR = 1.70; 95% confidence interval (CI): 1.09, 2.64] and the second tertile of DDE exposure (RR = 1.67; 95% CI: 1.10, 2.55), but no association with DDT exposure in the population overall. Associations between overweight and PCB and DDE concentrations were strongest in girls (*p*-interaction between 0.01 and 0.28); DDT was associated with overweight only in boys. For DDT we observed stronger associations in children with fat intakes at or above compared with below the median, but this interaction was not significant (*p*-interaction > 0.05).

Conclusions: This study suggests that prenatal OC exposures may be associated with overweight in children and that sex and high-fat intake may influence susceptibility.

Disease Outcomes

Role of Environmental Chemicals in Diabetes and Obesity: A National Toxicology Program Workshop Review

Kristina A. Thayer, Jerrold J. Heindel, John R. Bucher, and Michael A. Gallo

120:779–789 (2012) | http://dx.doi.org/10.1289/ehp.1104597

Background: There has been increasing interest in the concept that exposures to environmental chemicals may be contributing factors to the epidemics of diabetes and obesity. On 11–13 January 2011, the National Institute of Environmental Health Sciences (NIEHS) Division of the National Toxicology Program (NTP) organized a workshop to evaluate the current state of the science on these topics of increasing public health concern.

Objective: The main objective of the workshop was to develop recommendations for a research agenda after completing a critical analysis of the literature for humans and experimental animals exposed to certain environmental chemicals. The environmental exposures considered at the workshop were arsenic, persistent organic pollutants, maternal smoking/nicotine, organotins, phthalates, bisphenol A, and pesticides. High-throughput screening data from Toxicology in the 21st Century (Tox21) were also considered as a way to evaluate potential cellular pathways and generate hypotheses for testing which and how certain chemicals might perturb biological processes related to diabetes and obesity.

Conclusions: Overall, the review of the existing literature identified linkages between several of the environmental exposures and type 2 diabetes. There was also support for the "developmental obesogen" hypothesis, which suggests that chemical exposures may increase the risk of obesity by altering the differentiation of adipocytes or the development of neural circuits that regulate feeding behavior. The effects may be most apparent when the developmental exposure is combined with consumption of a high-calorie, high-carbohydrate, or high-fat diet later in life. Research on environmental chemical exposures and type 1 diabetes was very limited. This lack of research was considered a critical data gap. In this workshop review, we outline the major themes that emerged from the workshop and discuss activities that NIEHS/NTP is undertaking to address research recommendations. This review also serves as an introduction to an upcoming series of articles that review the literature regarding specific exposures and outcomes in more detail.

STRESS AND HEALTH

Stress during Pregnancy and Offspring Pediatric Disease: A National Cohort Study

Marion Tegethoff, Naomi Greene, Jørn Olsen, Emmanuel Schaffner, and Gunther Meinlschmidt

119:1647–1652 (2011) | http://dx.doi.org/10.1289/ehp.1003253

Background: Identifying risk factors for adverse health outcomes in children is important. The intrauterine environment plays a pivotal role for health and disease across life.

Objectives: We conducted a comprehensive study to determine whether common psychosocial stress during pregnancy is a risk factor for a wide spectrum of pediatric diseases in the offspring.

Methods: The study was conducted using prospective data in a population-based sample of mothers with live singleton births (n = 66,203; 71.4% of those eligible) from the Danish National Birth Cohort. We estimated the association between maternal stress during pregnancy (classified based on two *a priori*–defined indicators of common stress forms, life stress and emotional stress) and offspring diseases during childhood (grouped into 16 categories of diagnoses from the *International Classification of Diseases, 10th Revision*, based on data from national registries), controlling for maternal stress after pregnancy.

Results: Median age at end of follow-up was 6.2 (range, 3.6–8.9) years. Life stress (highest compared with lowest quartile) was associated with an increased risk of conditions originating in the perinatal period [odds ratio (OR) = 1.13; 95% confidence interval (CI): 1.06, 1.21] and congenital malformations (OR=1.17; CI: 1.06, 1.28) and of the first diagnosis of infection [hazard ratio (HR) = 1.28; CI: 1.17, 1.39], mental disorders (age 0–2.5 years: HR = 2.03; CI: 1.32, 3.14), and eye (age 0–4.5 years: HR = 1.27; CI: 1.06, 1.53), ear (HR = 1.36; CI: 1.23, 1.51), respiratory (HR = 1.27; CI; 1.19, 1.35), digestive (HR = 1.23; CI: 1.11, 1.37), skin (HR = 1.24; CI: 1.09, 1.43), musculoskeletal (HR = 1.15; CI: 1.01–1.30), and genitourinary diseases (HR = 1.25; CI; 1.08, 1.45). Emotional stress was associated with an increased risk for the first diagnosis of infection (HR = 1.09; CI: 1.01, 1.18) and a decreased risk for the first diagnosis of endocrine (HR = 0.81; CI; 0.67, 0.99), eye (HR = 0.84; CI; 0.71, 0.99), and circulatory diseases (age 0–3 years: HR = 0.63; CI: 0.42, 0.95).

Conclusions: Maternal life stress during pregnancy may be a common risk factor for impaired child health. The results suggest new approaches to reduce childhood diseases.

▾ NEWS | SCIENCE SELECTION

An Emotional Bond: The Relationship between Maternal Stress and Offspring Disease

Tanya Tillett | 119:A488

http://dx.doi.org/10.1289/ehp.119-a488a

HEAVY METALS (E.G., LEAD, MERCURY)

Prenatal Lead Exposure and Weight of 0- to 5-Year-Old Children in Mexico City

Myriam Afeiche, Karen E. Peterson, Brisa N. Sánchez, David Cantonwine, Héctor Lamadrid-Figueroa, Lourdes Schnaas, Adrienne S. Ettinger, Mauricio Hernández-Avila, Howard Hu, and Martha M. Téllez-Rojo

119:1436–1441 (2011) | http://dx.doi.org/10.1289/ehp.1003184

Background: Cumulative prenatal lead exposure, as measured by maternal bone lead burden, has been associated with smaller weight of offspring at birth and 1 month of age, but no study has examined whether this effect persists into early childhood.

Objective: We investigated the association of perinatal maternal bone lead, a biomarker of cumulative prenatal lead exposure, with children's attained weight over time from birth to 5 years of age.

Methods: Children were weighed at birth and at several intervals up until 60 months. Maternal tibia and patella lead were measured at 1 month postpartum using *in vivo* K-shell X-ray fluorescence. We used varying coefficient models with random effects to assess the association of maternal bone lead with weight trajectories of 522 boys and 477 girls born between 1994 and 2005 in Mexico City.

Results: After controlling for breast-feeding duration, maternal anthropometry, and sociodemographic characteristics, a 1-SD increase in maternal patella lead (micrograms per gram) was associated with a 130.9-g decrease in weight [95% confidence interval (CI), –227.4 to –34.4 g] among females and a 13.0-g non-significant increase in weight among males (95% CI, –73.7 to 99.9 g) at 5 years of age. These associations were similar after controlling for concurrent blood lead levels between birth and 5 years.

Conclusions: Maternal bone lead was associated with lower weight over time among female but not male children up to 5 years of age. Given that the association was evident for patellar but not tibial lead levels, and was limited to females, results need to be confirmed in other studies.

Manganese Exposure from Drinking Water and Children's Classroom Behavior in Bangladesh

Khalid Khan, Pam Factor-Litvak, Gail A. Wasserman, Xinhua Liu, Ershad Ahmed, Faruque Parvez, Vesna Slavkovich, Diane Levy, Jacob Mey, Alexander van Geen, and Joseph H. Graziano

119:1501–1506 (2011) | http://dx.doi.org/10.1289/ehp.1003397

Background: Evidence of neurological, cognitive, and neuropsychological effects of manganese (Mn) exposure from drinking water (WMn) in children has generated widespread public health concern. At elevated exposures, Mn has been associated with increased levels of externalizing behaviors, including irritability, aggression, and impulsivity. Little is known about potential effects at lower exposures, especially in children. Moreover, little is known regarding potential interactions between exposure to Mn and other metals, especially arsenic (As).

Objectives: We conducted a cross-sectional study of 201 children to investigate associations of Mn and As in tube well water with classroom behavior among elementary school children, 8–11 years of age, in Araihazar, Bangladesh.

Methods: Data on exposures and behavioral outcomes were collected from the participants at the baseline of an ongoing longitudinal study of child intelligence. Study children were rated by their school teachers on externalizing and internalizing items of classroom behavior using the standardized Child Behavior Checklist–Teacher's Report Form (CBCL-TRF).

Results: Log-transformed WMn was positively and significantly associated with TRF internalizing [estimated $\beta = 0.82$; 95% confidence interval (CI), 0.08–1.56; $p = 0.03$], TRF externalizing (estimated $\beta = 2.59$; 95% CI, 0.81–4.37; $p = 0.004$), and TRF total scores (estimated $\beta = 3.35$; 95% CI, 0.86–5.83; $p = 0.008$) in models that adjusted for log-transformed water arsenic (WAs) and sociodemographic covariates. We also observed a positive monotonic dose–response relationship between WMn and TRF externalizing and TRF total scores among the participants of the study. We did not find any significant associations between WAs and various scales of TRF scores.

Conclusion: These observations reinforce the growing concern regarding the neurotoxicologic effects of WMn in children.

Exposures

A Geospatial Analysis of the Effects of Aviation Gasoline on Childhood Blood Lead Levels

Marie Lynn Miranda, Rebecca Anthopolos, and Douglas Hastings

119:1513–1516 (2011) | http://dx.doi.org/10.1289/ehp.1003231

Background: Aviation gasoline, commonly referred to as avgas, is a leaded fuel used in small aircraft. Recent concern about the effects of lead emissions from planes has motivated the U.S. Environmental Protection to consider regulating leaded avgas.

Objective: In this study we investigated the relationship between lead from avgas and blood lead levels in children living in six counties in North Carolina.

Methods: We used geographic information systems to approximate areas surrounding airports in which lead from avgas may be present in elevated concentrations in air and may also be deposited to soil. We then used regression analysis to examine the relationship between residential proximity to airports and North Carolina blood lead surveillance data in children 9 months to 7 years of age while controlling for factors including age of housing, socioeconomic characteristics, and seasonality.

Results: Our results suggest that children living within 500 m of an airport at which planes use leaded avgas have higher blood lead levels than other children. This apparent effect of avgas on blood lead levels was evident also among children living within 1,000 m of airports. The estimated effect on blood lead levels exhibited a monotonically decreasing dose–response pattern, with the largest impact on children living within 500 m.

Conclusions: We estimated a significant association between potential exposure to lead emissions from avgas and blood lead levels in children. Although the estimated increase was not especially large, the results of this study are nonetheless directly relevant to the policy debate surrounding the regulation of leaded avgas.

Arsenic Exposure and Motor Function among Children in Bangladesh

Faruque Parvez, Gail A. Wasserman, Pam Factor-Litvak, Xinhua Liu, Vesna Slavkovich, Abu B. Siddique, Rebeka Sultana, Ruksana Sultana, Tariqul Islam, Diane Levy, Jacob L. Mey, Alexander van Geen, Khalid Khan, Jennie Kline, Habibul Ahsan, and Joseph H. Graziano

119:1665–1670 (2011) | http://dx.doi.org/10.1289/ehp.1103548

Background: Several reports indicate that drinking water arsenic (WAs) and manganese (WMn) are associated with children's intellectual function. Very little is known, however, about possible associations with other neurologic outcomes such as motor function.

Methods: We investigated the associations of WAs and WMn with motor function in 304 children in Bangladesh, 8–11 years of age. We measured As and Mn concentrations in drinking water, blood, urine, and toenails. We assessed motor function with the Bruininks–Oseretsky test, version 2, in four subscales—fine manual control (FMC), manual coordination (MC), body coordination (BC), and strength and agility—which can be summarized with a total motor composite score (TMC).

Results: Log-transformed blood As was associated with decreases in TMC [$\beta = -3.63$; 95% confidence interval (CI): −6.72, −0.54; $p < 0.01$], FMC ($\beta = -1.68$; 95% CI: −3.19, −0.18; $p < 0.05$), and BC ($\beta = -1.61$; 95% CI: −2.72, −0.51; $p < 0.01$), with adjustment for sex, school attendance, head circumference, mother's intelligence, plasma ferritin, and blood Mn, lead, and selenium. Other measures of As exposure (WAs, urinary As, and toenail As) also were inversely associated with motor function scores, particularly TMC and BC. Square-transformed blood selenium was positively associated with TMC ($\beta = 3.54$; 95% CI: 1.10, 6.0; $p < 0.01$), FMC ($\beta = 1.55$; 95% CI: 0.40, 2.70; $p < 0.005$), and MC ($\beta = 1.57$; 95% CI: 0.60, 2.75; $p < 0.005$) in the unadjusted models. Mn exposure was not significantly associated with motor function.

Conclusion: Our research demonstrates an adverse association of As exposure and a protective association of Se on motor function in children.

Exposures

Associations of Early Childhood Manganese and Lead Coexposure with Neurodevelopment

Birgit Claus Henn, Lourdes Schnaas, Adrienne S. Ettinger, Joel Schwartz, Héctor Lamadrid-Figueroa, Mauricio Hernández-Avila, Chitra Amarasiriwardena, Howard Hu, David C. Bellinger, Robert O. Wright, and Martha María Téllez-Rojo

120:126–131 (2012) | http://dx.doi.org/10.1289/ehp.1003300

Background: Most toxicologic studies focus on a single agent, although this does not reflect real-world scenarios in which humans are exposed to multiple chemicals.

Objectives: We prospectively studied manganese–lead interactions in early childhood to examine whether manganese–lead coexposure is associated with neurodevelopmental deficiencies that are more severe than expected based on effects of exposure to each metal alone.

Methods: Four hundred fifty-five children were enrolled at birth in an longitudinal cohort study in Mexico City, provided blood samples, and were followed until 36 months of age. We measured lead and manganese at 12 and 24 months and assessed neurodevelopment at 6-month intervals from 12 to 36 months of age using Bayley Scales of Infant Development–II.

Results: Mean (± SD) blood concentrations at 12 and 24 months were, respectively, 24.7 ± 5.9 μg/L and 21.5 ± 7.4 μg/L for manganese and 5.1 ± 2.6 μg/dL and 5.0 ± 2.9 μg/dL for lead. Mixed-effects models, including Bayley scores at five time points, showed a significant interaction over time: highest manganese quintile × continuous lead; mental development score, β = –1.27 [95% confidence interval (CI): –2.18, –0.37]; psychomotor development score, β = –0.92 (95% CI: –1.76, –0.09). Slopes for the estimated 12-month lead effect on 18-month mental development and 24- through 36-month psychomotor development scores were steeper for children with high manganese than for children with midrange manganese levels.

Conclusions: We observed evidence of synergism between lead and manganese, whereby lead toxicity was increased among children with high manganese coexposure. Findings highlight the importance of understanding health effects of mixed exposures, particularly during potentially sensitive developmental stages such as early childhood.

▾ NEWS | SCIENCE SELECTION

Mixed Metals Toxicity: More than the Sum of Its Parts?
Angela Spivey | 120:A35
http://dx.doi.org/10.1289/ehp.120-a35b

Rochester's Lead Law: Evaluation of a Local Environmental Health Policy Innovation

Katrina Smith Korfmacher, Maria Ayoob, and Rebecca Morley

120:309–315 (2012) | http://dx.doi.org/10.1289/ehp.1103606

Background: Significant progress has been made in reducing the incidence of childhood lead poisoning in the United States in the past three decades. However, the prevalence of elevated blood lead in children (≥ 10 μg/dL) remains high in some communities, particularly those with high proportions of pre-1978 housing in poor condition. Increasingly, municipalities are using local policy tools to reduce lead poisoning in high-risk areas, but little is known about the effectiveness of such policies.

Objectives: In this article, we evaluated the effectiveness of a comprehensive rental housing–based lead law adopted in Rochester, New York, in 2005.

Methods: This policy evaluation integrates analyses of city inspections data, a survey of landlords, landlord focus groups, and health department data on children's blood lead levels from the first 4 years of implementation of the 2005 law.

