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CHILDREN'S HEALTH COLLECTION 2013

OCTOBER 2012–SEPTEMBER 2013
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Disease Outcomes

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

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
- Radiation
- Built Environment
- Food Safety/Insecurity, Nutrition

Methodologies *and* Populations

- Community-based Participatory Research and Translation/Environmental Justice
- Epigenetics
- Methodologies

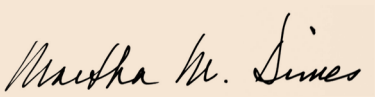
PREFACE

Children's Health Collection 2013 comprises all relevant articles published in *EHP* from October 2012 through September 2013: peer-reviewed research articles, news articles, podcasts, Science Selections, and editorials. Abstracts are featured for each research article, and hyperlinks take readers directly to the full article online (http://www.ehponline.org/). The Science Selections are noted just below the related research.

Under three main sections—Disease Outcomes, Exposures, and Methodologies and Populations—the collection includes all research that has appeared in the Children's Health section of each *EHP* issue as well as relevant reviews and commentaries, research that involves both adult and child cohorts, adult diseases with early origins, experimental models with direct application to children's health, and topics of general interest to children's health researchers and advocates. Some specific topics (e.g., Built Environment) have news articles but not research.

This year has seen a large increase in articles on a variety of heavy metals as well as pesticides and other compounds, indicating that problems involving these exposures are still very much with us. Throughout the topics, study populations are from Asia, Africa, Europe (large pan-European cohorts and others in single countries), Central and South America, arctic Canada, and various rural and urban areas within the United States. Longitudinal birth cohort studies will continue to produce valuable research; and collaboration among cohort studies can suggest ways to integrate measures and methodologies for detailed comparison.

Please see http://www.ehponline.org/collections/ for all the yearly Children's Health collections.



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Disease Outcomes

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ASTHMA/RESPIRATORY DISEASE, LUNG DEVELOPMENT, ALLERGY

The Head-off Environmental Asthma in Louisiana (HEAL) Study—Methods and Study Population

Patricia C. Chulada, Suzanne Kennedy, Mosanda M. Mvula, Katy Jaffee, Jeremy Wildfire, Eleanor Thornton, Richard D. Cohn, L. Faye Grimsley, Herman Mitchell, Jane El-Dahr, Yvonne Sterling, William J. Martin, LuAnn White, Kevin U. Stephens, and Maureen Lichtveld

120:1592–1599 (2012) | http://dx.doi.org/10.1289/ehp.1104239

Background: In the city of New Orleans, Louisiana, and surrounding parishes (NOLA), children with asthma were perilously impacted by Hurricane Katrina as a result of disrupted health care, high home mold and allergen levels, and high stress.

Objectives: The Head-off Environmental Asthma in Louisiana (HEAL) study was conducted to examine relationships between the post-Katrina environment and childhood asthma in NOLA and assess a novel asthma counselor intervention that provided case management and guidance for reducing home mold and allergen levels.

Methods: Children (4–12 years old) with moderate-to-severe asthma were recruited from NOLA schools. Over 1 year, they received two clinical evaluations, three home environmental evaluations, and the asthma intervention. Quarterly end points included symptom days, medication use, and unscheduled emergency department or clinic visits. A community advisory group was assembled and informed HEAL at all phases.

Results: Of the children (n = 182) enrolled in HEAL, 67% were African American, and 25% came from households with annual incomes < $15,000. HEAL children were symptomatic, averaging 6.6 symptom days in the 2 weeks before baseline, and had frequent unscheduled visits to clinics or emergency departments (76% had at least one unscheduled visit in the preceding 3 months). In this report, we describe study design and baseline characteristics of HEAL children.

Conclusions: Despite numerous challenges faced by investigators, study staff, and participants, including destroyed infrastructure, disrupted lives, and lost jobs, HEAL was successful in terms of recruitment and retention, the high quality of data collected that will provide insight into asthma-allergen relationships, and the asthma intervention. This success was attributable to using an adaptive approach and refining processes as needed.

Indoor Environmental Exposures for Children with Asthma Enrolled in the HEAL Study, Post-Katrina New Orleans

L. Faye Grimsley, Patricia C. Chulada, Suzanne Kennedy, LuAnn White, Jeremy Wildfire, Richard D. Cohn, Herman Mitchell, Eleanor Thornton, Jane El-Dahr, Mosanda M. Mvula, Yvonne Sterling, William J. Martin, Kevin U. Stephens, and Maureen Lichtveld

120:1600–1606 (2012) | http://dx.doi.org/10.1289/ehp.1104840

Background: Rain and flooding from Hurricane Katrina resulted in widespread growth of mold and bacteria and production of allergens in New Orleans, Louisiana, which may have led to increased exposures and morbidity in children with asthma.

Objectives: The goal of the Head-off Environmental Asthma in Louisiana (HEAL) study was to characterize post-Katrina exposures to mold and allergens in children with asthma.

Methods: The homes of 182 children with asthma in New Orleans and surrounding parishes were evaluated by visual inspection, temperature and moisture measurements, and air and dust sampling. Air was collected using vacuum-pump spore traps and analyzed for > 30 mold taxa using bright field microscopy. Dust was collected from the children's beds and bedroom floors and analyzed for mouse (Mus m 1), dust mite (Der p 1), cockroach (Bla g 1), and mold (*Alternaria* mix) allergens using ELISA.

Results: More than half (62%) of the children were living in homes that had been damaged by rain, flooding, or both. Geometric mean indoor and outdoor airborne mold levels were 501 and 3,958 spores/m^3, respectively. *Alternaria* antigen was detected in dust from 98% of homes, with 58% having concentrations > 10 µg/g. Mus m 1, Der p 1, and Bla g 1 were detected in 60%, 35%, and 20% of homes, respectively, at low mean concentrations.

Conclusions: Except for *Alternaria* antigen in dust, concentrations of airborne mold (ratio of indoor to outdoor mold) and dust allergens in the homes of HEAL children were lower than measurements found in other studies, possibly because of extensive post-Katrina mold remediation and renovations, or because children moved into cleaner homes upon returning to New Orleans.

Disease Outcomes

Implementation of Evidence-based Asthma Interventions in Post-Katrina New Orleans: The Head-off Environmental Asthma in Louisiana (HEAL) Study

Herman Mitchell, Richard D. Cohn, Jeremy Wildfire, Eleanor Thornton, Suzanne Kennedy, Jane M. El-Dahr, Patricia C. Chulada, Mosanda M. Mvula, L. Faye Grimsley, Maureen Y. Lichtveld, LuAnn E. White, Yvonne M. Sterling, Kevin U. Stephens Sr., and William J. Martin II

120:1607–1612 (2012) | http://dx.doi.org/10.1289/ehp.1104242

Background: Childhood asthma morbidity and mortality in New Orleans, Louisiana, is among the highest in the nation. In August 2005, Hurricane Katrina created an environmental disaster that led to high levels of mold and other allergens and disrupted health care for children with asthma.

Objectives: We implemented a unique hybrid asthma counselor and environmental intervention based on successful National Institutes of Health asthma interventions from the National Cooperative Inner City Asthma (NCICAS) and Inner-City Asthma (ICAS) Studies with the goal of reducing asthma symptoms in New Orleans children after Hurricane Katrina.

Methods: Children (4–12 years old) with moderate-to-severe asthma ($n = 182$) received asthma counseling and environmental intervention for approximately 1 year. HEAL was evaluated employing several analytical approaches including a pre–post evaluation of symptom changes over the entire year, an analysis of symptoms according to the timing of asthma counselor contact, and a comparison to previous evidence-based interventions.

Results: Asthma symptoms during the previous 2 weeks decreased from 6.5 days at enrollment to 3.6 days at the 12-month symptom assessment (a 45% reduction, $p < 0.001$), consistent with changes observed after NCICAS and ICAS interventions (35% and 62% reductions in symptom days, respectively). Children whose families had contact with a HEAL asthma counselor by 6 months showed a 4.09-day decrease [95% confidence interval (CI): 3.25 to 4.94-day decrease] in symptom days, compared with a 1.79-day decrease (95% CI: 0.90, 2.67) among those who had not yet seen an asthma counselor ($p < 0.001$).

Conclusions: The novel combination of evidence-based asthma interventions was associated with improved asthma symptoms among children in post-Katrina New Orleans. Post-intervention changes in symptoms were consistent with previous randomized trials of NCICAS and ICAS interventions.

Near-Roadway Pollution and Childhood Asthma: Implications for Developing "Win–Win" Compact Urban Development and Clean Vehicle Strategies

Laura Perez, Fred Lurmann, John Wilson, Manuel Pastor, Sylvia J. Brandt, Nino Künzli, and Rob McConnell

120:1619–1626 (2012) | http://dx.doi.org/10.1289/ehp.1104785

Background: The emerging consensus that exposure to near-roadway traffic-related pollution causes asthma has implications for compact urban development policies designed to reduce driving and greenhouse gases.

Objectives: We estimated the current burden of childhood asthma-related disease attributable to near-roadway and regional air pollution in Los Angeles County (LAC) and the potential health impact of regional pollution reduction associated with changes in population along major traffic corridors.

Methods: The burden of asthma attributable to the dual effects of near-roadway and regional air pollution was estimated, using nitrogen dioxide and ozone as markers of urban combustion-related and secondary oxidant pollution, respectively. We also estimated the impact of alternative scenarios that assumed a 20% reduction in regional pollution in combination with a 3.6% reduction or 3.6% increase in the proportion of the total population living near major roads, a proxy for near-roadway exposure.

Results: We estimated that 27,100 cases of childhood asthma (8% of total) in LAC were at least partly attributable to pollution associated with residential location within 75 m of a major road. As a result, a substantial proportion of asthma-related morbidity is a consequence of near-roadway pollution, even if symptoms are triggered by other factors. Benefits resulting from a 20% regional pollution reduction varied markedly depending on the associated change in near-roadway proximity.

Conclusions: Our findings suggest that there are large and previously unappreciated public health consequences of air pollution in LAC and probably in other metropolitan areas with dense traffic corridors. To maximize health benefits, compact urban development strategies should be coupled with policies to reduce near-roadway pollution exposure.

» NEWS | SCIENCE SELECTION

Proximity Plus Pollution: Understanding Factors in Asthma among Children Living near Major Roadways

Julia R. Barrett | A436 (November 2012)

http://dx.doi.org/10.1289/ehp.120-A436b

Disease Outcomes

The Air Quality Health Index and Asthma Morbidity: A Population-Based Study

Teresa To, Shixin Shen, Eshetu G. Atenafu, Jun Guan, Susan McLimont, Brian Stocks, and Christopher Licskai

121:46–52 (2013) | http://dx.doi.org/10.1289/ehp.1104816

Background: Exposure to air pollution has been linked to the exacerbation of respiratory diseases. The Air Quality Health Index (AQHI), developed in Canada, is a new health risk scale for reporting air quality and advising risk reduction actions.

Objective: We used the AQHI to estimate the impact of air quality on asthma morbidity, adjusting for potential confounders.

Methods: Daily air pollutant measures were obtained from 14 regional monitoring stations in Ontario. Daily counts of asthma-attributed hospitalizations, emergency department (ED) visits, and outpatient visits were obtained from a provincial registry of 1.5 million patients with asthma. Poisson regression was used to estimate health services rate ratios (RRs) as a measure of association between the AQHI or individual pollutants and health services use. We adjusted for age, sex, season, year, and region of residence.

Results: The AQHI values were significantly associated with increased use of asthma health services on the same day and on the 2 following days, depending on the specific outcome assessed. A 1-unit increase in the AQHI was associated with a 5.6% increase in asthma outpatient visits (RR = 1.056; 95% CI: 1.053, 1.058) and a 2.1% increase in the rate of hospitalization (RR = 1.021; 95% CI: 1.014, 1.028) on the same day and with a 1.3% increase in the rate of ED visits (RR = 1.013; 95% CI: 1.010, 1.017) after a 2-day lag.