Results: Implementation has proceeded consistent with projected numbers of inspections with nearly all target units inspected in the first 4 years. Higher than expected inspection passage rates suggest that landlords have reduced lead hazards in rental housing affected by the law. Implementation of the lead law does not appear to have had a significant impact on the housing market.

Conclusions: Although many uncertainties remain, our analysis suggests that the lead law has had a positive impact on children's health. Strong enforcement, support for community-based lead programs, and ongoing intergovernmental coordination will be necessary to maintain lead-safe housing in Rochester. Lessons learned from the Rochester experience may inform future local lead poisoning prevention policies in other communities.

Exposures

Association between Prenatal Lead Exposure and Blood Pressure in Children

Aimin Zhang, Howard Hu, Brisa N. Sánchez, Adrienne S. Ettinger, Sung Kyun Park, David Cantonwine, Lourdes Schnaas, Robert O. Wright, Hector Lamadrid-Figueroa, and Martha Maria Tellez-Rojo

120:445–450 (2012) | http://dx.doi.org/10.1289/ehp.1103736

Background: Lead exposure in adults is associated with hypertension. Altered prenatal nutrition is associated with subsequent risks of adult hypertension, but little is known about whether prenatal exposure to toxicants, such as lead, may also confer such risks.

Objectives: We investigated the relationship of prenatal lead exposure and blood pressure (BP) in 7- to 15-year-old boys and girls.

Methods: We evaluated 457 mother–child pairs, originally recruited for an environmental birth cohort study between 1994 and 2003 in Mexico City, at a follow-up visit in 2008–2010. Prenatal lead exposure was assessed by measurement of maternal tibia and patella lead using *in vivo* K-shell X-ray fluorescence and cord blood lead using atomic absorption spectrometry. BP was measured by mercury sphygmomanometer with appropriate-size cuffs.

Results: Adjusting for relevant covariates, maternal tibia lead was significantly associated with increases in systolic BP (SBP) and diastolic BP (DBP) in girls but not in boys (*p*-interaction with sex = 0.025 and 0.007 for SBP and DBP, respectively). Among girls, an interquartile range increase in tibia lead (13 μg/g) was associated with 2.11-mmHg [95% confidence interval (CI): 0.69, 3.52] and 1.60-mmHg (95% CI: 0.28, 2.91) increases in SBP and DBP, respectively. Neither patella nor cord lead was associated with child BP.

Conclusions: Maternal tibia lead, which reflects cumulative environmental lead exposure and a source of exposure to the fetus, is a predisposing factor to higher BP in girls but not boys. Sex-specific adaptive responses to lead toxicity during early-life development may explain these differences.

Outbreak of Fatal Childhood Lead Poisoning Related to Artisanal Gold Mining in Northwestern Nigeria, 2010

Carrie A. Dooyema, Antonio Neri, Yi-Chun Lo, James Durant, Paul I. Dargan, Todd Swarthout, Oladayo Biya, Saheed O. Gidado, Suleiman Haladu, Nasir Sani-Gwarzo, Patrick M. Nguku, Henry Akpan, Sa'ad Idris, Abdullahi M. Bashir, and Mary Jean Brown

120:601–607 (2012) | http://dx.doi.org/10.1289/ehp.1103965

Background: In May 2010, a team of national and international organizations was assembled to investigate children's deaths due to lead poisoning in villages in northwestern Nigeria.

Objectives: Our goal was to determine the cause of the childhood lead poisoning outbreak, investigate risk factors for child mortality, and identify children < 5 years of age in need of emergency chelation therapy for lead poisoning.

Methods: We administered a cross-sectional, door-to-door questionnaire in two affected villages, collected blood from children 2–59 months of age, and obtained soil samples from family compounds. Descriptive and bivariate analyses were performed with survey, blood lead, and environmental data. Multivariate logistic regression techniques were used to determine risk factors for childhood mortality.

Results: We surveyed 119 family compounds. Of 463 children < 5 years of age, 118 (25%) had died in the previous year. We tested 59% (204/345) of children < 5 years of age, and all were lead poisoned (≥ 10 μg/dL); 97% (198/204) of children had blood lead levels (BLLs) ≥ 45 μg/dL, the threshold for initiating chelation therapy. Gold ore was processed inside two-thirds of the family compounds surveyed. In multivariate modeling, significant risk factors for death in the previous year from suspected lead poisoning included the age of the child, the mother's work at ore-processing activities, community well as primary water source, and the soil lead concentration in the compound.

Conclusion: The high levels of environmental contamination, percentage of children < 5 years of age with elevated BLLs (97%, > 45 μg/dL), and incidence of convulsions among children before death (82%) suggest that most of the recent childhood deaths in the two surveyed villages were caused by acute lead poisoning from gold ore–processing activities. Control measures included environmental remediation, chelation therapy, public health education, and control of mining activities.

▾ NEWS | SCIENCE SELECTION

Massive Childhood Lead Poisoning: The Price of Nigerian Gold
Adrian Burton | 120:A165
http://dx.doi.org/10.1289/ehp.120-a165a

Exposures

Evidence on the Human Health Effects of Low-Level Methylmercury Exposure

Margaret R. Karagas, Anna L. Choi, Emily Oken, Milena Horvat, Rita Schoeny, Elizabeth Kamai, Whitney Cowell, Philippe Grandjean, and Susan Korrick

120:799–806 (2012) | http://dx.doi.org/10.1289/ehp.1104494

Background: Methylmercury (MeHg) is a known neurotoxicant. Emerging evidence indicates it may have adverse effects on the neurologic and other body systems at common low levels of exposure. Impacts of MeHg exposure could vary by individual susceptibility or be confounded by beneficial nutrients in fish containing MeHg. Despite its global relevance, synthesis of the available literature on low-level MeHg exposure has been limited.

Objectives: We undertook a synthesis of the current knowledge on the human health effects of low-level MeHg exposure to provide a basis for future research efforts, risk assessment, and exposure remediation policies worldwide.

Data sources and extraction: We reviewed the published literature for original human epidemiologic research articles that reported a direct biomarker of mercury exposure. To focus on high-quality studies and those specifically on low mercury exposure, we excluded case series, as well as studies of populations with unusually high fish consumption (e.g., the Seychelles), marine mammal consumption (e.g., the Faroe Islands, circumpolar, and other indigenous populations), or consumption of highly contaminated fish (e.g., gold-mining regions in the Amazon).

Data synthesis: Recent evidence raises the possibility of effects of low-level MeHg exposure on fetal growth among susceptible subgroups and on infant growth in the first 2 years of life. Low-level effects of MeHg on neurologic outcomes may differ by age, sex, and timing of exposure. No clear pattern has been observed for cardiovascular disease (CVD) risk across populations or for specific CVD end points. For the few studies evaluating immunologic effects associated with MeHg, results have been inconsistent.

Conclusions: Studies targeted at identifying potential mechanisms of low-level MeHg effects and characterizing individual susceptibility, sexual dimorphism, and nonlinearity in dose response would help guide future prevention, policy, and regulatory efforts surrounding MeHg exposure.

World Health Organization Discontinues Its Drinking-Water Guideline for Manganese

Seth H. Frisbie, Erika J. Mitchell, Hannah Dustin, Donald M. Maynard, and Bibudhendra Sarkar

120:775–778 (2012) | http://dx.doi.org/10.1289/ehp.1104693

Background: The World Health Organization (WHO) released the fourth edition of *Guidelines for Drinking-Water Quality* in July 2011. In this edition, the 400-µg/L drinking-water guideline for manganese (Mn) was discontinued with the assertion that because "this health-based value is well above concentrations of manganese normally found in drinking water, it is not considered necessary to derive a formal guideline value."

Objective: In this commentary, we review the WHO guideline for Mn in drinking water—from its introduction in 1958 through its discontinuation in 2011.

Methods: For the primary references, we used the WHO publications that documented the Mn guidelines. We used peer-reviewed journal articles, government reports, published conference proceedings, and theses to identify countries with drinking water or potential drinking-water supplies exceeding 400 µg/L Mn and peer-reviewed journal articles to summarize the health effects of Mn.

Discussion: Drinking water or potential drinking-water supplies with Mn concentrations > 400 µg/L are found in a substantial number of countries worldwide. The drinking water of many tens of millions of people has Mn concentrations > 400 µg/L. Recent research on the health effects of Mn suggests that the earlier WHO guideline of 400 µg/L may have been too high to adequately protect public health.

Conclusions: The toxic effects and geographic distribution of Mn in drinking-water supplies justify a reevaluation by the WHO of its decision to discontinue its drinking-water guideline for Mn.

Pre- and Postnatal Arsenic Exposure and Body Size to 2 Years of Age: A Cohort Study in Rural Bangladesh

Kuntal K. Saha, Annette Engström, Jena Derakhshani Hamadani, Fahmida Tofail, Kathleen M. Rasmussen, and Marie Vahter

120:1208–1214 (2012) | http://dx.doi.org/10.1289/ehp.1003378

Background: Exposure to arsenic via drinking water has been associated with adverse pregnancy outcomes and infant morbidity and mortality. Little is known, however, about the effects of arsenic on child growth.

Objective: We assessed potential effects of early-life arsenic exposure on weight and length of children from birth to 2 years of age.

Methods: We followed 2,372 infants born in a population-based intervention trial in rural Bangladesh. Exposure was assessed by arsenic concentrations in urine (U-As) of mothers (gestational weeks 8 and 30) and children (18 months old). Child anthropometry was measured monthly in the first year and quarterly in the second. Linear regression models were used to examine associations of U-As (by quintiles) with child weight and length, adjusted for age, maternal body mass index, socioeconomic status, and sex (or stratified by sex).

Results: Median (10th–90th percentiles) U-As concentrations were about 80 (25–400) µg/L in the mothers and 34 (12–159) µg/L in the children. Inverse associations of maternal U-As with child's attained weight and length at 3–24 months were markedly attenuated after adjustment. However, associations of U-As at 18 months with weight and length at 18–24 months were more robust, particularly in girls. Compared with girls in the first quintile of U-As (< 16 µg/L), those in the fourth quintile (26–46 µg/L) were almost 300 g lighter and 0.7 cm shorter, and had adjusted odds ratios (95% confidence interval) for underweight and stunting of 1.57 (1.02–2.40) and 1.58 (1.05–2.37), respectively, at 21 months.

Conclusions: Postnatal arsenic exposure was associated with lower body weight and length among girls, but not boys.

RELATED ARTICLES

NEWS | CDC Updates Guidelines for Children's Lead Exposure

Kellyn S. Betts | 120:A268
http://dx.doi.org/10.1289/ehp.120-a268

EDITORIAL | Methylmercury Effects and Exposures: Who Is at Risk?

Celia Chen | 120:A224–A225
http://dx.doi.org/10.1289/ehp.1205357

NEWS | Why Is It So Difficult to Choose Safer Alternatives for Hazardous Chemicals?

Valerie J. Brown | 120:A280–A283
http://dx.doi.org/10.1289/ehp.120-a280

PESTICIDES AND OTHER CHEMICALS/COMPOUNDS (E.G., BPA, PCBS, PBDES, PFCS, PHTHALATES, ENDOCRINE DISRUPTORS)

Relationship between Urinary Phthalate and Bisphenol A Concentrations and Serum Thyroid Measures in U.S. Adults and Adolescents from the National Health and Nutrition Examination Survey (NHANES) 2007–2008

John D. Meeker, Kelly K. Ferguson

119:1396–1402 (2011) | http://dx.doi.org/10.1289/ehp.1103582

Background: Limited animal, *in vitro*, and human studies have reported that exposure to phthalates or bisphenol A (BPA) may affect thyroid signaling.

Objective: We explored the cross-sectional relationship between urinary concentrations of metabolites of di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), and BPA with a panel of serum thyroid measures among a representative sample of U.S. adults and adolescents.

Methods: We analyzed data on urinary biomarkers of exposure to phthalates and BPA, serum thyroid measures, and important covariates from 1,346 adults (ages ≥ 20 years) and 329 adolescents (ages 12–19 years) from the National Health and Nutrition Examination Survey (NHANES) 2007–2008 using multivariable linear regression.

Results: Among adults, we observed significant inverse relationships between urinary DEHP metabolites and total thyroxine (T_4), free T_4, total triiodothyronine (T_3), and thyroglobulin, and positive relationships with thyroid-stimulating hormone (TSH). The strongest and most consistent relationships involved total T_4, where adjusted regression coefficients for quintiles of oxidative DEHP metabolites displayed monotonic dose-dependent decreases in total T_4 (p-value for trend < 0.0001). Suggestive inverse relationships between urinary BPA and total T_4 and TSH were also observed. Conversely, among adolescents, we observed significant positive relationships between DEHP metabolites and total T_3. Mono(3-carboxypropyl) phthalate, a secondary metabolite of both DBP and di-*n*-octyl phthalate, was associated with several thyroid measures in both age groups, whereas other DBP metabolites were not associated with thyroid measures.

Conclusions: These results support previous reports of associations between phthalates—and possibly BPA—and altered thyroid hormones. More detailed studies are needed to determine the temporal relationships and potential clinical and public health implications of these associations.

A Comparison of PBDE Serum Concentrations in Mexican and Mexican-American Children Living in California

Brenda Eskenazi, Laura Fenster, Rosemary Castorina, Amy R. Marks, Andreas Sjödin, Lisa Goldman Rosas, Nina Holland, Armando Garcia Guerra, Lizbeth Lopez-Carillo, and Asa Bradman

119:1442–1448 (2011) | http://dx.doi.org/10.1289/ehp.1002874

Background: Polybrominated diphenyl ethers (PBDE), which are used as flame retardants, have been found to be higher in residents of California than of other parts of the United States.

Objectives: We aimed to investigate the role of immigration to California on PBDE levels in Latino children.

Methods: We compared serum PBDE concentrations in a population of first-generation Mexican-American 7-year-old children (n = 264), who were born and raised in California [Center for Health Analysis of Mothers and Children of Salinas (CHAMACOS) study], with 5-year-old Mexican children (n = 283), who were raised in the states in Mexico where most CHAMACOS mothers had originated (Proyecto Mariposa).

Results: On average, PBDE serum concentrations in the California Mexican-American children were three times higher than their mothers' levels during pregnancy and seven times higher than concentrations in the children living in Mexico. The PBDE serum concentrations were higher in the Mexican-American children regardless of length of time their mother had resided in California or the duration of the child's breast-feeding. These data suggest that PBDE serum concentrations in these children resulted primarily from postnatal exposure.

Conclusions: Latino children living in California have much higher PBDE serum levels than their Mexican counterparts. Given the growing evidence documenting potential health effects of PBDE exposure, the levels in young children noted in this study potentially present a major public health challenge, especially in California. In addition, as PBDEs are being phased out and replaced by other flame retardants, the health consequences of these chemical replacements should be investigated and weighed against their purported fire safety benefits.

NEWS | SCIENCE SELECTION

Children's Exposure to PBDEs: Binational Comparison Highlights Dramatic Differences

Kellyn S. Betts | 119:A442

http://dx.doi.org/10.1289/ehp.119-a442a

Associations between Polybrominated Diphenyl Ether (PBDE) Flame Retardants, Phenolic Metabolites, and Thyroid Hormones during Pregnancy

Heather M. Stapleton, Sarah Eagle, Rebecca Anthopolos, Amy Wolkin, and Marie Lynn Miranda

119:1454–1459 (2011) | http://dx.doi.org/10.1289/ehp.1003235

Background: Polybrominated diphenyl ethers (PBDEs) are chemical additives used as flame retardants in commercial products. PBDEs are bioaccumulative and persistent and have been linked to several adverse health outcomes.

Objectives: This study leverages an ongoing pregnancy cohort to measure PBDEs and PBDE metabolites in serum collected from an understudied population of pregnant women late in their third trimester. A secondary objective was to determine whether the PBDEs or their metabolites were associated with maternal thyroid hormones.

Methods: One hundred forty pregnant women > 34 weeks into their pregnancy were recruited into this study between 2008 and 2010. Blood samples were collected during a routine prenatal clinic visit. Serum was analyzed for a suite of PBDEs, three phenolic metabolites (i.e., containing an –OH moiety), and five thyroid hormones.