Conclusions: The AQHI values were significantly associated with the use of asthma-related health services. Timely AQHI health risk advisories with integrated risk reduction messages may reduce morbidity associated with air pollution in patients with asthma.

Urinary Biomarkers for Phthalates Associated with Asthma in Norwegian Children

Randi J. Bertelsen, Karin C. Lødrup Carlsen, Antonia M. Calafat, Jane A. Hoppin, Geir Håland, Petter Mowinckel, Kai-Håkon Carlsen, and Martinus Løvik

121:251–256 (2013) | http://dx.doi.org/10.1289/ehp.1205256

Background: High-molecular-weight phthalates in indoor dust have been associated with asthma in children, but few studies have evaluated phthalate biomarkers in association with respiratory outcomes.

Objectives: We explored the association between urinary concentrations of phthalate metabolites and current asthma.

Methods: In a cross-sectional analysis, 11 metabolites of 8 phthalates [including four metabolites of di(2-ethylhexyl) phthalate] were measured in one first morning void collected from 2001 through 2004 from 623 10-year-old Norwegian children. Logistic regression models controlling for urine specific gravity, sex, parental asthma, and income were used to estimate associations between current asthma and phthalate metabolite concentrations by quartiles or as $\log_{10}$-transformed variables.

Results: Current asthma was associated with both mono(carboxyoctyl) phthalate (MCOP) and mono(carboxynonyl) phthalate (MCNP), although the association was limited to those in the highest quartile of these chemicals. The adjusted odds ratio (aOR) for current asthma was 1.9 (95% CI: 1.0, 3.3) for the highest MCOP quartile compared with the lowest quartile, and 1.3 (95% CI: 0.98, 1.7) for an interquartile-range increase. The aOR for current asthma was 2.2 (95% CI: 1.2, 4.0) for the highest MCNP quartile and 1.3 (95% CI: 1.0, 1.7) for an interquartile-range increase. The other phthalate metabolites were not associated with current asthma.

Conclusions: Current asthma was associated with the highest quartiles of MCOP and MCNP, metabolites of two high molecular weight phthalates, diisononyl phthalate and diisodecyl phthalate, respectively. Given the short biological half-life of the phthalates and the cross-sectional design, our findings should be interpreted cautiously.

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Phthalates and Childhood Asthma: Revealing an Association through Urinary Biomarkers

Tanya Tillett | A59 (February 2013)

http://dx.doi.org/10.1289/ehp.121-A59

Urban Tree Canopy and Asthma, Wheeze, Rhinitis, and Allergic Sensitization to Tree Pollen in a New York City Birth Cohort

Gina S. Lovasi, Jarlath P.M. O'Neil-Dunne, Jacqueline W.T. Lu, Daniel Sheehan, Matthew S. Perzanowski, Sean W. MacFaden, Kristen L. King, Thomas Matte, Rachel L. Miller, Lori A. Hoepner, Frederica P. Perera, and Andrew Rundle

121:494–500 (2013) | http://dx.doi.org/10.1289/ehp.1205513

Background: Urban landscape elements, particularly trees, have the potential to affect airflow, air quality, and production of aeroallergens. Several large-scale urban tree planting projects have sought to promote respiratory health, yet evidence linking tree cover to human health is limited.

Objectives: We sought to investigate the association of tree canopy cover with subsequent development of childhood asthma, wheeze, rhinitis, and allergic sensitization.

Methods: Birth cohort study data were linked to detailed geographic information systems data characterizing 2001 tree canopy coverage based on LiDAR (light detection and ranging) and multispectral imagery within 0.25 km of the prenatal address. A total of 549 Dominican or African-American children born in 1998–2006 had outcome data assessed by validated questionnaire or based on IgE antibody response to specific allergens, including a tree pollen mix.

Results: Tree canopy coverage did not significantly predict outcomes at 5 years of age, but was positively associated with asthma and allergic sensitization at 7 years. Adjusted risk ratios (RRs) per standard deviation of tree canopy coverage were 1.17 for asthma (95% CI: 1.02, 1.33), 1.20 for any specific allergic sensitization (95% CI: 1.05, 1.37), and 1.43 for tree pollen allergic sensitization (95% CI: 1.19, 1.72).

Conclusions: Results did not support the hypothesized protective association of urban tree canopy coverage with asthma or allergy-related outcomes. Tree canopy cover near the prenatal address was associated with higher prevalence of allergic sensitization to tree pollen. Information was not available on sensitization to specific tree species or individual pollen exposures, and results may not be generalizable to other populations or geographic areas.

Serum Polyfluoroalkyl Concentrations, Asthma Outcomes, and Immunological Markers in a Case–Control Study of Taiwanese Children

Guang-Hui Dong, Kuan-Yen Tung, Ching-Hui Tsai, Miao-Miao Liu, Da Wang, Wei Liu, Yi-He Jin, Wu-Shiun Hsieh, Yungling Leo Lee, and Pau-Chung Chen

121:507–513 (2013) | http://dx.doi.org/10.1289/ehp.1205351

Background: Perfluorinated compounds (PFCs) are ubiquitous pollutants. Experimental data suggest that they may be associated with adverse health outcomes, including asthma. However, there is little supporting epidemiological evidence.

Methods: A total of 231 asthmatic children and 225 nonasthmatic controls, all from northern Taiwan, were recruited in the Genetic and Biomarkers study for Childhood Asthma. Structure questionnaires were administered by face-to-face interview. Serum concentrations of 11 PFCs and levels of immunological markers were also measured. Associations of PFC quartiles with concentrations of immunological markers and asthma outcomes were estimated using multivariable regression models.