Results: PBDEs were detected in all samples and ranged from 3.6 to 694 ng/g lipid. Two hydroxylated BDE congeners (4′-OH-BDE 49 and 6-OH-BDE 47) were detected in > 67% of the samples. BDEs 47, 99, and 100 were significantly and positively associated with free and total thyroxine (T_4) levels and with total triiodothyronine levels above the normal range. Associations between T_4 and PBDEs remained after controlling for smoking status, maternal age, race, gestational age, and parity.

Conclusions: PBDEs and OH-BDEs are prevalent in this cohort, and levels are similar to those in the general population. Given their long half-lives, PBDEs may be affecting thyroid regulation throughout pregnancy. Further research is warranted to determine mechanisms through which PBDEs affect thyroid hormone levels in developing fetuses and newborn babies.

Prenatal Exposure to Phthalates and Infant Development at 6 Months: Prospective Mothers and Children's Environmental Health (MOCEH) Study

Yeni Kim, Eun–Hee Ha, Eui–Jung Kim, Hyesook Park, Mina Ha, Ja–Hyeong Kim, Yun–Chul Hong, Namsoo Chang, and Bung–Nyun Kim

119:1495–1500 (2011) | http://dx.doi.org/10.1289/ehp.1003178

Background: There are increasing concerns over adverse effects of prenatal phthalate exposure on the neurodevelopment of infants.

Objectives: Our goal was to explore the association between prenatal di(2-ethylhexyl) phthalate and dibutyl phthalate exposure and the Mental and Psychomotor Developmental Indices (MDI and PDI, respectively) of the Bayley Scales of Infant Development at 6 months, as part of the Mothers and Children's Environmental Health Study.

Methods: Between 2006 and 2009, 460 mother–infant pairs from Seoul, Cheonan, and Ulsan, Korea, participated. Prenatal mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-*n*-butyl phthalate (MBP) were measured in one urine sample acquired from each mother during the third trimester of pregnancy. Associations with log-transformed creatinine-corrected phthalate concentrations were estimated using linear regression models adjusted for potential confounders.

Results: MDI was inversely associated with the natural log concentrations (micrograms per gram creatinine) of MEHHP [β = –0.97; 95% confidence interval (CI), –1.85 to –0.08] and MEOHP (β = –0.95; CI, –1.87 to –0.03), and PDI was inversely associated with MEHHP (β = –1.20; CI, –2.33 to –0.08). In males, MDI was inversely associated with MEHHP (β = –1.46; CI, –2.70 to –0.22), MEOHP (β = –1.57; CI, –2.87 to –0.28), and MBP (β = –0.93; CI, –1.82 to –0.05); PDI was inversely associated with MEHHP (β = –2.36; CI, –3.94 to –0.79), MEOHP (β = –2.05; CI, –3.71 to –0.39), and MBP (β = –1.25; CI, –2.40 to –0.11). No significant linear associations were observed for females.

Conclusions: The results suggest that prenatal exposure to phthalates may be inversely associated with the MDI and PDI of infants, particularly males, at 6 months.

Exposures

Isomer Profiles of Perfluorochemicals in Matched Maternal, Cord, and House Dust Samples: Manufacturing Sources and Transplacental Transfer

Sanjay Beesoon, Glenys M. Webster, Mahiba Shoeib, Tom Harner, Jonathan P. Benskin, and Jonathan W. Martin

119:1659–1664 (2011) | http://dx.doi.org/10.1289/ehp.1003265

Background: Perfluorochemicals (PFCs) are detectable in the general population and in the human environment, including house dust. Sources are not well characterized, but isomer patterns should enable differentiation of historical and contemporary manufacturing sources. Isomer-specific maternal–fetal transfer of PFCs has not been examined despite known developmental toxicity of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in rodents.

Objectives: We elucidated relative contributions of electrochemical (phased out in 2001) and telomer (contemporary) PFCs in dust and measured how transplacental transfer efficiency (TTE; based on a comparison of maternal and cord sera concentrations) is affected by perfluorinated chain length and isomer branching pattern.

Methods: We analyzed matching samples of house dust ($n = 18$), maternal sera ($n = 20$), and umbilical cord sera ($n = 20$) by isomer-specific high-performance liquid chromatography tandem mass spectrometry.

Results: PFOA isomer signatures revealed that telomer sources accounted for 0–95% of total PFOA in house dust (median, 31%). This may partly explain why serum PFOA concentrations are not declining in some countries despite the phase-out of electrochemical PFOA. TTE data indicate that total branched isomers crossed the placenta more efficiently than did linear isomers for both PFOS ($p < 0.01$) and PFOA ($p = 0.02$) and that placental transfer of branched isomers of PFOS increased as the branching point moved closer to the sulfonate (SO_3–) end of the molecule.

Conclusions: Results suggest that humans are exposed to telomer PFOA, but larger studies that also account for dietary sources should be conducted. The exposure profile of PFOS and PFOA isomers can differ between the mother and fetus—an important consideration for perinatal epidemiology studies of PFCs.

Serum Concentrations of Organochlorine Pesticides and Growth among Russian Boys

Jane S. Burns, Paige L. Williams, Oleg Sergeyev, Susan A. Korrick, Mary M. Lee, Boris Revich, Larisa Altshul, Julie T. Del Prato, Olivier Humblet, Donald G. Patterson Jr., Wayman E. Turner, Mikhail Starovoytov, and Russ Hauser

120:303–308 (2012) | http://dx.doi.org/10.1289/ehp.1103743

Background: Limited human data suggest an association of organochlorine pesticides (OCPs) with adverse effects on children's growth.

Objective: We evaluated the associations of OCPs with longitudinally assessed growth among peripubertal boys from a Russian cohort with high environmental OCP levels.

Methods: A cohort of 499 boys enrolled in the Russian Children's Study between 2003 and 2005 at 8–9 years of age were followed prospectively for 4 years. At study entry, 350 boys had serum OCPs measured. Physical examinations were conducted at entry and annually. The longitudinal associations of serum OCPs with annual measurements of body mass index (BMI), height, and height velocity were examined by multivariate mixed-effects regression models for repeated measures, controlling for potential confounders.

Results: Among the 350 boys with OCP measurements, median serum hexachlorobenzene (HCB), β-hexachlorocyclohexane (βHCH), and *p,p´*-dichlorodiphenyldichloroethylene (*p,p´*-DDE) concentrations were 159 ng/g lipid, 168 ng/g lipid, and 287 ng/g lipid, respectively. Age-adjusted BMI and height *z*-scores generally fell within the normal range per World Health Organization standards at entry and during follow-up. However, in adjusted models, boys with higher serum HCB, βHCH, and *p,p´*-DDE had significantly lower mean [95% confidence interval (CI)] BMI *z*-scores, by –0.84 (–1.23, –0.46), –1.32 (–1.70, –0.95), and –1.37 (–1.75, –0.98), respectively, for the highest versus lowest quintile. In addition, the highest quintile of *p,p´*-DDE was associated with a significantly lower mean (95% CI) height *z*-score, by –0.69 (–1.00, –0.39) than that of the lowest quintile.

Conclusions: Serum OCP concentrations measured at 8–9 years of age were associated with reduced growth, particularly reduced BMI, during the peripubertal period, which may affect attainment of optimal adult body mass and height.

Exposures

Association of Hexachlorobenzene (HCB), Dichlorodiphenyltrichloroethane (DDT), and Dichlorodiphenyldichloroethylene (DDE) with *in Vitro* Fertilization (IVF) Outcomes

Shruthi Mahalingaiah, Stacey A. Missmer, Arnab Maity, Paige L. Williams, John D. Meeker, Katharine Berry, Shelley Ehrlich, Melissa J. Perry, Daniel W. Cramer, and Russ Hauser

120:316–320 (2012) | http://dx.doi.org/10.1289/ehp.1103696

Background: Hexachlorobenzene (HCB), dichlorodiphenyltrichloroethane (DDT), and dichlorodiphenyldichloroethylene (DDE) are persistent chlorinated pesticides with endocrine activity that may adversely affect the early stages of human reproduction.

Objective: Our goal was to determine the association of serum levels of HCB, DDT, and DDE with implantation failure, chemical pregnancy, and spontaneous abortion in women undergoing *in vitro* fertilization (IVF) from 1994 to 2003.

Methods: Levels of HCB and congeners of DDT and DDE were measured in serum collected during the follicular phase. Multivariable-adjusted statistical models accommodating multiple outcomes and multiple cycles per woman were used to estimate the relation between serum pesticide levels and IVF outcomes.

Results: A total of 720 women with a mean ± SD age 35.4 ± 4.2 years at enrollment contributed 774 IVF cycles. All samples had detectable levels of HCB, DDT, and DDE, with median levels of 0.087 ng/g serum for HCB, 1.12 ng/g serum for total DDT, and 1.04 ng/g serum for *p,p´*-DDE. Compared with the lowest quartile (Q1) of HCB, the lipid- and multivariable-adjusted odds ratio (OR) for failed implantation was significantly elevated for those with higher HCB quartiles [Q2–Q4; adjusted ORs: for Q2, 1.71; 95% confidence interval (CI): 1.03, 2.82; for Q3, 2.30; 95% CI: 1.39, 3.81; for Q4, 2.32; 95% CI: 1.38, 3.90] and showed a significantly increasing trend ($p = 0.001$). No statistically significant associations were observed between DDT/DDE and IVF outcomes or between HCB and chemical pregnancy or spontaneous abortion.

Conclusions: Serum HCB concentrations were on average lower than that of the general U.S. population and associated with failed implantation among women undergoing IVF.

Polyfluoroalkyl Compounds in Texas Children from Birth through 12 Years of Age

Arnold Schecter, Noor Malik-Bass, Antonia M. Calafat, Kayoko Kato, Justin A. Colacino, Tyra L. Gent, Linda S. Hynan, T. Robert Harris, Sunitha Malla, and Linda Birnbaum

120:590–594 (2012) | http://dx.doi.org/10.1289/ehp.1104325

Background: For > 50 years, polyfluoroalkyl compounds (PFCs) have been used worldwide, mainly as surfactants and emulsifiers, and human exposure to some PFCs is widespread.

Objectives: Our goal was to report PFC serum concentrations from a convenience sample of Dallas, Texas, children from birth to < 13 years of age, and to examine age and sex differences in PFC concentrations.

Methods: We analyzed 300 serum samples collected in 2009 for eight PFCs by online solid phase extraction–high performance liquid chromatography–isotope dilution–tandem mass spectrometry.

Results: Perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA) were detected in > 92% of participants; the other PFCs measured were detected less frequently. Overall median concentrations of PFOS (4.1 ng/mL) were higher than those for PFOA (2.85 ng/mL), PFNA (1.2 ng/mL), and PFHxS (1.2 ng/mL). For PFOS, PFOA, PFNA, and PFHxS, we found no significant differences ($p < 0.05$) by sex, significantly increasing concentrations for all four chemicals by age, and significantly positive correlations between all four compounds.

Conclusions: We found no significant differences in the serum concentrations of PFOS, PFOA, PFNA, and PFHxS by sex, but increasing concentrations with age. Our results suggest that these 300 Texas children from birth through 12 years of age continued to be exposed to several PFCs in late 2009, years after changes in production of some PFCs in the United States.

Exposures

Pre- and Postnatal Polychlorinated Biphenyl Concentrations and Longitudinal Measures of Thymus Volume in Infants

Todd A. Jusko, Dean Sonneborn, Lubica Palkovicova, Anton Kocan, Beata Drobna, Tomas Trnovec, and Irva Hertz-Picciotto

120:595–600 (2012) | http://dx.doi.org/10.1289/ehp.1104229

Background: Previously, we reported an association between higher maternal polychlorinated biphenyl (PCB) concentrations and smaller thymus volume in newborns in a birth cohort residing in eastern Slovakia.

Objective: In the present report we address whether thymus volume at later ages is influenced by prenatal and early postnatal PCB exposure.

Methods: At the time of delivery, 1,134 mother–infant pairs were enrolled. Maternal and 6- and 16-month infant blood samples were collected and analyzed for 15 PCB congeners. Thymus volume was measured in infants shortly after birth and at ages 6 and 16 months using ultrasonography.

Results: Higher maternal PCB concentration was associated with reduced thymus volume at birth [a 0.21 SD reduction in thymus volume for an increase in total maternal PCB concentration from the 10th to the 90th percentile; 95% confidence interval (CI): −0.37, −0.05], whereas maternal PCB concentration was not predictive of 6- and 16-month thymus volume. Six-month infant PCB concentration was associated with a 0.40 SD decrease in 6-month thymus volume (95% CI: −0.76, −0.04). There was also some suggestion that thymus volume at 16 months was positively associated with concurrent infant PCB concentration.

Conclusions: The potential adverse effects of *in utero* PCB exposure on thymic development may extend beyond the neonatal period. Results from this highly exposed cohort provide suggestive evidence that postnatal PCB concentrations may be influential, but a smaller set of 6-month PCB measurements limited statistical power at that time point. Implications regarding impaired immunologic maturation or long-term clinical implications remain to be determined.

Variability of Urinary Phthalate Metabolite and Bisphenol A Concentrations before and during Pregnancy

Joe M. Braun, Kristen W. Smith, Paige L. Williams, Antonia M. Calafat, Katharine Berry, Shelley Ehrlich, and Russ Hauser

120:739–745 (2012) | http://dx.doi.org/10.1289/ehp.1104139

Background: Gestational phthalate and bisphenol A (BPA) exposure may increase the risk of adverse maternal/child health outcomes, but there are few data on the variability of urinary biomarkers before and during pregnancy.

Objective: We characterized the variability of urinary phthalate metabolite and BPA concentrations before and during pregnancy and the ability of a single spot urine sample to classify average gestational exposure.

Methods: We collected 1,001 urine samples before and during pregnancy from 137 women who were partners in couples attending a Boston fertility clinic and who had a live birth. Women provided spot urine samples before ($n \geq 2$) and during ($n \geq 2$) pregnancy. We measured urinary concentrations of monoethyl phthalate (MEP), mono-*n*-butyl phthalate (MBP), mono-iso-butyl phthalate, monobenzyl phthalate (MBzP), four metabolites of di-(2-ethylhexyl) phthalate (DEHP), and BPA. After adjusting for specific gravity, we characterized biomarker variability using intraclass correlation coefficients (ICCs) and conducted several surrogate category analyses to determine whether a single spot urine sample could adequately classify average gestational exposure.

Results: Absolute concentrations of phthalate metabolites and BPA were similar before and during pregnancy. Variability was higher during pregnancy than before pregnancy for BPA and MBzP, but similar during and before pregnancy for MBP, MEP, and ÓDEHP. During pregnancy, MEP (ICC = 0.50) and MBP (ICC = 0.45) were less variable than BPA (ICC = 0.12), MBzP (ICC = 0.25), and ÓDEHP metabolites (ICC = 0.08). Surrogate analyses suggested that a single spot urine sample may reasonably classify MEP and MBP concentrations during pregnancy, but more than one sample may be necessary for MBzP, DEHP, and BPA.

Conclusions: Urinary phthalate metabolites and BPA concentrations were variable before and during pregnancy, but the magnitude of variability was biomarker specific. A single spot urine sample adequately classified MBP and MEP concentrations during pregnancy. The present results may be related to unique features of the women studied, and replication in other pregnancy cohorts is recommended.

Exposures

Relationships of Perfluorooctanoate and Perfluorooctane Sulfonate Serum Concentrations between Mother–Child Pairs in a Population with Perfluorooctanoate Exposure from Drinking Water

Debapriya Mondal, Maria-Jose Lopez-Espinosa, Ben Armstrong, Cheryl R. Stein, and Tony Fletcher

120:752–757 (2012) | http://dx.doi.org/10.1289/ehp.1104538

Background: There are limited data on the associations between maternal or newborn and child exposure to perfluoroalkyl acids (PFAAs), including perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS). This study provides an opportunity to assess the association between PFAA concentrations in mother–child pairs in a population exposed to PFOA via drinking water.

Objectives: We aimed to determine the relationship between mother–child PFAA serum concentrations and to examine how the child:mother ratio varies with child's age, child's sex, drinking-water PFOA concentration, reported bottled water use, and mother's breast-feeding intention.

Methods: We studied 4,943 mother–child pairs (children, 1–19 years of age). The child:mother PFAA ratio was stratified by possible determinants. Results are summarized as geometric mean ratios and correlation coefficients between mother–child pairs, overall and within strata.