Results: Nine PFCs were detectable in most children (≥ 84.4%), of which perfluorooctane sulfonate (PFOS) was the most abundant (median serum concentrations of 33.9 ng/mL in asthmatics and 28.9 ng/mL in controls). Adjusted odds ratios for asthma among those with the highest versus lowest quartile of PFC exposure ranged from 1.81 (95% CI: 1.02, 3.23) for the perfluorododecanoic acid (PFDoA) to 4.05 (95% CI: 2.21, 7.42) for perfluorooctanic acid (PFOA). PFOS, PFOA, and subsets of the other PFCs were positively associated with serum IgE concentrations, absolute eosinophil counts (AEC), eosinophilic cationic protein (ECP) concentrations, and asthma severity scores among asthmatics.

Conclusions: This study suggests an association between PFC exposure and juvenile asthma. Because of widespread exposure to these chemicals, these findings may be of potential public health concern.

NEURODEVELOPMENTAL/NEUROBEHAVIORAL DISORDERS

Developmental Fluoride Neurotoxicity: A Systematic Review and Meta-Analysis

Anna L. Choi, Guifan Sun, Ying Zhang, and Philippe Grandjean

120:1362–1368 (2012) | http://dx.doi.org/10.1289/ehp.1104912

Background: Although fluoride may cause neurotoxicity in animal models and acute fluoride poisoning causes neurotoxicity in adults, very little is known of its effects on children's neurodevelopment.

Objective: We performed a systematic review and meta-analysis of published studies to investigate the effects of increased fluoride exposure and delayed neurobehavioral development.

Methods: We searched the MEDLINE, EMBASE, Water Resources Abstracts, and TOXNET databases through 2011 for eligible studies. We also searched the China National Knowledge Infrastructure (CNKI) database, because many studies on fluoride neurotoxicity have been published in Chinese journals only. In total, we identified 27 eligible epidemiological studies with high and reference exposures, end points of IQ scores, or related cognitive function measures with means and variances for the two exposure groups. Using random-effects models, we estimated the standardized mean difference between exposed and reference groups across all studies. We conducted sensitivity analyses restricted to studies using the same outcome assessment and having drinking-water fluoride as the only exposure. We performed the Cochran test for heterogeneity between studies, Begg's funnel plot, and Egger test to assess publication bias, and conducted meta-regressions to explore sources of variation in mean differences among the studies.

Results: The standardized weighted mean difference in IQ score between exposed and reference populations was –0.45 (95% confidence interval: –0.56, –0.35) using a random-effects model. Thus, children in high-fluoride areas had significantly lower IQ scores than those who lived in low-fluoride areas. Subgroup and sensitivity analyses also indicated inverse associations, although the substantial heterogeneity did not appear to decrease.

Conclusions: The results support the possibility of an adverse effect of high fluoride exposure on children's neurodevelopment. Future research should include detailed individual-level information on prenatal exposure, neurobehavioral performance, and covariates for adjustment.

In Utero and Childhood Polybrominated Diphenyl Ether (PBDE) Exposures and Neurodevelopment in the CHAMACOS Study

Brenda Eskenazi, Jonathan Chevrier, Stephen A. Rauch, Katherine Kogut, Kim G. Harley, Caroline Johnson, Celina Trujillo, Andreas Sjödin, and Asa Bradman

121:257–262 (2013) | http://dx.doi.org/10.1289/ehp.1205597

Background: California children's exposures to polybrominated diphenyl ether flame retardants (PBDEs) are among the highest worldwide. PBDEs are known endocrine disruptors and neurotoxicants in animals.

Objective: Here we investigate the relation of *in utero* and child PBDE exposure to neurobehavioral development among participants in CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas), a California birth cohort.

Methods: We measured PBDEs in maternal prenatal and child serum samples and examined the association of PBDE concentrations with children's attention, motor functioning, and cognition at 5 (n = 310) and 7 years of age (n = 323).

Results: Maternal prenatal PBDE concentrations were associated with impaired attention as measured by a continuous performance task at 5 years and maternal report at 5 and 7 years of age, with poorer fine motor coordination—particularly in the nondominant—at both age points, and with decrements in Verbal and Full-Scale IQ at 7 years. PBDE concentrations in children 7 years of age were significantly or marginally associated with concurrent teacher reports of attention problems and decrements in Processing Speed, Perceptual Reasoning, Verbal Comprehension, and Full-Scale IQ. These associations were not altered by adjustment for birth weight, gestational age, or maternal thyroid hormone levels.

Conclusions: Both prenatal and childhood PBDE exposures were associated with poorer attention, fine motor coordination, and cognition in the CHAMACOS cohort of school-age children. This study, the largest to date, contributes to growing evidence suggesting that PBDEs have adverse impacts on child neurobehavioral development.

» NEWS | SCIENCE SELECTION

Lasting Impacts: Pre- and Postnatal PBDE Exposures Linked to IQ Deficits

Kellyn S. Betts | A58 (February 2013)

http://dx.doi.org/10.1289/ehp.121-A58

Prenatal *p,p´*-DDE Exposure and Neurodevelopment among Children 3.5–5 Years of Age

Luisa Torres-Sánchez, Lourdes Schnaas, Stephen J. Rothenberg, Mariano E. Cebrián, Erika Osorio-Valencia, María del Carmen Hernández, Rosa María García-Hernández, and Lizbeth López-Carrillo

121:263–268 (2013) | http://dx.doi.org/10.1289/ehp.12050

Background: The results of previous studies suggest that prenatal exposure to bis[*p*-chlorophenyl]-1,1,1-trichloroethane (DDT) and to its main metabolite, 2,2-bis(*p*-chlorophenyl)-1,1-dichloroethylene (DDE), impairs psychomotor development during the first year of life. However, information about the persistence of this association at later ages is limited.

Objectives: We assessed the association of prenatal DDE exposure with child neurodevelopment at 42–60 months of age.

Methods: Since 2001 we have been monitoring the neurodevelopment in children who were recruited at birth into a perinatal cohort exposed to DDT, in the state of Morelos, Mexico. We report McCarthy Scales of Children's Abilities for 203 children at 42, 48, 54, and 60 months of age. Maternal DDE serum levels were available for at least one trimester of pregnancy. The Home Observation for Measurement of the Environment scale and other covariables of interest were also available.

Results: After adjustment, a doubling of DDE during the third trimester of pregnancy was associated with statistically significant reductions of –1.37, –0.88, –0.84, and –0.80 points in the general cognitive index, quantitative, verbal, and memory components respectively. The association between prenatal DDE and the quantitative component was weaker at 42 months than at older ages. No significant statistical interactions with sex or breastfeeding were observed.

Conclusions: These findings support the hypothesis that prenatal DDE impairs early child neurodevelopment; the potential for adverse effects on development should be considered when using DDT for malaria control.

Traffic-Related Air Pollution Exposure in the First Year of Life and Behavioral Scores at 7 Years of Age

Nicholas C. Newman, Patrick Ryan, Grace LeMasters, Linda Levin, David Bernstein, Gurjit K. Khurana Hershey, James E. Lockey, Manuel Villareal, Tiina Reponen, Sergey Grinshpun, Heidi Sucharew, and Kim N. Dietrich

121:731–736 (2013) | http://dx.doi.org/10.1289/ehp.1205555

Background: There is increasing concern about the potential effects of traffic-related air pollution (TRAP) on the developing brain. The impact of TRAP exposure on childhood behavior is not fully understood because of limited epidemiologic studies.

Objective: We explored the association between early-life exposure to TRAP using a surrogate, elemental carbon attributed to traffic (ECAT), and attention deficit/hyperactivity disorder (ADHD) symptoms at 7 years of age.

Methods: From the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) birth cohort we collected data on exposure to ECAT during infancy and behavioral scores at 7 years of age. Children enrolled in CCAAPS had at least one atopic parent and a birth residence either < 400 m or > 1,500 m from a major highway. Children were followed from infancy through 7 years of age. ECAT exposure during the first year of life was estimated based on measurements from 27 air sampling sites and land use regression modeling. Parents completed the Behavioral Assessment System for Children, 2nd Edition, when the child was 7 years of age. ADHD-related symptoms were assessed using the Hyperactivity, Attention Problems, Aggression, Conduct Problems, and Atypicality subscales.

Results: Exposure to the highest tertile of ECAT during the child's first year of life was significantly associated with Hyperactivity *T*-scores in the "at risk" range at 7 years of age, after adjustment [adjusted odds ratio (aOR) = 1.7; 95% CI: 1.0, 2.7]. Stratification by maternal education revealed a stronger association in children whose mothers had higher education (aOR = 2.3; 95% CI: 1.3, 4.1).

Conclusions: ECAT exposure during infancy was associated with higher Hyperactivity scores in children; this association was limited to children whose mothers had more than a high school education.

Associations between Traffic-Related Black Carbon Exposure and Attention in a Prospective Birth Cohort of Urban Children

Yueh-Hsiu Mathilda Chiu, David C. Bellinger, Brent A. Coull, Shawn Anderson, Rachel Barber, Robert O. Wright, and Rosalind J. Wright

121:859–864 (2013) | http://dx.doi.org/10.1289/ehp.1205940

Background: Ambient air pollution may have neurotoxic effects in children. Data examining associations between traffic-related air pollution and attention domains remain sparse.

Objectives: We examined associations between black carbon (BC), a marker of traffic particles, and attention measures ascertained at 7–14 years of age among 174 children in a birth cohort based in the Boston, Massachusetts, area.

Methods: We estimated BC levels using a validated spatial–temporal land-use regression model based on residence during children's lifetime. Children completed the Conner's Continuous Performance Test (CPT) measuring omission errors, commission errors, and hit reaction time (HRT), with higher scores indicating increased errors or slower reaction time. Multivariable-adjusted linear regression analyses were used to examine associations between BC and each attention outcome.

Results: Children were primarily Hispanic (56%) and Caucasian (41%); 53% were boys. We found a positive association between higher BC levels with increased commission errors and slower HRT, adjusting for child IQ, age, sex, blood lead level, maternal education, pre- and postnatal tobacco smoke exposure, and community-level social stress. Notably, the association was weaker, though still positive, for the highest BC quartile relative to the middle two quartiles. Sex-stratified analysis demonstrated statistically significant associations between BC and both commission errors and HRT in boys, but BC was not significantly associated with any of the CPT outcomes in girls.

Conclusions: In this population of urban children, we found associations between BC exposure and higher commission errors and slower reaction time. These associations were overall more apparent in boys than girls.

AUTISM

Ambient Air Pollution and Autism in Los Angeles County, California

Tracy Ann Becerra, Michelle Wilhelm, Jørn Olsen, Myles Cockburn, and Beate Ritz

121:380–386 (2013) | http://dx.doi.org/10.1289/ehp.1205827

Background: The prevalence of autistic disorder (AD), a serious developmental condition, has risen dramatically over the past two decades, but high-quality population-based research addressing etiology is limited.

Objectives: We studied the influence of exposures to traffic-related air pollution during pregnancy on the development of autism using data from air monitoring stations and a land use regression (LUR) model to estimate exposures.

Methods: Children of mothers who gave birth in Los Angeles, California, who were diagnosed with a primary AD diagnosis at 3–5 years of age during 1998–2009 were identified through the California Department of Developmental Services and linked to 1995–2006 California birth certificates. For 7,603 children with autism and 10 controls per case matched by sex, birth year, and minimum gestational age, birth addresses were mapped and linked to the nearest air monitoring station and a LUR model. We used conditional logistic regression, adjusting for maternal and perinatal characteristics including indicators of SES.

Results: Per interquartile range (IQR) increase, we estimated a 12–15% relative increase in odds of autism for ozone [odds ratio (OR) = 1.12, 95% CI: 1.06, 1.19; per 11.54-ppb increase] and particulate matter ≤ 2.5 μm (OR = 1.15; 95% CI: 1.06, 1.24; per 4.68-$\mu g/m^3$ increase) when mutually adjusting for both pollutants. Furthermore, we estimated 3–9% relative increases in odds per IQR increase for LUR-based nitric oxide and nitrogen dioxide exposure estimates. LUR-based associations were strongest for children of mothers with less than a high school education.