Results: Child and mother PFOA and PFOS concentrations were correlated ($r = 0.82$ and 0.26, respectively). Up to about 12 years of age, children had higher serum PFOA concentrations than did their mothers. The highest child:mother PFOA ratio was found among children ≤ 5 years (44% higher than their mothers), which we attribute to *in utero* exposure and to exposure via breast milk and drinking water. Higher PFOS concentrations in children persisted until at least 19 years of age (42% higher than their mothers). Boys > 5 years of age had significantly higher PFOA and PFOS child:mother ratios than did girls.

Conclusion: Concentrations of both PFOA and PFOS tended to be higher in children than in their mothers. This difference persisted until they were about 12 years of age for PFOA and at least 19 years of age for PFOS.

Phthalates and Perfluorooctanesulfonic Acid in Human Amniotic Fluid: Temporal Trends and Timing of Amniocentesis in Pregnancy

Morten Søndergaard Jensen, Bent Nørgaard-Pedersen, Gunnar Toft, David M. Hougaard, Jens Peter Bonde, Arieh Cohen, Ane Marie Thulstrup, Richard Ivell, Ravinder Anand-Ivell, Christian H. Lindh, and Bo A.G. Jönsson

120:897–903 (2012) | http://dx.doi.org/10.1289/ehp.1104522

Background: Measures of prenatal environmental exposures are important, and amniotic fluid levels may directly reflect fetal exposures during hypothesized windows of vulnerability.

Objectives: We aimed to detect various phthalate metabolites and perfluorooctanesulfonic acid (PFOS) in human amniotic fluid, to study temporal exposure trends, and to estimate potential associations with gestational week of amniocentesis and maternal age and parity at amniocentesis.

Methods: We studied 300 randomly selected second-trimester amniotic fluid samples from a Danish pregnancy-screening biobank covering 1980 through 1996. We used only samples from male offspring pregnancies. We assayed the environmental pollutants by liquid chromatography/triple quadrupole mass spectrometry and analyzed data using generalized linear regression models.

Results: We detected the di(2-ethylhexyl) phthalate (DEHP) metabolite mono(2-ethyl-5-carboxypentyl) phthalate (5cx-MEPP) at a median concentration of 0.27 ng/mL [interquartile range (IQR): 0.20–0.37 ng/mL], the diisononyl phthalate (DiNP) metabolite mono(4-methyl-7-carboxyheptyl) phthalate (7cx-MMeHP) at 0.07 ng/mL (IQR: 0.05–0.11 ng/mL), and PFOS at 1.1 ng/mL (IQR: 0.66–1.60 ng/mL). An increase of 1 calendar year was associated with 3.5% lower [95% confidence interval (CI): –4.8%, –2.1%] 5cx-MEPP levels and with 7.1% higher (95% CI: 5.3%, 9.0%) 7cx-MMeHP levels. For each later gestational week of amniocentesis, 5cx-MEPP was 9.9% higher (95% CI: 4.8%, 15.2%), 7cx-MMeHP was 8.6% higher (95: CI: 2.7%, 14.9%), and PFOS was 9.4% higher (95: CI: 3.3%, 15.9%). We observed no associations with maternal age or parity.

Conclusions: Measured metabolite levels appeared to parallel decreasing DEHP exposure and increasing DiNP exposure during the study period. The environmental pollutant levels were positively associated with later gestational age at amniocentesis during pregnancy weeks 12–22.

Exposures

Prenatal Exposure to Bisphenol A and Child Wheeze from Birth to 3 Years of Age

Adam J. Spanier, Robert S. Kahn, Allen R. Kunselman, Richard Hornung, Yingying Xu, Antonia M. Calafat, and Bruce P. Lanphear

120:916–920 (2012) | http://dx.doi.org/10.1289/ehp.1104175

Background: Bisphenol A (BPA), an endocrine-disrupting chemical that is routinely detected in > 90% of Americans, promotes experimental asthma in mice. The association of prenatal BPA exposure and wheeze has not been evaluated in humans.

Objective: We examined the relationship between prenatal BPA exposure and wheeze in early childhood.

Methods: We measured BPA concentrations in serial maternal urine samples from a prospective birth cohort of 398 mother–infant pairs and assessed parent-reported child wheeze every 6 months for 3 years. We used generalized estimating equations with a logit link to evaluate the association of prenatal urinary BPA concentration with the dichotomous outcome wheeze (wheeze over the previous 6 months).

Results: Data were available for 365 children; BPA was detected in 99% of maternal urine samples during pregnancy. In multivariable analysis, a one-unit increase in log-transformed creatinine-standardized mean prenatal urinary BPA concentration was not significantly associated with child wheeze from birth to 3 years of age, but there was an interaction of BPA concentration with time ($p = 0.003$). Mean prenatal BPA above versus below the median was positively associated with wheeze at 6 months of age [adjusted odds ratio (AOR) = 2.3; 95% confidence interval (CI): 1.3, 4.1] but not at 3 years (AOR = 0.6; 95% CI: 0.3, 1.1). In secondary analyses evaluating associations of each prenatal BPA concentration separately, urinary BPA concentrations measured at 16 weeks gestation were associated with wheeze (AOR = 1.2; 95% CI: 1.0, 1.5), but BPA concentrations at 26 weeks of gestation or at birth were not.

Conclusions: Mean prenatal BPA was associated with increased odds of wheeze in early life, and the effect diminished over time. Evaluating exposure at each prenatal time point demonstrated an association between wheeze from 6 months to 3 years and log-transformed BPA concentration at 16 weeks gestation only.

Endocrine Disruptors and Asthma-Associated Chemicals in Consumer Products

Robin E. Dodson, Marcia Nishioka, Laurel J. Standley, Laura J. Perovich, Julia Green Brody, and Ruthann A. Rudel

120:935–943 (2012) | http://dx.doi.org/10.1289/ehp.1104052

Background: Laboratory and human studies raise concerns about endocrine disruption and asthma resulting from exposure to chemicals in consumer products. Limited labeling or testing information is available to evaluate products as exposure sources.

Objectives: We analytically quantified endocrine disruptors and asthma-related chemicals in a range of cosmetics, personal care products, cleaners, sunscreens, and vinyl products. We also evaluated whether product labels provide information that can be used to select products without these chemicals.

Methods: We selected 213 commercial products representing 50 product types. We tested 42 composited samples of high-market-share products, and we tested 43 alternative products identified using criteria expected to minimize target compounds. Analytes included parabens, phthalates, bisphenol A (BPA), triclosan, ethanolamines, alkylphenols, fragrances, glycol ethers, cyclosiloxanes, and ultraviolet (UV) filters.

Results: We detected 55 compounds, indicating a wide range of exposures from common products. Vinyl products contained > 10% bis(2-ethylhexyl) phthalate (DEHP) and could be an important source of DEHP in homes. In other products, the highest concentrations and numbers of detects were in the fragranced products (e.g., perfume, air fresheners, and dryer sheets) and in sunscreens. Some products that did not contain the well-known endocrine-disrupting phthalates contained other less-studied phthalates (dicyclohexyl phthalate, diisononyl phthalate, and di-n-propyl phthalate; also endocrine-disrupting compounds), suggesting a substitution. Many detected chemicals were not listed on product labels.

Conclusions: Common products contain complex mixtures of EDCs and asthma-related compounds. Toxicological studies of these mixtures are needed to understand their biological activity. Regarding epidemiology, our findings raise concern about potential confounding from co-occurring chemicals and misclassification due to variability in product composition. Consumers should be able to avoid some target chemicals—synthetic fragrances, BPA, and regulated active ingredients—using purchasing criteria. More complete product labeling would enable consumers to avoid the rest of the target chemicals.

Thyroid Function and Perfluoroalkyl Acids in Children Living Near a Chemical Plant

Maria-Jose Lopez-Espinosa, Debapriya Mondal, Ben Armstrong, Michael S. Bloom, and Tony Fletcher

120:1036–1041 (2012) | http://dx.doi.org/10.1289/ehp.1104370

Background: Animal studies suggest that some perfluoroalkyl acids (PFAAs), including perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS), and perfluorononanoic acid (PFNA) may impair thyroid function. Epidemiological findings, mostly related to adults, are inconsistent.

Objectives: We investigated whether concentrations of PFAAs were associated with thyroid function among 10,725 children (1–17 years of age) living near a Teflon manufacturing facility in the Mid-Ohio Valley (USA).

Methods: Serum levels of thyroid-stimulating hormone (TSH), total thyroxine (TT_4), and PFAAs were measured during 2005–2006, and information on diagnosed thyroid disease was collected by questionnaire. Modeled *in utero* PFOA concentrations were based on historical information on PFOA releases, environmental distribution, pharmacokinetic modeling, and residential histories. We performed multivariate regression analyses.

Results: Median concentrations of modeled *in utero* PFOA and measured serum PFOA, PFOS, and PFNA were 12, 29, 20, and 1.5 ng/mL, respectively. The odds ratio for hypothyroidism ($n = 39$) was 1.54 [95% confidence interval (CI): 1.00, 2.37] for an interquartile range (IQR) contrast of 13 to 68 ng/mL in serum PFOA measured in 2005–2006. However, an IQR shift in serum PFOA was not associated with TSH or TT_4 levels in all children combined. IQR shifts in serum PFOS (15 to 28 ng/mL) and serum PFNA (1.2 to 2.0 ng/mL) were both associated with a 1.1% increase in TT_4 in children 1–17 years old (95% CIs: 0.6, 1.5 and 0.7, 1.5 respectively).

Conclusions: This is the first large-scale report in children suggesting associations of serum PFOS and PFNA with thyroid hormone levels and of serum PFOA and hypothyroidism.

Serum PBDEs in a North Carolina Toddler Cohort: Associations with Handwipes, House Dust, and Socioeconomic Variables

Heather M. Stapleton, Sarah Eagle, Andreas Sjödin, and Thomas F. Webster

120:1049–1054 (2012) | http://dx.doi.org/10.1289/ehp.1104802

Background: Polybrominated diphenyl ethers (PBDEs) are persistent, bioaccumulative, and endocrine-disrupting chemicals.

Objectives: We used handwipes to estimate exposure to PBDEs in house dust among toddlers and examined sex, age, breast-feeding, race, and parents' education as predictors of serum PBDEs.

Methods: Eighty-three children from 12 to 36 months of age were enrolled in North Carolina between May 2009 and November 2010. Blood, handwipe, and house dust samples were collected and analyzed for PBDEs. A questionnaire was administered to collect demographic data.

Results: PBDEs were detected in all serum samples (geometric mean for ∑pentaBDE in serum was 43.3 ng/g lipid), 98% of the handwipe samples, and 100% of the dust samples. Serum ∑pentaBDEs were significantly correlated with both handwipe and house dust ∑pentaBDE levels, but were more strongly associated with handwipe levels ($r = 0.57$; $p < 0.001$ vs. $r = 0.35$; $p < 0.01$). Multivariate model estimates revealed that handwipe levels, child's sex, child's age, and father's education accounted for 39% of the variation in serum ∑BDE3 levels (sum of BDEs 47, 99, and 100). In contrast, age, handwipe levels, and breast-feeding duration explained 39% of the variation in serum BDE 153.

Conclusions: Our study suggests that hand-to-mouth activity may be a significant source of exposure to PBDEs. Furthermore, age, socioeconomic status, and breast-feeding were significant predictors of exposure, but associations varied by congener. Specifically, serum ∑BDE3 was inversely associated with socioeconomic status, whereas serum BDE-153 was positively associated with duration of breast-feeding and mother's education.

Exposures

Relationship of Perfluorooctanoic Acid Exposure to Pregnancy Outcome Based on Birth Records in the Mid-Ohio Valley

David A. Savitz, Cheryl R. Stein, Beth Elston, Gregory A. Wellenius, Scott M. Bartell, Hyeong-Moo Shin, Veronica M. Vieira, and Tony Fletcher

120:1201–1207 (2012) | http://dx.doi.org/10.1289/ehp.1104752

Background: Perfluorooctanoic acid (PFOA) is a potential cause of adverse pregnancy outcomes, but previous studies have been limited by low exposures and small study size.

Objectives: Using birth certificate information, we examined the relation between estimated PFOA exposure and birth outcomes in an area of West Virginia and Ohio whose drinking water was contaminated by a chemical plant.

Methods: Births in the study area from 1990 through 2004 were examined to generate case groups of stillbirth ($n = 106$), pregnancy-induced hypertension ($n = 224$), preterm birth ($n = 3,613$), term low birth weight ($n = 918$), term small-for-gestational-age (SGA) ($n = 353$), and a continuous measure of birth weight among a sample of term births ($n = 4,534$). A 10% sample of term births ≥ 2,500 g were selected as a source of controls ($n = 3,616$). Historical estimates of serum PFOA were derived from a previously developed fate and transport model. In a second study, we examined 4,547 area births linked to a survey with residential history data.

Results: In the analysis based only on birth records, we found no consistent evidence of an association between estimated PFOA exposure and stillbirth, pregnancy-induced hypertension, preterm birth, or indices of fetal growth. In the analysis of birth records linked to the survey, PFOA was unrelated to pregnancy-induced hypertension or preterm birth but showed some suggestion of an association with early preterm birth. Measures of growth restriction showed weak and inconsistent associations with PFOA.

Conclusions: Based on the analysis using the health survey, these results provide little support for an effect of PFOA exposure on most pregnancy outcomes, except for early preterm birth and possibly fetal growth restriction.

AIR POLLUTION: PARTICULATE MATTER/SMOKE/INDOOR AIR

Residential Traffic-Related Pollution Exposures and Exhaled Nitric Oxide in the Children's Health Study

Sandrah P. Eckel, Kiros Berhane, Muhammad T. Salam, Edward B. Rappaport, William S. Linn, Theresa M. Bastain, Yue Zhang, Frederick Lurmann, Edward L. Avol, and Frank D. Gilliland

119:1472–1477 (2011) | http://dx.doi.org/10.1289/ehp.1103516

Background: The fractional concentration of nitric oxide in exhaled air (Fe_{NO}) potentially detects airway inflammation related to air pollution exposure. Existing studies have not yet provided conclusive evidence on the association of Fe_{NO} with traffic-related pollution (TRP).

Objectives: We evaluated the association of Fe_{NO} with residential TRP exposure in a large cohort of children.

Methods: We related Fe_{NO} measured on 2,143 children (ages 7–11 years) who participated in the Southern California Children's Health Study (CHS) to five classes of metrics of residential TRP: distances to freeways and major roads; length of all and local roads within circular buffers around the home; traffic densities within buffers; annual average line source dispersion modeled nitrogen oxides (NO_x) from freeways and nonfreeway roads; and predicted annual average nitrogen oxide, nitrogen dioxide, and NO_x from a model based on intracommunity sampling in the CHS.

Results: In children with asthma, length of roads was positively associated with Fe_{NO}, with stronger associations in smaller buffers [46.7%; 95% confidence interval (CI), 14.3–88.4], 12.4% (95% CI, –8.8 to 38.4), and 4.1% (95% CI, –14.6 to 26.8) higher Fe_{NO} for 100-, 300-, and 1,000-m increases in the length of all roads in 50-, 100-, and 200-m buffers, respectively. Other TRP metrics were not significantly associated with Fe_{NO}, even though the study design was powered to detect exposures explaining as little as 0.4% of the variation in natural log-transformed Fe_{NO} ($R^2 = 0.004$).

Conclusion: Length of road was the only indicator of residential TRP exposure associated with airway inflammation in children with asthma, as measured by Fe_{NO}.

Exposures

Traffic Air Pollution and Other Risk Factors for Respiratory Illness in Schoolchildren in the Niger-Delta Region of Nigeria

B. Adetoun Mustapha, Marta Blangiardo, David J. Briggs, and Anna L. Hansell

119:1478–1482 (2011) | http://dx.doi.org/10.1289/ehp.1003099

Background: Association of childhood respiratory illness with traffic air pollution has been investigated largely in developed but not in developing countries, where pollution levels are often very high.

Objectives: In this study we investigated associations between respiratory health and outdoor and indoor air pollution in schoolchildren 7–14 years of age in low socioeconomic status areas in the Niger Delta.