Conclusion: Measured and estimated exposures from ambient pollutant monitors and LUR model suggest associations between autism and prenatal air pollution exposure, mostly related to traffic sources.

Perinatal Air Pollutant Exposures and Autism Spectrum Disorder in the Children of Nurses' Health Study II Participants

Andrea L. Roberts, Kristen Lyall, Jaime E. Hart, Francine Laden, Allan C. Just, Jennifer F. Bobb, Karestan C. Koenen, Alberto Ascherio, and Marc G. Weisskopf

121:978–984 (2013) | http://dx.doi.org/10.1289/ehp.1206187

Objective: Air pollution contains many toxicants known to affect neurological function and to have effects on the fetus *in utero*. Recent studies have reported associations between perinatal exposure to air pollutants and autism spectrum disorder (ASD) in children. We tested the hypothesis that perinatal exposure to air pollutants is associated with ASD, focusing on pollutants associated with ASD in prior studies.

Methods: We estimated associations between U.S. Environmental Protection Agency–modeled levels of hazardous air pollutants at the time and place of birth and ASD in the children of participants in the Nurses' Health Study II (325 cases, 22,101 controls). Our analyses focused on pollutants associated with ASD in prior research. We accounted for possible confounding and ascertainment bias by adjusting for family-level socioeconomic status (maternal grandparents' education) and census tract–level socioeconomic measures (e.g., tract median income and percent college educated), as well as maternal age at birth and year of birth. We also examined possible differences in the relationship between ASD and pollutant exposures by child's sex.

Results: Perinatal exposures to the highest versus lowest quintile of diesel, lead, manganese, mercury, methylene chloride, and an overall measure of metals were significantly associated with ASD, with odds ratios ranging from 1.5 (for overall metals measure) to 2.0 (for diesel and mercury). In addition, linear trends were positive and statistically significant for these exposures ($p < .05$ for each). For most pollutants, associations were stronger for boys (279 cases) than for girls (46 cases) and significantly different according to sex.

Conclusions: Perinatal exposure to air pollutants may increase risk for ASD. Additionally, future studies should consider sex-specific biological pathways connecting perinatal exposure to pollutants with ASD.

CANCERS

In Utero Pesticide Exposure and Leukemia in Brazilian Children < 2 Years of Age

Jeniffer Dantas Ferreira, Arnaldo Cézar Couto, Maria S. Pombo-de-Oliveira, Sergio Koifman, and the Brazilian Collaborative Study Group of Infant Acute Leukemia

121:269–275 (2013) | http://dx.doi.org/10.1289/ehp.1103942

Background: An association between pesticide exposure and cancer has been suggested. Infant leukemia is a rare neoplasm and its association with maternal pesticide exposure has been poorly explored.

Objectives: We investigated the association between pesticide exposure during pregnancy and leukemia in children < 2 years of age.

Methods: A hospital-based case–control study was carried out in 13 Brazilian states during 1999–2007. Mothers of 252 cases and those of 423 controls were interviewed. Information on pesticide exposures 3 months before pregnancy, throughout pregnancy, and during breastfeeding was obtained. Unconditional logistic regression was used to estimate adjusted odds ratios (aORs) for associations between pesticide exposures and leukemia.

Results: Associations with ever use of pesticides during pregnancy were observed for acute lymphoid leukemia (ALL) (aOR = 2.10; 95% CI: 1.14, 3.86) and acute myeloid leukemia (AML) (aOR = 5.01; 95% CI: 1.97, 12.7) in children 0–11 months of age, and with ALL (aOR = 1.88; 95% CI: 1.05, 5.23) at 12–23 months of age. According to reported maternal exposure to permethrin, higher risk estimates were verified for children 0–11 months of age (aOR = 2.47; 95% CI: 1.17, 5.25 for ALL; and aOR = 7.28; 95% CI: 2.60, 20.38 for AML). Maternal pesticide exposure related to agricultural activities showed an aOR of 5.25 (95% CI: 1.83, 15.08) for ALL, and an aOR of 7.56 (95% CI: 1.83, 31.23) for AML.

Conclusions: These results support the hypothesis that pesticide exposure during pregnancy may be involved in the etiology of acute leukemia in children < 2 years of age.

Disease Outcomes

Characterization of Residential Pesticide Use and Chemical Formulations through Self-Report and Household Inventory: The Northern California Childhood Leukemia Study

Neela Guha, Mary H. Ward, Robert Gunier, Joanne S. Colt, C. Suzanne Lea, Patricia A. Buffler, and Catherine Metayer

121:276–282 (2013) | http://dx.doi.org/10.1289/ehp.1204926

Background: Home and garden pesticide use has been linked to cancer and other health outcomes in numerous epidemiological studies. Exposure has generally been self-reported, so the assessment is potentially limited by recall bias and lack of information on specific chemicals.

Objectives: As part of an integrated assessment of residential pesticide exposure, we identified active ingredients and described patterns of storage and use.

Methods: During a home interview of 500 residentially stable households enrolled in the Northern California Childhood Leukemia Study during 2001–2006, trained interviewers inventoried residential pesticide products and queried participants about their storage and use. U.S. Environmental Protection Agency registration numbers, recorded from pesticide product labels, and pesticide chemical codes were matched to public databases to obtain information on active ingredients and chemical class. Poisson regression was used to identify independent predictors of pesticide storage. Analyses were restricted to 259 participating control households.

Results: Ninety-five percent (246 of 259) of the control households stored at least one pesticide product (median, 4). Indicators of higher sociodemographic status predicted more products in storage. We identified the most common characteristics: storage areas (garage, 40%; kitchen, 20%), pests treated (ants, 33%; weeds, 20%), pesticide types (insecticides, 46%; herbicides, 24%), chemical classes (pyrethroids, 77%; botanicals, 50%), active ingredients (pyrethrins, 43%) and synergists (piperonyl butoxide, 42%). Products could contain multiple active ingredients.

Conclusions: Our data on specific active ingredients and patterns of storage and use will inform future etiologic analyses of residential pesticide exposures from self-reported data, particularly among households with young children.

Environmental and Occupational Interventions for Primary Prevention of Cancer: A Cross-Sectorial Policy Framework

Carolina Espina, Miquel Porta, Joachim Schüz, Ildefonso Hernández Aguado, Robert V. Percival, Carlos Dora, Terry Slevin, Julietta Rodriguez Guzman, Tim Meredith, Philip J. Landrigan, and Maria Neira

121:420–426 (2013) | http://dx.doi.org/10.1289/ehp.1205897

Background: Nearly 13 million new cancer cases and 7.6 million cancer deaths occur worldwide each year; 63% of cancer deaths occur in low- and middle-income countries. A substantial proportion of all cancers are attributable to carcinogenic exposures in the environment and the workplace.

Objective: We aimed to develop an evidence-based global vision and strategy for the primary prevention of environmental and occupational cancer.

Methods: We identified relevant studies through PubMed by using combinations of the search terms "environmental," "occupational," "exposure," "cancer," "primary prevention," and "interventions." To supplement the literature review, we convened an international conference titled "Environmental and Occupational Determinants of Cancer: Interventions for Primary Prevention" under the auspices of the World Health Organization, in Asturias, Spain, on 17–18 March 2011.

Discussion: Many cancers of environmental and occupational origin could be prevented. Prevention is most effectively achieved through primary prevention policies that reduce or eliminate involuntary exposures to proven and probable carcinogens. Such strategies can be implemented in a straightforward and cost-effective way based on current knowledge, and they have the added benefit of synergistically reducing risks for other noncommunicable diseases by reducing exposures to shared risk factors.

Conclusions: Opportunities exist to revitalize comprehensive global cancer control policies by incorporating primary interventions against environmental and occupational carcinogens.

BIRTH DEFECTS

A Population-Based Case–Control Study of Extreme Summer Temperature and Birth Defects

Alissa R. Van Zutphen, Shao Lin, Barbara A. Fletcher, and Syni-An Hwang

120:1443–1449 (2012) | http://dx.doi.org/10.1289/ehp.1104671

Background: Although hyperthermia is a recognized animal teratogen and maternal fever has been associated with birth defects in humans, data on the relationship between high environmental temperatures and birth defects are limited.

Objective: To determine whether pregnancies are potentially vulnerable to the weather extremes anticipated with climate change, we evaluated the relationship between extreme summer temperature and the occurrence of birth defects.

Methods: We performed a population-based case–control study by linking the New York State Congenital Malformations Registry to birth certificates for the years 1992–2006. We selected nonmalformed infants from a 10% random sample of live births as controls. We assigned meteorologic data based on maternal residence at birth, summarized universal apparent temperature (UAT; degrees Fahrenheit) across the critical period of embryogenesis, and estimated adjusted odds ratios (aOR) and 95% confidence intervals (CI) with multivariable logistic regression, controlling for confounders available on the birth certificate.

Results: Among 6,422 cases and 59,328 controls that shared at least 1 week of the critical period in summer, a 5-degree increase in mean daily minimum UAT was significantly associated with congenital cataracts (aOR = 1.51; 95% CI: 1.14, 1.99). Congenital cataracts were significantly associated with all ambient temperature indicators as well: heat wave, number of heat waves, and number of days above the 90th percentile. Inconsistent associations with a subset of temperature indicators were observed for renal agenesis/hypoplasia (positive) and anophthalmia/microphthalmia and gastroschisis (negative).

Conclusions: We found positive and consistent associations between multiple heat indicators during the relevant developmental window and congenital cataracts which should be confirmed with other data sources.

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David C. Holzman | A75 (March 2013)
http://dx.doi.org/10.1289/ehp.121-A75

In Utero Exposure to Dioxins and Dioxin-like Compounds and Anogenital Distance in Newborns and Infants

Marina Vafeiadi, Silvia Agramunt, Eleni Papadopoulou, Harrie Besselink, Kleopatra Mathianaki, Polyxeni Karakosta, Ariana Spanaki, Antonis Koutis, Leda Chatzi, Martine Vrijheid, and Manolis Kogevinas

121:125–130 (2013) | http://dx.doi.org/10.1289/ehp.1205221

Background: Anogenital distance in animals is used as a measure of fetal androgen action. Prenatal exposure to dioxins and dioxin-like compounds in rodents causes reproductive changes in male offspring and decreases anogenital distance.

Objective: We assessed whether *in utero* exposure to dioxins and dioxin-like compounds adversely influences anogenital distance in newborns and young children (median age, 16 months; range, 1–31 months).

Methods: We measured anogenital distance among participants of the "Rhea" mother–child cohort study in Crete and the Hospital del Mar (HMAR) cohort in Barcelona. Anogenital distance (AGD; anus to upper penis), anoscrotal distance (ASD; anus to scrotum), and penis width (PW) were measured in 119 newborn and 239 young boys; anoclitoral (ACD; anus to clitoris) and anofourchetal distance (AFD; anus to fourchette) were measured in 118 newborn and 223 young girls. We estimated plasma dioxin-like activity in maternal blood samples collected at delivery with the Dioxin-Responsive Chemically Activated LUciferase eXpression (DR CALUX®) bioassay.

Results: Anogenital distances were sexually dimorphic, being longer in males than females. Plasma dioxin-like activity was negatively associated with AGD in male newborns. The estimated change in AGD per 10 pg CALUX®–toxic equivalent/g lipid increase was –0.44 mm (95% CI: –0.80, –0.08) after adjusting for confounders. Negative but smaller and nonsignificant associations were observed for AGD in young boys. No associations were found in girls.