Methods: A cross-sectional survey was carried out among 1,397 schoolchildren. Exposure to home outdoor and indoor air pollution was assessed by self-report questionnaire. School air pollution exposures were assessed using traffic counts, distance of schools to major streets, and particulate matter and carbon monoxide measurements, combined using principal components analysis. Hierarchical logistic regression was used to examine associations with reported respiratory health, adjusting for potential confounders.

Results: Traffic disturbance at home (i.e., traffic noise and/or fumes evident inside the home vs. none) was associated with wheeze [odds ratio (OR) = 2.16; 95% confidence interval (CI), 1.28–3.64], night cough (OR = 1.37; 95% CI, 1.03–1.82), phlegm (OR = 1.49; 95% CI, 1.09–2.04), and nose symptoms (OR = 1.40; 95% CI, 1.03–1.90), whereas school exposure to a component variable indicating exposure to fine particles was associated with increased phlegm (OR = 1.38; 95% CI, 1.09–1.75). Nonsignificant positive associations were found between cooking with wood/coal (OR = 2.99; 95% CI, 0.88–10.18) or kerosene (OR = 2.83; 95% CI, 0.85–9.44) and phlegm compared with cooking with gas.

Conclusion: Traffic pollution is associated with respiratory symptoms in schoolchildren in a deprived area of western Africa. Associations may have been underestimated because of nondifferential misclassification resulting from limitations in exposure measurement.

Impact of Reduced Maternal Exposures to Wood Smoke from an Introduced Chimney Stove on Newborn Birth Weight in Rural Guatemala

Lisa M. Thompson, Nigel Bruce, Brenda Eskenazi, Anaite Diaz, Daniel Pope, and Kirk R. Smith

119:1489–1494 (2011) | http://dx.doi.org/10.1289/ehp.1002928

Background: A growing body of evidence indicates a relationship between household indoor air pollution from cooking fires and adverse neonatal outcomes, such as low birth weight (LBW), in resource-poor countries.

Objective: We examined the effect of reduced wood smoke exposure in pregnancy on LBW of Guatemalan infants in RESPIRE (Randomized Exposure Study of Pollution Indoors and Respiratory Effects).

Methods: Pregnant women ($n = 266$) either received a chimney stove (intervention) or continued to cook over an open fire (control). Between October 2002 and December 2004 we weighed 174 eligible infants (69 to mothers who used a chimney stove and 105 to mothers who used an open fire during pregnancy) within 48 hr of birth. Multivariate linear regression and adjusted odds ratios (ORs) were used to estimate differences in birth weight and LBW (< 2,500 g) associated with chimney-stove versus open-fire use during pregnancy.

Results: Pregnant women using chimney stoves had a 39% reduction in mean exposure to carbon monoxide compared with those using open fires. LBW prevalence was high at 22.4%. On average, infants born to mothers who used a stove weighed 89 g more [95% confidence interval (CI), –27 to 204 g] than infants whose mothers used open fires after adjusting for maternal height, diastolic blood pressure, gravidity, and season of birth. The adjusted OR for LBW was 0.74 (95% CI, 0.33–1.66) among infants of stove users compared with open-fire users. Average birth weight was 296 g higher (95% CI, 109–482 g) in infants born during the cold season (after harvest) than in other infants; this unanticipated finding may reflect the role of maternal nutrition on birth weight in an impoverished region.

Conclusions: A chimney stove reduced wood smoke exposures and was associated with reduced LBW occurrence. Although not statistically significant, the estimated effect was consistent with previous studies.

Exposures

Black Carbon as an Additional Indicator of the Adverse Health Effects of Airborne Particles Compared with PM_{10} and $PM_{2.5}$

Nicole A.H. Janssen, Gerard Hoek, Milena Simic-Lawson, Paul Fischer, Leendert van Bree, Harry ten Brink, Menno Keuken, Richard W. Atkinson, H. Ross Anderson, Bert Brunekreef, and Flemming R. Cassee

119:1691–1699 (2011) | http://dx.doi.org/10.1289/ehp.1003369

Background: Current air quality standards for particulate matter (PM) use the PM mass concentration [PM with aerodynamic diameters ≤ 10 µm (PM_{10}) or ≤ 2.5 µm ($PM_{2.5}$)] as a metric. It has been suggested that particles from combustion sources are more relevant to human health than are particles from other sources, but the impact of policies directed at reducing PM from combustion processes is usually relatively small when effects are estimated for a reduction in the total mass concentration.

Objectives: We evaluated the value of black carbon particles (BCP) as an additional indicator in air quality management.

Methods: We performed a systematic review and meta-analysis of health effects of BCP compared with PM mass based on data from time-series studies and cohort studies that measured both exposures. We compared the potential health benefits of a hypothetical traffic abatement measure, using near-roadway concentration increments of BCP and $PM_{2.5}$ based on data from prior studies.

Results: Estimated health effects of a 1-µg/m^3 increase in exposure were greater for BCP than for PM_{10} or $PM_{2.5}$, but estimated effects of an interquartile range increase were similar. Two-pollutant models in time-series studies suggested that the effect of BCP was more robust than the effect of PM mass. The estimated increase in life expectancy associated with a hypothetical traffic abatement measure was four to nine times higher when expressed in BCP compared with an equivalent change in $PM_{2.5}$ mass.

Conclusion: BCP is a valuable additional air quality indicator to evaluate the health risks of air quality dominated by primary combustion particles.

Chronic Air Pollution Exposure during Pregnancy and Maternal and Fetal C-Reactive Protein Levels: The Generation R Study

Edith H. van den Hooven, Yvonne de Kluizenaar, Frank H. Pierik, Albert Hofman, Sjoerd W. van Ratingen, Peter Y.J. Zandveld, Jan Lindemans, Henk Russcher, Eric A.P. Steegers, Henk M.E. Miedema, and Vincent W.V. Jaddoe

120:746–751 (2012) | http://dx.doi.org/10.1289/ehp.1104345

Background: Exposure to air pollution has been associated with higher C-reactive protein (CRP) levels, suggesting an inflammatory response. Not much is known about this association in pregnancy.

Objectives: We investigated the associations of air pollution exposure during pregnancy with maternal and fetal CRP levels in a population-based cohort study in the Netherlands.

Methods: Particulate matter (PM) with an aerodynamic diameter ≤ 10 µm (PM_{10}) and nitrogen dioxide (NO_2) levels were estimated at the home address using dispersion modeling for different averaging periods preceding the blood sampling (1 week, 2 weeks, 4 weeks, and total pregnancy). High-sensitivity CRP levels were measured in maternal blood samples in early pregnancy (n = 5,067) and in fetal cord blood samples at birth (n = 4,450).

Results: Compared with the lowest quartile, higher PM_{10} exposure levels for the prior 1 and 2 weeks were associated with elevated maternal CRP levels (> 8 mg/L) in the first trimester [fourth PM_{10} quartile for the prior week: odds ratio (OR), 1.32; 95% confidence interval (CI): 1.08, 1.61; third PM_{10} quartile for the prior 2 weeks: OR, 1.28; 95% CI: 1.06, 1.56]; however, no clear dose–response relationships were observed. PM_{10} and NO_2 exposure levels for 1, 2, and 4 weeks preceding delivery were not consistently associated with fetal CRP levels at delivery. Higher long-term PM_{10} and NO_2 exposure levels (total pregnancy) were associated with elevated fetal CRP levels (> 1 mg/L) at delivery (fourth quartile PM_{10}: OR, 2.18; 95% CI: 1.08, 4.38; fourth quartile NO_2: OR, 3.42; 95% CI: 1.36, 8.58; p-values for trend < 0.05).

Conclusions: Our results suggest that exposure to air pollution during pregnancy may lead to maternal and fetal inflammatory responses.

Exposures

Placental Mitochondrial DNA Content and Particulate Air Pollution during *in Utero* Life

Bram G. Janssen, Elke Munters, Nicky Pieters, Karen Smeets, Bianca Cox, Ann Cuypers, Frans Fierens, Joris Penders, Jaco Vangronsveld, Wilfried Gyselaers, and Tim S. Nawrot

120:1346–1352 (2012) | http://dx.doi.org/10.1289/ehp.1104458

Background: Studies emphasize the importance of particulate matter (PM) in the formation of reactive oxygen species and inflammation. We hypothesized that these processes can influence mitochondrial function of the placenta and fetus.

Objective: We investigated the influence of PM_{10} exposure during pregnancy on the mitochondrial DNA content (mtDNA content) of the placenta and umbilical cord blood.

Methods: DNA was extracted from placental tissue ($n = 174$) and umbilical cord leukocytes ($n = 176$). Relative mtDNA copy numbers (i.e., mtDNA content) were determined by real-time polymerase chain reaction. Multiple regression models were used to link mtDNA content and *in utero* exposure to PM_{10} over various time windows during pregnancy.

Results: In multivariate-adjusted analysis, a 10-μg/m^3 increase in PM_{10} exposure during the last month of pregnancy was associated with a 16.1% decrease [95% confidence interval (CI): –25.2, –6.0%, $p = 0.003$] in placental mtDNA content. The corresponding effect size for average PM_{10} exposure during the third trimester was 17.4% (95% CI: –31.8, –0.1%, $p = 0.05$). Furthermore, we found that each doubling in residential distance to major roads was associated with an increase in placental mtDNA content of 4.0% (95% CI: 0.4, 7.8%, $p = 0.03$). No association was found between cord blood mtDNA content and PM_{10} exposure.

Conclusions: Prenatal PM_{10} exposure was associated with placental mitochondrial alterations, which may both reflect and intensify oxidative stress production. The potential health consequences of decreased placental mtDNA content in early life must be further elucidated.

▾NEWS | SCIENCE SELECTION

Potential Mechanism for PM_{10} Effects on Birth Outcomes: In Utero Exposure Linked to Mitochondrial Damage

Tanya Tillett | 120:A363

http://dx.doi.org/10.1289/ehp.120-a363b

Surrounding Greenness and Exposure to Air Pollution During Pregnancy: An Analysis of Personal Monitoring Data

Payam Dadvand, Audrey de Nazelle, Margarita Triguero-Mas, Anna Schembari, Marta Cirach, Elmira Amoly, Francesc Figueras, Xavier Basagaña, Bart Ostro, and Mark Nieuwenhuijsen

120:1286–1290 (2012) | http://dx.doi.org/10.1289/ehp.1104609

Background: Green spaces are reported to improve health status, including beneficial effects on pregnancy outcomes. Despite the suggestions of air pollution–related health benefits of green spaces, there is no available evidence on the impact of greenness on personal exposure to air pollution.

Objectives: We investigated the association between surrounding greenness and personal exposure to air pollution among pregnant women and to explore the potential mechanisms, if any, behind this association.

Methods: In total, 65 rounds of sampling were carried out for 54 pregnant women who resided in Barcelona during 2008–2009. Each round consisted of a 2-day measurement of particulate matter with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$) and a 1-week measurement of nitric oxides collected simultaneously at both the personal and microenvironmental levels. The study participants were also asked to fill out a time–microenvironment–activity diary during the sampling period. We used satellite retrievals to determine the surrounding greenness as the average of Normalized Difference Vegetation Index (NDVI) in a buffer of 100 m around each maternal residential address. We estimated the impact of surrounding greenness on personal exposure levels, home-outdoor and home-indoor pollutant levels, and maternal time-activity.

Results: Higher residential surrounding greenness was associated with lower personal, home-indoor, and home-outdoor $PM_{2.5}$ levels, and more time spent at home-outdoor.

Conclusions: We found lower levels of personal exposure to air pollution among pregnant women residing in greener areas. This finding may be partly explained by lower home-indoor pollutant levels and more time spent in less polluted home-outdoor environment by pregnant women in greener areas.

ENDOTOXINS AND WATER TOXINS

A Cross-Sectional Investigation of Chronic Exposure to Microcystin in Relationship to Childhood Liver Damage in the Three Gorges Reservoir Region, China

Yan Li, Ji-an Chen, Qing Zhao, Chaowen Pu, Zhiqun Qiu, Renping Zhang, and Weiqun Shu

119:1483–1488 (2011) | http://dx.doi.org/10.1289/ehp.1002412

Background: Microcystin-producing *Microcystis* bloom is a severe water problem in the world. Some reports indicate that chronic exposure to microcystin may result in liver damage in adults, but information on effects in children is limited.

Objective: We investigated the relationship between microcystin exposure and liver damage in children.

Methods: We measured microcystin concentrations in drinking water and aquatic food (carp and duck) from two lakes and four wells. Participants were 1,322 children 7–15 years of age who obtained drinking water from one of the tested sources, completed questionnaires, and provided blood samples for serum liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and γ-glutamyltransferase (GGT)] and serum microcystin analysis. Multivariable logistic regression was used to identify risk factors associated with liver damage (two or more abnormal serum enzyme levels in ALT, AST, ALP, or GGT).

Results: Microcystin was detected in most samples of water and aquatic food from two lakes. Children who drank water from the lake with the highest microcystin concentrations had a total estimated daily microcystin intake of 2.03 μg, a value much higher than the tolerable daily intake (0.40 μg) proposed by the World Health Organization for children. Hepatitis B virus (HBV) infection, use of hepatotoxic medicines, and microcystin exposure were associated with liver damage. AST and ALP levels were significantly higher in high-microcystin-exposed children than in low-exposed children and unexposed children when participants who were HBV-positive or hepatotoxic medicine users were excluded from the analysis.

Conclusion: These results suggest that chronic exposure to microcystin may be associated with liver damage in children in the Three Gorges Reservoir Region.

Health Risks of Limited-Contact Water Recreation

Samuel Dorevitch, Preethi Pratap, Meredith Wroblewski, Daniel O. Hryhorczuk, Hong Li, Li C. Liu, and Peter A. Scheff

120:192–197 (2012) | http://dx.doi.org/10.1289/ehp.1103934

Background: Wastewater-impacted waters that do not support swimming are often used for boating, canoeing, fishing, kayaking, and rowing. Little is known about the health risks of these limited-contact water recreation activities.

Objectives: We evaluated the incidence of illness, severity of illness, associations between water exposure and illness, and risk of illness attributable to limited-contact water recreation on waters dominated by wastewater effluent and on waters approved for general use recreation (such as swimming).

Methods: The Chicago Health, Environmental Exposure, and Recreation Study was a prospective cohort study that evaluated five health outcomes among three groups of people: those who engaged in limited-contact water recreation on effluent-dominated waters, those who engaged in limited-contact recreation on general-use waters, and those who engaged in non–water recreation. Data analysis included survival analysis, logistic regression, and estimates of risk for counterfactual exposure scenarios using G-computation.

Results: Telephone follow-up data were available for 11,297 participants. With non–water recreation as the reference group, we found that limited-contact water recreation was associated with the development of acute gastrointestinal illness in the first 3 days after water recreation at both effluent-dominated waters [adjusted odds ratio (AOR) 1.46; 95% confidence interval (CI): 1.08, 1.96] and general-use waters (1.50; 95% CI: 1.09, 2.07). For every 1,000 recreators, 13.7 (95% CI: 3.1, 24.9) and 15.1 (95% CI: 2.6, 25.7) cases of gastrointestinal illness were attributable to limited-contact recreation at effluent-dominated waters and general-use waters, respectively. Eye symptoms were associated with use of effluent-dominated waters only (AOR 1.50; 95% CI: 1.10, 2.06). Among water recreators, our results indicate that illness was associated with the amount of water exposure.

Conclusions: Limited-contact recreation, both on effluent-dominated waters and on waters designated for general use, was associated with an elevated risk of gastrointestinal illness.

▾NEWS | SCIENCE SELECTION

In the Same Boat? Health Risks of Water Recreation Are Not Limited to Full-Contact Activities

Wendee Holtcamp | 120:A77

http://dx.doi.org/10.1289/ehp.120-a77a

Aflatoxin Exposure May Contribute to Chronic Hepatomegaly in Kenyan School Children

Yun Yun Gong, Shona Wilson, Joseph K. Mwatha, Michael N. Routledge, Jovita M. Castelino, Bin Zhao, Gachuhi Kimani, H. Curtis Kariuki, Birgitte J. Vennervald, David W. Dunne, and Christopher P. Wild

120:893–896 (2012) | http://dx.doi.org/10.1289/ehp.1104357

Background: Presentation with a firm type of chronic hepatomegaly of multifactorial etiology is common among school-age children in sub-Saharan Africa.

Objective: Aflatoxin is a liver toxin and carcinogen contaminating staple maize food. In this study we examined its role in chronic hepatomegaly.

Methods: Plasma samples collected in 2002 and again in 2004 from 218 children attending two schools in neighboring villages were assayed for aflatoxin exposure using the aflatoxin–albumin adduct (AF-alb) biomarker. Data were previously examined for associations among hepatomegaly, malaria, and schistosomiasis.

Results: AF-alb levels were high in children from both schools, but the geometric mean (95% confidence interval) in year 2002 was significantly higher in Matangini [206.5 (175.5, 243.0) pg/mg albumin] than in Yumbuni [73.2 (61.6, 87.0) pg/mg; $p < 0.001$]. AF-alb levels also were higher in children with firm hepatomegaly [176.6 (129.6, 240.7) pg/mg] than in normal children [79.9 (49.6, 128.7) pg/mg; $p = 0.029$]. After adjusting for *Schistosoma mansoni* and *Plasmodium* infection, we estimated a significant 43% increase in the prevalence of hepatomegaly/hepatosplenomegaly for every natural-log-unit increase in AF-alb. In 2004, AF-alb levels were markedly higher than in 2002 [539.7 (463.3, 628.7) vs. 114.5 (99.7, 131.4) pg/mg; $p < 0.001$] but with no significant difference between the villages or between hepatomegaly and normal groups [539.7 (436.7, 666.9) vs. 512.6 (297.3, 883.8) pg/mg], possibly because acute exposures during an aflatoxicosis outbreak in 2004 may have masked any potential underlying relationship.

Conclusions: Exposure to aflatoxin was associated with childhood chronic hepatomegaly in 2002. These preliminary data suggest an additional health risk that may be related to aflatoxin exposure in children, a hypothesis that merits further testing.

RELATED ARTICLES

NEWS | Planting Healthier Indoor Air

Luz Claudio | 119:A426–A427
http://dx.doi.org/10.1289/ehp.119-a426

NEWS | EPA Proposes Tighter Particulate Air Pollution Standards

Bob Weinhold | 120:A348–A349
http://dx.doi.org/10.1289/ehp.120-a348a

NEWS | Our Food: Packaging and Public Health

Luz Claudio | 120:A232–A237
http://dx.doi.org/10.1289/ehp.120-a232

PODCAST | Climate Change, Crop Yields, and Undernutrition, with Sari Kovats

http://dx.doi.org/10.1289/ehp.trp120111

PODCAST | A Bite of Arsenic, with Kathryn Cottingham

http://dx.doi.org/10.1289/ehp.trp050112

Exposures

BUILT ENVIRONMENT

Associations between the Quality of the Residential Built Environment and Pregnancy Outcomes among Women in North Carolina

Marie Lynn Miranda, Lynne C. Messer, and Gretchen L. Kroeger

120:471–477 (2012) | http://dx.doi.org/10.1289/ehp.1103578

Background: The built environment, a key component of environmental health, may be an important contributor to health disparities, particularly for reproductive health outcomes.

Objective: In this study we investigated the relationship between seven indices of residential built environment quality and adverse reproductive outcomes for the City of Durham, North Carolina (USA).

Methods: We surveyed approximately 17,000 residential tax parcels in central Durham, assessing > 50 individual variables on each. These data, collected using direct observation, were combined with tax assessor, public safety, and U.S. Census data to construct seven indices representing important domains of the residential built environment: housing damage, property disorder, security measures, tenure (owner or renter occupied), vacancy, crime count, and nuisance count. Fixed-slope random-intercept multilevel models estimated the association between the residential built environment and five adverse birth outcomes. Models were adjusted for maternal characteristics and clustered at the primary adjacency community unit, defined as the index block, plus all adjacent blocks that share any portion of a line segment (block boundary) or vertex.

Results: Five built environment indices (housing damage, property disorder, tenure, vacancy, and nuisance count) were associated with each of the five outcomes in the unadjusted context: preterm birth, small for gestational age (SGA), low birth weight (LBW), continuous birth weight, and birth weight percentile for gestational age (BWPGA; sex-specific birth weight distributions for infants delivered at each gestational age using National Center for Health Statistics referent births for 2000–2004). However, some estimates were attenuated after adjustment. In models adjusted for individual-level covariates, housing damage remained statistically significantly associated with SGA, birth weight, and BWPGA.

Conclusion: This work suggests a real and meaningful relationship between the quality of the residential built environment and birth outcomes, which we argue are a good measure of general community health.

CLIMATE CHANGE

Climate Extremes and the Length of Gestation

Payam Dadvand, Xavier Basagaña, Claudio Sartini, Francesc Figueras, Martine Vrijheid, Audrey de Nazelle, Jordi Sunyer, and Mark J. Nieuwenhuijsen

119:1449–1453 (2011) | http://dx.doi.org/10.1289/ehp.1003241

Background: Although future climate is predicted to have more extreme heat conditions, the available evidence on the impact of these conditions on pregnancy length is very scarce and inconclusive.

Objectives: We investigated the impact of maternal short-term exposure to extreme ambient heat on the length of pregnancy.

Methods: This study was based on a cohort of births that occurred in a major university hospital in Barcelona during 2001–2005. Three indicators of extreme heat conditions based on 1-day exposure to an unusually high heat–humidity index were applied. Each mother was assigned the measures made by the meteorological station closest to maternal residential postcodes. A two-stage analysis was developed to quantify the change in pregnancy length after maternal exposure to extreme heat conditions adjusted for a range of covariates. The second step was repeated for lags 0 (delivery date) to 6 days.

Results: We included data from 7,585 pregnant women in our analysis. We estimated a 5-day reduction in average gestational age at delivery after an unusually high heat–humidity index on the day before delivery.

Conclusion: Extreme heat was associated with a reduction in the average gestational age of children delivered the next day, suggesting an immediate effect of this exposure on pregnant women. Further studies are required to confirm our findings in different settings.

▾ NEWS | SCIENCE SELECTION

Pregnancy Pause: Extreme Heat Linked to Shortened Gestation
Tanya Tillett | 119:A443
http://dx.doi.org/10.1289/ehp.119-a443b

Climate Change, Crop Yields, and Undernutrition: Development of a Model to Quantify the Impact of Climate Scenarios on Child Undernutrition

Simon J. Lloyd, R. Sari Kovats, and Zaid Chalabi

119:1817–1823 (2011) | http://dx.doi.org/10.1289/ehp.1003311

Background: Global climate change is anticipated to reduce future cereal yields and threaten food security, thus potentially increasing the risk of undernutrition. The causation of undernutrition is complex, and there is a need to develop models that better quantify the potential impacts of climate change on population health.

Objectives: We developed a model for estimating future undernutrition that accounts for food and nonfood (socioeconomic) causes and can be linked to available regional scenario data. We estimated child stunting attributable to climate change in five regions in South Asia and sub-Saharan Africa (SSA) in 2050.

Methods: We used current national food availability and undernutrition data to parameterize and validate a global model, using a process-driven approach based on estimations of the physiological relationship between a lack of food and stunting. We estimated stunting in 2050 using published modeled national calorie availability under two climate scenarios and a reference scenario (no climate change).

Results: We estimated that climate change will lead to a relative increase in moderate stunting of 1–29% in 2050 compared with a future without climate change. Climate change will have a greater impact on rates of severe stunting, which we estimated will increase by 23% (central SSA) to 62% (South Asia).

Conclusions: Climate change is likely to impair future efforts to reduce child malnutrition in South Asia and SSA, even when economic growth is taken into account. Our model suggests that to reduce and prevent future undernutrition, it is necessary to both increase food access and improve socioeconomic conditions, as well as reduce greenhouse gas emissions.

▾NEWS | SCIENCE SELECTION

More Lack in the World: The Complex Connection between Undernutrition and Climate Change

Angela Spivey | 119:A524

http://dx.doi.org/10.1289/ehp.119-a524a

NATURAL DISASTERS

Environmental Lead after Hurricane Katrina: Implications for Future Populations

Felicia A. Rabito, Shahed Iqbal, Sara Perry, Whitney Arroyave, and Janet C. Rice

120:180–184 (2012) | http://dx.doi.org/10.1289/ehp.1103774

Background: As a result of Hurricane Katrina, > 100,000 homes were destroyed or damaged and a significant amount of sediment was deposited throughout the city of New Orleans, Louisiana. Researchers have identified the potential for increased lead hazards from environmental lead contamination of soils.

Objectives: We assessed the distribution of residential soil and dust lead 2 years poststorm and compared soil lead before and after the storm.

Methods: We conducted a cross-sectional study in New Orleans in which households were selected by stratified random sampling. A standard residential questionnaire was administered, and lead testing was performed for both the interior and exterior of homes. Logistic regression was used to identify significant predictors of interior and exterior lead levels in excess of allowable levels.

Results: One hundred nine households were enrolled; 61% had at least one lead measurement above federal standards. Of homes with bare soil, 47% had elevated lead and 27% had levels exceeding 1,200 ppm. Housing age was associated with soil lead, and housing age and soil lead were associated with interior lead. Race, income, and ownership status were not significantly associated with either interior or exterior lead levels. The median soil lead level of 560 ppm was significantly higher than the median level of samples collected before Hurricane Katrina.

Conclusions: The high prevalence (61%) of lead above recommended levels in soil and dust samples in and around residences raises concern about potential health risks to the New Orleans population, most notably children. Steps should be taken to mitigate the risk of exposure to lead-contaminated soil and dust. Further research is needed to quantify the possible contribution of reconstruction activities to environmental lead levels.

Exposures

Estimated Effects of Asian Dust Storms on Spatiotemporal Distributions of Clinic Visits for Respiratory Diseases in Taipei Children (Taiwan)

Lung-Chang Chien, Chiang-Hsing Yang, and Hwa-Lung Yu

120:1215–1220 (2012) | http://dx.doi.org/10.1289/ehp.1104417

Background: Increases in certain cause-specific hospital admissions have been reported during Asian dust storms (ADS), which primarily originate from north and northwest China during winter and spring. However, few studies have investigated the relationship between the ADS and clinic visits for respiratory diseases in children.

Objective: We investigated the general impact to children's health across space and time by analyzing daily clinic visits for respiratory diseases among preschool and schoolchildren registered in 12 districts of Taipei City during 1997–2007 from the National Health Insurance dataset.

Methods: We applied a structural additive regression model to estimate the association between ADS episodes and children's clinic visits for respiratory diseases, controlling for space and time variations.

Results: Compared with weeks before ADS events, the rate of clinic visits during weeks after ADS events increased 2.54% (95% credible interval = 2.43, 2.66) for preschool children (≤ 6 years of age) and 5.03% (95% credible interval = 4.87, 5.20) for schoolchildren (7–14 years of age). Spatial heterogeneity in relative rates of clinic visits was also identified. Compared with the mean level of Taipei City, higher relative rates appeared in districts with or near large hospitals and medical centers.

Conclusion: To our knowledge, this is the first population-based study to assess the impact of ADS on children's respiratory health. Our analysis suggests that children's respiratory health was affected by ADS events across all of Taipei, especially among schoolchildren.

Birth Weight following Pregnancy during the 2003 Southern California Wildfires

David M. Holstius, Colleen E. Reid, Bill M. Jesdale, and Rachel Morello-Frosch

120:1340–1345 (2012) | http://dx.doi.org/10.1289/ehp.1104515

Background: In late October 2003, a series of wildfires exposed urban populations in Southern California to elevated levels of air pollution over several weeks. Previous research suggests that short-term hospital admissions for respiratory outcomes increased specifically as a result of these fires.

Objective: We assessed the impact of a wildfire event during pregnancy on birth weight among term infants.

Methods: Using records for singleton term births delivered to mothers residing in California's South Coast Air Basin (SoCAB) during 2001–2005 (n = 886,034), we compared birth weights from pregnancies that took place entirely before or after the wildfire event (n = 747,590) with those where wildfires occurred during the first (n = 60,270), second (n = 39,435), or third (n = 38,739) trimester. The trimester-specific effects of wildfire exposure were estimated using a fixed-effects regression model with several maternal characteristics included as covariates.

Results: Compared with pregnancies before and after the wildfires, mean birth weight was estimated to be 7.0 g lower [95% confidence interval (CI): –11.8, –2.2] when the wildfire occurred during the third trimester, 9.7 g lower when it occurred during the second trimester (95% CI: –14.5, –4.8), and 3.3 g lower when it occurred during the first trimester (95% CI: –7.2, 0.6).

Conclusions: Pregnancy during the 2003 Southern California wildfires was associated with slightly reduced average birth weight among infants exposed *in utero*. The extent and increasing frequency of wildfire events may have implications for infant health and development.

▾ NEWS | SCIENCE SELECTION

Followup in Southern California: Decreased Birth Weight following Prenatal Wildfire Smoke Exposure

Rebecca Kessler | 120:A362

http://dx.doi.org/10.1289/ehp.120-a362b

FOOD SAFETY/INSECURITY/NUTRITION

Arsenic, Organic Foods, and Brown Rice Syrup

Brian P. Jackson, Vivien F. Taylor, Margaret R. Karagas, Tracy Punshon, and Kathryn L. Cottingham

120:623–626 (2012) | http://dx.doi.org/10.1289/ehp.1104619

Background: Rice can be a major source of inorganic arsenic (As_i) for many subpopulations. Rice products are also used as ingredients in prepared foods, some of which may not be obviously rice based. Organic brown rice syrup (OBRS) is used as a sweetener in organic food products as an alternative to high-fructose corn syrup. We hypothesized that OBRS introduces As into these products.

Objective: We determined the concentration and speciation of As in commercially available brown rice syrups and in products containing OBRS, including toddler formula, cereal/energy bars, and high-energy foods used by endurance athletes.

Methods: We used inductively coupled plasma mass spectrometry (ICP-MS) and ion chromatography coupled to ICP-MS to determine total As (As_{total}) concentrations and As speciation in products purchased via the Internet or in stores in the Hanover, New Hampshire, area.

Discussion: We found that OBRS can contain high concentrations of As_i and dimethylarsenate (DMA). An "organic" toddler milk formula containing OBRS as the primary ingredient had As_{total} concentrations up to six times the U.S. Environmental Protection Agency safe drinking water limit. Cereal bars and high-energy foods containing OBRS also had higher As concentrations than equivalent products that did not contain OBRS. As_i was the main As species in most food products tested in this study.

Conclusions: There are currently no U.S. regulations applicable to As in food, but our findings suggest that the OBRS products we evaluated may introduce significant concentrations of As_i into an individual's diet. Thus, we conclude that there is an urgent need for regulatory limits on As in food.

▾NEWS | SCIENCE SELECTION

Suspect Sweetener: Arsenic Detected in Organic Brown Rice Syrup

Wendee Holtcamp | 120:A204

http://dx.doi.org/10.1289/ehp.120-a204a

Which Fish Should I Eat? Perspectives Influencing Fish Consumption Choices

Emily Oken, Anna L. Choi, Margaret R. Karagas, Koenraad Mariën, Christoph M. Rheinberger, Rita Schoeny, Elsie Sunderland, and Susan Korrick

120:790–798 (2012) | http://dx.doi.org/10.1289/ehp.1104500

Background: Diverse perspectives have influenced fish consumption choices.

Objectives: We summarized the issue of fish consumption choice from toxicological, nutritional, ecological, and economic points of view; identified areas of overlap and disagreement among these viewpoints; and reviewed effects of previous fish consumption advisories.

Methods: We reviewed published scientific literature, public health guidelines, and advisories related to fish consumption, focusing on advisories targeted at U.S. populations. However, our conclusions apply to groups having similar fish consumption patterns.

Discussion: There are many possible combinations of matters related to fish consumption, but few, if any, fish consumption patterns optimize all domains. Fish provides a rich source of protein and other nutrients, but because of contamination by methylmercury and other toxicants, higher fish intake often leads to greater toxicant exposure. Furthermore, stocks of wild fish are not adequate to meet the nutrient demands of the growing world population, and fish consumption choices also have a broad economic impact on the fishing industry. Most guidance does not account for ecological and economic impacts of different fish consumption choices.

Conclusion: Despite the relative lack of information integrating the health, ecological, and economic impacts of different fish choices, clear and simple guidance is necessary to effect desired changes. Thus, more comprehensive advice can be developed to describe the multiple impacts of fish consumption. In addition, policy and fishery management interventions will be necessary to ensure long-term availability of fish as an important source of human nutrition.

▾NEWS | SCIENCE SELECTION

Casting a Wider Net: The Quest for Better Guidance on Seafood Consumption

Kellyn S. Betts | 120:A244

http://dx.doi.org/10.1289/ehp.120-a244b

Exposures

Nutrition Can Modulate the Toxicity of Environmental Pollutants: Implications in Risk Assessment and Human Health

Bernhard Hennig, Lindell Ormsbee, Craig J. McClain, Bruce A. Watkins, Bruce Blumberg, Leonidas G. Bachas, Wayne Sanderson, Claudia Thompson, and William A. Suk

120:771–774 (2012) | http://dx.doi.org/10.1289/ehp.1104712

Background: The paradigm of human risk assessment includes many variables that must be viewed collectively in order to improve human health and prevent chronic disease. The pathology of chronic diseases is complex, however, and may be influenced by exposure to environmental pollutants, a sedentary lifestyle, and poor dietary habits. Much of the emerging evidence suggests that nutrition can modulate the toxicity of environmental pollutants, which may alter human risks associated with toxicant exposures.

Objectives: In this commentary, we discuss the basis for recommending that nutrition be considered a critical variable in disease outcomes associated with exposure to environmental pollutants, thus establishing the importance of incorporating nutrition within the context of cumulative risk assessment.

Discussion: A convincing body of research indicates that nutrition is a modulator of vulnerability to environmental insults; thus, it is timely to consider nutrition as a vital component of human risk assessment. Nutrition may serve as either an agonist or an antagonist (e.g., high-fat foods or foods rich in antioxidants, respectively) of the health impacts associated with exposure to environmental pollutants. Dietary practices and food choices may help explain the large variability observed in human risk assessment.

Conclusion: We recommend that nutrition and dietary practices be incorporated into future environmental research and the development of risk assessment paradigms. Healthful nutrition interventions might be a powerful approach to reduce disease risks associated with many environmental toxic insults and should be considered a variable within the context of cumulative risk assessment and, where appropriate, a potential tool for subsequent risk reduction.

Hexabromocyclododecane (HBCD) Stereoisomers in U.S. Food from Dallas, Texas

Arnold Schecter, David T. Szabo, James Miller, Tyra L. Gent, Noor Malik-Bass, Malte Petersen, Olaf Paepke, Justin A. Colacino, Linda S. Hynan, T. Robert Harris, Sunitha Malla, and Linda S. Birnbaum

120:1260–1264 (2012) | http://dx.doi.org/10.1289/ehp.1204993

Background: Hexabromocyclododecane (HBCD) is a brominated flame retardant used in polystyrene foams in thermal insulation and electrical equipment. The HBCD commercial mixture consists mainly of α, β, and γ stereoisomers. Health concerns of HBCD exposure include alterations in immune and reproductive systems, neurotoxic effects, and endocrine disruption. Stereoisomer-specific levels of HBCD have not been measured previously in U.S. food.

Objectives: We measured HBCD stereoisomer levels in U.S. foods from Dallas, Texas, supermarkets.

Methods: Convenience samples of commonly consumed foods were purchased from supermarkets in Dallas in 2009–2010. Food samples included a wide variety of lipid-rich foods: fish, peanut butter, poultry, pork, and beef. Thirty-six individual food samples were collected in 2010 and analyzed for α-, β-, and γ-HBCD stereoisomers using liquid chromatography–tandem mass spectrometry (LC-MS/MS). Ten pooled food samples previously collected in 2009 for a study of total HBCD levels using gas chromatography–mass spectrometry (GC-MS), were reanalyzed for α-, β-, and γ-HBCD stereoisomers using LC-MS/MS.

Results: Of the 36 measured individual foods, 15 (42%) had detectable levels of HBCD. Median (ranges) of α- and γ-HBCD concentrations were 0.003 (< 0.005–1.307) and 0.005 (< 0.010–0.143) ng/g wet weight (ww), respectively; β-HBCD was present in three samples with a median (range) of 0.003 (< 0.005–0.019) ng/g ww. Median levels (range) for α-, β-, and γ-HBCD, in pooled samples were 0.077 (0.010–0.310), 0.008 (< 0.002–0.070), and 0.024 (0.012–0.170) ng/g ww, respectively.

Conclusions: α-HBCD was detected most frequently and at highest concentrations, followed by γ-, and then β-HBCD, in food samples from Dallas, Texas. Food may be a substantial contributor to the elevated α-HBCD levels observed in humans. These data suggest that larger and more representative sampling should be conducted.

Methodologies *and* Populations

BIOMARKERS AND BIOMONITORING

Maternal and Gestational Factors and Micronucleus Frequencies in Umbilical Blood: The NewGeneris Rhea Cohort in Crete

Kim Vande Loock, Eleni Fthenou, Ilse Decordier, Georgia Chalkiadaki, Maria Keramarou, Gina Plas, Mathieu Roelants, Jos Kleinjans, Leda Chatzi, Franco Merlo, Manolis Kogevinas, and Micheline Kirsch-Volders

119:1460–1465 (2011) | http://dx.doi.org/10.1289/ehp.1003246

Background: The use of cancer-related biomarkers in newborns has been very limited.

Objective: We investigated the formation of micronuclei (MN) in full-term and preterm newborns and their mothers from the Rhea cohort (Crete), applying for the first time in cord blood a validated semiautomated analysis system, in both mono- and binucleated T lymphocytes.

Methods: We assessed MN frequencies in peripheral blood samples from the mothers and in umbilical cord blood samples. We calculated MN in mononucleated (MNMONO) and binucleated (MNBN) T lymphocytes and the cytokinesis block proliferation index (CBPI) in 251 newborns (224 full term) and 223 mothers, including 182 mother–child pairs. Demographic and lifestyle characteristics were collected.

Results: We observed significantly higher MNBN and CBPI levels in mothers than in newborns. In newborns, MNMONO and MNBN were correlated ($r = 0.35$, $p < 0.001$), and we found a moderate correlation between MNMONO in mothers and newborns ($r = 0.26$, $p < 0.001$). MNMONO frequencies in newborns were positively associated with the mother's body mass index and inversely associated with gestational age and mother's age, but we found no significant predictors of MNBN or CBPI in newborns.

Conclusions: Although confirmation is needed by a larger study population, the results indicate the importance of taking into account both mono- and binucleated T lymphocytes for biomonitoring of newborns, because the first reflects damage expressed during *in vivo* cell division and accumulated *in utero*, and the latter includes additional damage expressed as MN during the *in vitro* culture step.

Prioritization of Biomarker Targets in Human Umbilical Cord Blood: Identification of Proteins in Infant Blood Serving as Validated Biomarkers in Adults

Nicole Hansmeier, Tzu-Chiao Chao, Lynn R. Goldman, Frank R. Witter, and Rolf U. Halden

120:764–769 (2012) | http://dx.doi.org/10.1289/ehp.1104190

Background: Early diagnosis represents one of the best lines of defense in the fight against a wide array of human diseases. Umbilical cord blood (UCB) is one of the first easily available diagnostic biofluids and can inform about the health status of newborns. However, compared with adult blood, its diagnostic potential remains largely untapped.

Objectives: Our goal was to accelerate biomarker research on UCB by exploring its detectable protein content and providing a priority list of potential biomarkers based on known proteins involved in disease pathways.

Methods: We explored cord blood serum proteins by profiling a UCB pool of 12 neonates with different backgrounds using a combination of isoelectric focusing and liquid chromatography coupled with matrix-assisted laser desorption/ionization tandem mass spectrometry (MALDI-MS/MS) and by comparing results with information contained in metabolic and disease databases available for adult blood.

Results: A total of 1,210 UCB proteins were identified with a protein-level false discovery rate of ~ 5% as estimated by naïve target-decoy and MAYU approaches, signifying a 6-fold increase in the number of UCB proteins described to date. Identified proteins correspond to 138 different metabolic and disease pathways and provide a platform of mechanistically linked biomarker candidates for tracking disruptions in cellular processes. Moreover, among the identified proteins, 38 were found to be approved biomarkers for adult blood.

Conclusions: The results of this study advance current knowledge of the human cord blood serum proteome. They showcase the potential of UCB as a diagnostic medium for assessing infant health by detection and identification of candidate biomarkers for known disease pathways using a global, nontargeted approach. These biomarkers may inform about mechanisms of exposure–disease relationships. Furthermore, biomarkers approved by the U.S. Food and Drug Administration for screening in adult blood were detected in UCB and represent high-priority targets for immediate validation.

Methodologies *and* Populations

COMMUNITY-BASED PARTICIPATORY RESEARCH AND TRANSLATION

Developing a Bidirectional Academic–Community Partnership with an Appalachian-American Community for Environmental Health Research and Risk Communication

Erin N. Haynes, Caroline Beidler, Richard Wittberg, Lisa Meloncon, Megan Parin, Elizabeth J. Kopras, Paul Succop, and Kim N. Dietrich

119:1364–1372 (2011) | http://dx.doi.org/10.1289/ehp.1003164

Background: Marietta, Ohio, is an Appalachian-American community whose residents have long struggled with understanding their exposure to airborne manganese (Mn). Although community engagement in research is strongly endorsed by the National Institutes of Health and the National Institute of Environmental Health Sciences in particular, little has been documented demonstrating how an academic–community partnership that implements the community-based participatory research (CBPR) principles can be created and mobilized for research.

Objectives: We created a bidirectional, academic–community partnership with an Appalachian-American community to a) identify the community's thoughts and perceptions about local air quality, its effect on health, and the perception of risk communication sources and b) jointly develop and conduct environmental health research.

Methods: We formed a community advisory board (CAB), jointly conducted pilot research studies, and used the results to develop a community-driven research agenda.

Results: Persons in the community were "very concerned" to "concerned" about local air quality (91%) and perceived the air quality to have a direct impact on their health and on their children's health (93% and 94%, respectively). The CAB identified the primary research question: "Does Mn affect the cognition and behavior of children?" Although the community members perceived research scientists as the most trusted and knowledgeable regarding risks from industrial emissions, they received very little risk information from research scientists.

Conclusions: Engaging a community in environmental health research from its onset enhanced the quality and relevance of the research investigation. The CBPR principles were a useful framework in building a strong academic–community partnership. Because of the current disconnect between communities and research scientists, academic researchers should consider working collaboratively with community-based risk communication sources.

EPIGENETICS

In Utero Exposures, Infant Growth, and DNA Methylation of Repetitive Elements and Developmentally Related Genes in Human Placenta

Charlotte S. Wilhelm-Benartzi, E. Andres Houseman, Matthew A. Maccani, Graham M. Poage, Devin C. Koestler, Scott M. Langevin, Luc A. Gagne, Carolyn E. Banister, James F. Padbury, and Carmen J. Marsit

120:296–302 (2012) | http://dx.doi.org/10.1289/ehp.1103927

Background: Fetal programming describes the theory linking environmental conditions during embryonic and fetal development with risk of diseases later in life. Environmental insults *in utero* may lead to changes in epigenetic mechanisms potentially affecting fetal development.

Objectives: We examined associations between *in utero* exposures, infant growth, and methylation of repetitive elements and gene-associated DNA in human term placenta tissue samples.

Methods: Placental tissues and associated demographic and clinical data were obtained from subjects delivering at Women and Infants Hospital in Providence, Rhode Island (USA). Methylation levels of long interspersed nuclear element-1 (LINE-1) and the Alu element AluYb8 were determined in 380 placental samples from term deliveries using bisulfite pyrosequencing. Genomewide DNA methylation profiles were obtained in a subset of 184 samples using the Illumina Infinium HumanMethylation27 BeadArray. Multiple linear regression, model-based clustering methods, and gene set enrichment analysis examined the association between birth weight percentile, demographic variables, and repetitive element methylation and gene-associated CpG locus methylation.

Results: LINE-1 and AluYb8 methylation levels were found to be significantly positively associated with birth weight percentile ($p = 0.01$ and $p < 0.0001$, respectively) and were found to differ significantly among infants exposed to tobacco smoke and alcohol. Increased placental AluYb8 methylation was positively associated with average methylation among CpG loci found in polycomb group target genes; developmentally related transcription factor binding sites were overrepresented for differentially methylated loci associated with both elements.

Conclusions: Our results suggest that repetitive element methylation markers, most notably AluYb8 methylation, may be susceptible to epigenetic alterations resulting from the intrauterine environment and play a critical role in mediating placenta function, and may ultimately inform on the developmental basis of health and disease.

Methodologies *and* Populations

Prenatal Exposure to Polycyclic Aromatic Hydrocarbons, Benzo[*a*]pyrene–DNA Adducts, and Genomic DNA Methylation in Cord Blood

Julie B. Herbstman, Deliang Tang, Deguang Zhu, Lirong Qu, Andreas Sjödin, Zheng Li, David Camann, and Frederica P. Perera

120:733–738 (2012) | http://dx.doi.org/10.1289/ehp.1104056

Background: Polycyclic aromatic hydrocarbons (PAHs) are carcinogenic environmental pollutants generated during incomplete combustion. After exposure and during metabolism, PAHs can form reactive epoxides that can covalently bind to DNA. These PAH–DNA adducts are established markers of cancer risk. PAH exposure has been associated with epigenetic alterations, including genomic cytosine methylation. Both global hypomethylation and hypermethylation of specific genes have been associated with cancer and other diseases in humans. Experimental evidence suggests that PAH–DNA adduct formation may preferentially target methylated genomic regions. Early embryonic development may be a particularly susceptible period for PAH exposure, resulting in both increased PAH–DNA adducts and altered DNA methylation.

Objective: We explored whether prenatal exposure to PAHs is associated with genomic DNA methylation in cord blood and whether methylation levels are associated with the presence of detectable PAH–DNA adducts.

Methods: In a longitudinal cohort study of nonsmoking women in New York City, we measured PAH exposure during pregnancy using personal air monitors, assessed PAH internal dose using prenatal urinary metabolites (in a subset), and quantified benzo[*a*]pyrene–DNA adducts and genomic DNA methylation in cord blood DNA among 164 participants.

Results: Prenatal PAH exposure was associated with lower global methylation in umbilical cord white blood cells ($p = 0.05$), but global methylation levels were positively associated with the presence of detectable adducts in cord blood ($p = 0.01$).

Conclusions: These observations suggest that PAH exposure was adequate to alter global methylation in our study population. Additional epidemiologic studies that can measure site-specific cytosine methylation and adduct formation will improve our ability to understand this complex molecular pathway *in vivo*.

RELATED ARTICLES

EDITORIAL | The Challenge Facing Translation of Basic Science into Clinical and Community Settings to Improve Health Outcomes
Shari Barkin, David Schlundt | 119:A418–A419
http://dx.doi.org/10.1289/ehp.1104467

NEWS | Characterizing Exposomes: Tools for Measuring Personal Environmental Exposures
Kellyn S. Betts | 120:A158–A163
http://dx.doi.org/10.1289/ehp.120-a158

NEWS | Advising Parents in the Face of Scientific Uncertainty: An Environmental Health Dilemma
Naomi Lubick | 119:A436–A441
http://dx.doi.org/10.1289/ehp.119-a436

NEWS | Are We on the Same Page? Action Agenda of the National Conversation on Public Health and Chemical Exposures
Valerie J. Brown | 119:A484–A487
http://dx.doi.org/10.1289/ehp.119-a484

EDITORIAL | The Launch of the International Society for Children's Environmental Health and the Environment (ISCHE)
David C. Bellinger, Lynn R. Goldman, Bruce P. Lanphear, Brenda Eskenazi, David E. Jacobs, Mark Miller | 119:A420–A421
http://dx.doi.org/10.1289/ehp.1104435

PODCAST | Epigenomics and Maternal Smoking, with Bonnie Joubert and Stephanie London
http://dx.doi.org/10.1289/ehp.trp083112

Methodologies *and* Populations

Prenatal Arsenic Exposure and DNA Methylation in Maternal and Umbilical Cord Blood Leukocytes

Molly L. Kile, Andrea Baccarelli, Elaine Hoffman, Letizia Tarantini, Quazi Quamruzzaman, Mahmuder Rahman, Golam Mahiuddin, Golam Mostofa, Yu-Mei Hsueh, Robert O. Wright, and David C. Christiani

120:1061–1066 (2012) | http://dx.doi.org/10.1289/ehp.1104173

Background: Arsenic is an epigenetic toxicant and could influence fetal developmental programming.

Objectives: We evaluated the association between arsenic exposure and DNA methylation in maternal and umbilical cord leukocytes.

Methods: Drinking-water and urine samples were collected when women were at ≤ 28 weeks gestation; the samples were analyzed for arsenic using inductively coupled plasma mass spectrometry. DNA methylation at CpG sites in *p16* ($n = 7$) and *p53* ($n = 4$), and in LINE-1 and Alu repetitive elements (3 CpG sites in each), was quantified using pyrosequencing in 113 pairs of maternal and umbilical blood samples. We used general linear models to evaluate the relationship between DNA methylation and tertiles of arsenic exposure.

Results: Mean (± SD) drinking-water arsenic concentration was 14.8 ± 36.2 µg/L (range: < 1–230 µg/L). Methylation in LINE-1 increased by 1.36% [95% confidence interval (CI): 0.52, 2.21%] and 1.08% (95% CI: 0.07, 2.10%) in umbilical cord and maternal leukocytes, respectively, in association with the highest versus lowest tertile of total urinary arsenic per gram creatinine. Arsenic exposure was also associated with higher methylation of some of the tested CpG sites in the promoter region of *p16* in umbilical cord and maternal leukocytes. No associations were observed for Alu or *p53* methylation.

Conclusions: Exposure to higher levels of arsenic was positively associated with DNA methylation in LINE-1 repeated elements, and to a lesser degree at CpG sites within the promoter region of the tumor suppressor gene *p16*. Associations were observed in both maternal and fetal leukocytes. Future research is needed to confirm these results and determine if these small increases in methylation are associated with any health effects.

Maternal Exposure to Polycyclic Aromatic Hydrocarbons and 5′-CpG Methylation of Interferon-γ in Cord White Blood Cells

Wan-yee Tang, Linda Levin, Glenn Talaska, Yuk Yin Cheung, Julie Herbstman, Deliang Tang, Rachel L. Miller, Frederica Perera, and Shuk-Mei Ho

120:1195–1200 (2012) | http://dx.doi.org/10.1289/ehp.1103744

Background: Maternal factors are implicated in the onset of childhood asthma. Differentiation of naïve $CD4^+$ T lymphocytes into pro-allergic T-helper 2 cells induces interleukin *(IL)4* expression and inhibits interferon *(IFN)*γ expression accompanied by concordant methylation changes in the promoters of these genes. However, it has yet to be established whether maternal exposure to polycyclic aromatic hydrocarbons (PAHs) can alter these gene promoters epigenetically during fetal development.

Objectives: In this study we sought to elucidate the relationship between maternal PAH exposure and promoter methylation status of *IFN*γ and *IL4*.

Methods: We assessed the effects of benzo[*a*]pyrene (BaP), a representative airborne PAH, on the methylation status of the *IFN*γ and *IL4* promoters in Jurkat cells and two lung adenocarcinoma cell lines, and on gene expression. In addition, we evaluated methylation status of the *IFN*γ promoter in cord white blood cells from 53 participants in the Columbia Center for Children's Environmental Health cohort. Maternal PAH exposure was estimated by personal air monitoring during pregnancy.

Results: *In vitro* exposure of the cell models to low, noncytotoxic doses (0.1 and 1 nM) of BaP elicited increased promoter hypermethylation and reduced expression of *IFN*γ but not *IL4*. *IFN*γ promoter methylation in cord white blood cells was associated with maternal PAH exposure in the cohort study subsample.

Conclusion: Consistent with the results for the cell lines, maternal exposure to PAHs was associated with hypermethylation of *IFN*γ in cord blood DNA from cohort children. These findings support a potential role of epigenetics in fetal reprogramming by PAH-induced environmental diseases.

Methodologies *and* Populations

Particulate Matter, DNA Methylation in Nitric Oxide Synthase, and Childhood Respiratory Disease

Carrie V. Breton, Muhammad T. Salam, Xinhui Wang, Hyang-Min Byun, Kimberly D. Siegmund, and Frank D. Gilliland

120:1320–1326 (2012) | http://dx.doi.org/10.1289/ehp.1104439

Background: Air pollutants have been associated with childhood asthma and wheeze. Epigenetic regulation of nitric oxide synthase—the gene responsible for nitric oxide production—may be affected by air pollutants and contribute to the pathogenesis of asthma and wheeze.

Objective: Our goal was to investigate the association between air pollutants, DNA methylation, and respiratory outcomes in children.

Methods: Given residential address and buccal sample collection date, we estimated 7-day, 1-month, 6-month, and 1-year cumulative average $PM_{2.5}$ and PM_{10} (particulate matter ≤ 2.5 and ≤ 10 μm aerodynamic diameter, respectively) exposures for 940 participants in the Children's Health Study. Methylation of 12 CpG sites in three *NOS* (nitric oxide synthase) genes was measured using a bisulfite-polymerase chain reaction Pyrosequencing assay. Beta regression models were used to estimate associations between air pollutants, percent DNA methylation, and respiratory outcomes.

Results: A 5-μg/m^3 increase in $PM_{2.5}$ was associated with a 0.20% [95% confidence interval (CI): −0.32, −0.07] to 1.0% (95% CI: −1.61, −0.56) lower DNA methylation at *NOS2A* position 1, 0.06% (95% CI: −0.18, 0.06) to 0.58% (95% CI: −1.13, −0.02) lower methylation at position 2, and 0.34% (95% CI: −0.57, −0.11) to 0.89% (95% CI: −1.57, −0.21) lower methylation at position 3, depending on the length of exposure and CpG locus. One-year $PM_{2.5}$ exposure was associated with 0.33% (95% CI: 0.01, 0.65) higher in average DNA methylation of 4 loci in the *NOS2A* CpG island. A 5-μg/m^3 increase in 7-day and 1-year $PM_{2.5}$ was associated with 0.6% (95% CI: 0.13, 0.99) and 2.8% (95% CI: 1.77, 3.75) higher *NOS3* DNA methylation. No associations were observed for *NOS1*. PM_{10} showed similar but weaker associations with DNA methylation in these genes.

Conclusions: $PM_{2.5}$ exposure was associated with percent DNA methylation of several CpG loci in NOS genes, suggesting an epigenetic mechanism through which these pollutants may alter production of nitric oxide.

METHODOLOGIES

European Birth Cohorts for Environmental Health Research

Martine Vrijheid, Maribel Casas, Anna Bergström, Amanda Carmichael, Sylvaine Cordier, Merete Eggesbø, Esben Eller, Maria P. Fantini, Mariana F. Fernández, Ana Fernández-Somoano, Ulrike Gehring, Regina Grazuleviciene, Cynthia Hohmann, Anne M. Karvonen, Thomas Keil, Manolis Kogevinas, Gudrun Koppen, Ursula Krämer, Claudia E. Kuehni, Per Magnus, Renata Majewska, Anne-Marie Nybo Andersen, Evridiki Patelarou, Maria Skaalum Petersen, Frank H. Pierik, Kinga Polanska, Daniela Porta, Lorenzo Richiardi, Ana Cristina Santos, Rémy Slama, Radim J. Sram, Carel Thijs, Christina Tischer, Gunnar Toft, Tomáš Trnovec, Stephanie Vandentorren, Tanja G.M. Vrijkotte, Michael Wilhelm, John Wright, and Mark Nieuwenhuijsen

120:29–37 (2012) | http://dx.doi.org/10.1289/ehp.1103823

Background: Many pregnancy and birth cohort studies investigate the health effects of early-life environmental contaminant exposure. An overview of existing studies and their data is needed to improve collaboration, harmonization, and future project planning.

Objectives: Our goal was to create a comprehensive overview of European birth cohorts with environmental exposure data.

Methods: Birth cohort studies were included if they *a*) collected data on at least one environmental exposure, *b*) started enrollment during pregnancy or at birth, *c*) included at least one follow-up point after birth, *d*) included at least 200 mother–child pairs, and *e*) were based in a European country. A questionnaire collected information on basic protocol details and exposure and health outcome assessments, including specific contaminants, methods and samples, timing, and number of subjects. A full inventory can be searched on www.birthcohortsenrieco.net.

Results: Questionnaires were completed by 37 cohort studies of > 350,000 mother–child pairs in 19 European countries. Only three cohorts did not participate. All cohorts collected biological specimens of children or parents. Many cohorts collected information on passive smoking (n = 36), maternal occupation (n = 33), outdoor air pollution (n = 27), and allergens/biological organisms (n = 27). Fewer cohorts (n = 12–19) collected information on water contamination, ionizing or nonionizing radiation exposures, noise, metals, persistent organic pollutants, or other pollutants. All cohorts have information on birth outcomes; nearly all on asthma, allergies, childhood growth and obesity; and 26 collected information on child neurodevelopment.

Conclusion: Combining forces in this field will yield more efficient and conclusive studies and ultimately improve causal inference. This impressive resource of existing birth cohort data could form the basis for longer-term and worldwide coordination of research on environment and child health.

Methodologies *and* Populations

A Method to Estimate the Chronic Health Impact of Air Pollutants in U.S. Residences

Jennifer M. Logue, Phillip N. Price, Max H. Sherman, and Brett C. Singer

120:216–222 (2012) | http://dx.doi.org/10.1289/ehp.1104035

Background: Indoor air pollutants (IAPs) cause multiple health impacts. Prioritizing mitigation options that differentially affect individual pollutants and comparing IAPs with other environmental health hazards require a common metric of harm.

Objectives: Our objective was to demonstrate a methodology to quantify and compare health impacts from IAPs. The methodology is needed to assess population health impacts of large-scale initiatives—including energy efficiency upgrades and ventilation standards—that affect indoor air quality (IAQ).

Methods: Available disease incidence and disease impact models for specific pollutant–disease combinations were synthesized with data on measured concentrations to estimate the chronic heath impact, in disability-adjusted life-years (DALYs) lost, due to inhalation of a subset of IAPs in U.S. residences. Model results were compared with independent estimates of DALYs lost due to disease.

Results: Particulate matter ≤ 2.5 μm in aerodynamic diameter ($PM_{2.5}$), acrolein, and formaldehyde accounted for the vast majority of DALY losses caused by IAPs considered in this analysis, with impacts on par or greater than estimates for secondhand tobacco smoke and radon. Confidence intervals of DALYs lost derived from epidemiology-based response functions are tighter than those derived from toxicology-based, interspecies extrapolations. Statistics on disease incidence in the United States indicate that the upper-bound confidence interval for aggregate IAP harm is implausibly high.

Conclusions: The approach demonstrated in this study may be used to assess regional and national initiatives that affect IAQ at the population level. Cumulative health impacts from inhalation in U.S. residences of the IAPs assessed in this study are estimated at 400–1,100 DALYs lost annually per 100,000 persons.

Evaluation of Developmental Toxicants and Signaling Pathways in a Functional Test Based on the Migration of Human Neural Crest Cells

Bastian Zimmer, Gabsang Lee, Nina V. Balmer, Kesavan Meganathan, Agapios Sachinidis, Lorenz Studer, and Marcel Leist

120:1116–1122 (2012) | http://dx.doi.org/10.1289/ehp.1104489

Background: Information on the potential developmental toxicity (DT) of the majority of chemicals is scarce, and test capacities for further animal-based testing are limited. Therefore, new approaches with higher throughput are required. A screening strategy based on the use of relevant human cell types has been proposed by the U.S. Environmental Protection Agency and others. Because impaired neural crest (NC) function is one of the known causes for teratologic effects, testing of toxicant effects on NC cells is desirable for a DT test battery.

Objective: We developed a robust and widely applicable human-relevant NC function assay that would allow for sensitive screening of environmental toxicants and defining toxicity pathways.

Methods: We generated NC cells from human embryonic stem cells, and after establishing a migration assay of NC cells (MINC assay), we tested environmental toxicants as well as inhibitors of physiological signal transduction pathways.

Results: Methylmercury (50 nM), valproic acid (> 10 μM), and lead-acetate [$Pb(CH_3CO_2)_4$] (1 μM) affected the migration of NC cells more potently than migration of other cell types. The MINC assay correctly identified the NC toxicants triadimefon and triadimenol. Additionally, it showed different sensitivities to various organic and inorganic mercury compounds. Using the MINC assay and applying classic pharmacologic inhibitors and large-scale microarray gene expression profiling, we found several signaling pathways that are relevant for the migration of NC cells.

Conclusions: The MINC assay faithfully models human NC cell migration, and it reveals impairment of this function by developmental toxicants with good sensitivity and specificity.

Human Fetal Testis Xenografts Are Resistant to Phthalate-Induced Endocrine Disruption

Nicholas E. Heger, Susan J. Hall, Moses A. Sandrof, Elizabeth V. McDonnell, Janan B. Hensley, Erin N. McDowell, Kayla A. Martin, Kevin W. Gaido, Kamin J. Johnson, and Kim Boekelheide

120:1137–1143 (2012) | http://dx.doi.org/10.1289/ehp.1104711

Background: *In utero* exposure to endocrine-disrupting chemicals may contribute to testicular dysgenesis syndrome (TDS), a proposed constellation of increasingly common male reproductive tract abnormalities (including hypospadias, cryptorchidism, hypospermatogenesis, and testicular cancer). Male rats exposed *in utero* to certain phthalate plasticizers exhibit multinucleated germ cell (MNG) induction and suppressed steroidogenic gene expression and testosterone production in the fetal testis, causing TDS-consistent effects of hypospadias and cryptorchidism. Mice exposed to phthalates *in utero* exhibit MNG induction only. This disparity in response demonstrates a species-specific sensitivity to phthalate-induced suppression of fetal Leydig cell steroidogenesis. Importantly, *ex vivo* phthalate exposure of the fetal testis does not recapitulate the species-specific endocrine disruption, demonstrating the need for a new bioassay to assess the human response to phthalates.

Objectives: In this study, we aimed to develop and validate a rat and mouse testis xenograft bioassay of phthalate exposure and examine the human fetal testis response.

Methods: Fetal rat, mouse, and human testes were xenografted into immunodeficient rodent hosts, and hosts were gavaged with a range of phthalate doses over multiple days. Xenografts were harvested and assessed for histopathology and steroidogenic end points.

Results: Consistent with the *in utero* response, phthalate exposure induced MNG formation in rat and mouse xenografts, but only rats exhibited suppressed steroidogenesis. Across a range of doses, human fetal testis xenografts exhibited MNG induction but were resistant to suppression of steroidogenic gene expression.

Conclusions: Phthalate exposure of grafted human fetal testis altered fetal germ cells but did not reduce expression of genes that regulate fetal testosterone biosynthesis.

Environmental Health Perspectives (ISSN 0091-6765) is a peer-reviewed publication of the Public Health Service, U.S. Department of Health and Human Services. *EHP* is an open-access monthly journal of peer-reviewed research and news on the impact of the environment on human health. *EHP* also publishes a quarterly *Chinese Edition* (ISSN 1542-6351) and occasional special issues. The Secretary of Health and Human Services has deemed *EHP* to be necessary in the transaction of the public business required by law of this department.

Correspondence: Send all correspondence to Hugh A. Tilson, PhD, Editor-in-Chief, *EHP*, NIEHS/NIH, Mail Drop K3-01, PO Box 12233, Research Triangle Park, NC 27709 USA; phone: 919-541-3280; e-mail: EHPEditor@niehs.nih.gov.

Submissions: See Instructions to Authors online at http://www.ehponline.org/instructions/.

Subscriptions: Call 1-866-541-3841, or go online to http://www.ehponline.org/subscribe.

Address Changes: Send your mailing label(s) for each periodical with corrected information or a description of your subscription problem to Brogan & Partners, Attn: Order Processing, 14600 Weston Parkway, Suite 100, Cary, NC, 27513 USA; fax: 919-678-8696; phone (toll-free) 1-866-541-3841.

ehp | CHILDREN'S HEALTH COLLECTION 2012

OCTOBER 2011–SEPTEMBER 2012

www.ehponline.org