Conclusions: Male infants may be susceptible to endocrine-disrupting effects of dioxins. Our findings are consistent with the experimental animal evidence used by the Food and Agriculture Organization/World Health Organization to set recommendations for human dioxin intake.

Prenatal Nitrate Intake from Drinking Water and Selected Birth Defects in Offspring of Participants in the National Birth Defects Prevention Study

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121:1083–1089 (2013) | http://dx.doi.org/10.1289/ehp.1206249

Background: Previous studies of prenatal exposure to drinking-water nitrate and birth defects in offspring have not accounted for water consumption patterns or potential interaction with nitrosatable drugs.

Objectives: We examined the relation between prenatal exposure to drinking-water nitrate and selected birth defects, accounting for maternal water consumption patterns and nitrosatable drug exposure.

Methods: With data from the National Birth Defects Prevention Study, we linked addresses of 3,300 case mothers and 1,121 control mothers from the Iowa and Texas sites to public water supplies and respective nitrate measurements. We assigned nitrate levels for bottled water from collection of representative samples and standard laboratory testing. Daily nitrate consumption was estimated from self-reported water consumption at home and work.

Results: With the lowest tertile of nitrate intake around conception as the referent group, mothers of babies with spina bifida were 2.0 times more likely (95% CI: 1.3, 3.2) to ingest ≥ 5 mg nitrate daily from drinking water (vs. < 0.91 mg) than control mothers. During 1 month preconception through the first trimester, mothers of limb deficiency, cleft palate, and cleft lip cases were, respectively, 1.8 (95% CI: 1.1, 3.1), 1.9 (95% CI: 1.2, 3.1), and 1.8 (95% CI: 1.1, 3.1) times more likely than control mothers to ingest ≥ 5.42 mg of nitrate daily (vs. < 1.0 mg). Higher water nitrate intake did not increase associations between prenatal nitrosatable drug use and birth defects.

Conclusions: Higher water nitrate intake was associated with several birth defects in offspring, but did not strengthen associations between nitrosatable drugs and birth defects.

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

Surrounding Greenness and Pregnancy Outcomes in Four Spanish Birth Cohorts

Payam Dadvand, Jordi Sunyer, Xavier Basagaña, Ferran Ballester, Aitana Lertxundi, Ana Fernández-Somoano, Marisa Estarlich, Raquel García-Esteban, Michelle A. Mendez, and Mark J. Nieuwenhuijsen

120:1481–1487 (2012) | http://dx.doi.org/10.1289/ehp.1205244

Background: Green spaces have been associated with improved physical and mental health; however, the available evidence on the impact of green spaces on pregnancy is scarce.

Objectives: We investigated the association between surrounding greenness and birth weight, head circumference, and gestational age at delivery.

Methods: This study was based on 2,393 singleton live births from four Spanish birth cohorts (Asturias, Gipuzkoa, Sabadell, and Valencia) located in two regions of the Iberian Peninsula with distinct climates and vegetation patterns (2003–2008). We defined surrounding greenness as average of satellite-based Normalized Difference Vegetation Index (NDVI) (Landsat 4–5 TM data at 30 m × 30 m resolution) during 2007 in buffers of 100 m, 250 m, and 500 m around each maternal place of residence. Separate linear mixed models with adjustment for potential confounders and a random cohort effect were used to estimate the change in birth weight, head circumference, and gestational age for 1-interquartile range increase in surrounding greenness.

Results: Higher surrounding greenness was associated with increases in birth weight and head circumference [adjusted regression coefficients (95% confidence interval) of 44.2 g (20.2 g, 68.2 g) and 1.7 mm (0.5 mm, 2.9 mm) for an interquartile range increase in average NDVI within a 500-m buffer] but not gestational age. These findings were robust against the choice of the buffer size and the season of data acquisition for surrounding greenness, and when the analysis was limited to term births. Stratified analyses indicated stronger associations among children of mothers with lower education, suggesting greater benefits from surrounding greenness.

Conclusions: Our findings suggest a beneficial impact of surrounding greenness on measures of fetal growth but not pregnancy length.

Birth Weight, Head Circumference, and Prenatal Exposure to Acrylamide from Maternal Diet: The European Prospective Mother–Child Study (NewGeneris)

Marie Pedersen, Hans von Stedingk, Maria Botsivali, Silvia Agramunt, Jan Alexander, Gunnar Brunborg, Leda Chatzi, Sarah Fleming, Eleni Fthenou, Berit Granum, Kristine B. Gutzkow, Laura J. Hardie, Lisbeth E. Knudsen, Soterios A. Kyrtopoulos, Michelle A. Mendez, Domenico F. Merlo, Jeanette K. Nielsen, Per Rydberg, Dan Segerbäck, Jordi Sunyer, John Wright, Margareta Törnqvist, Jos C. Kleinjans, Manolis Kogevinas, and the NewGeneris Consortium

120:1739–1745 (2012) | http://dx.doi.org/10.1289/ehp.1205327

Background: Acrylamide is a common dietary exposure that crosses the human placenta. It is classified as a probable human carcinogen, and developmental toxicity has been observed in rodents.

Objectives: We examined the associations between prenatal exposure to acrylamide and birth outcomes in a prospective European mother–child study.

Methods: Hemoglobin (Hb) adducts of acrylamide and its metabolite glycidamide were measured in cord blood (reflecting cumulated exposure in the last months of pregnancy) from 1,101 singleton pregnant women recruited in Denmark, England, Greece, Norway, and Spain during 2006–2010. Maternal diet was estimated through food-frequency questionnaires.

Results: Both acrylamide and glycidamide Hb adducts were associated with a statistically significant reduction in birth weight and head circumference. The estimated difference in birth weight for infants in the highest versus lowest quartile of acrylamide Hb adduct levels after adjusting for gestational age and country was –132 g (95% CI: –207, –56); the corresponding difference for head circumference was –0.33 cm (95% CI: –0.61, –0.06). Findings were similar in infants of nonsmokers, were consistent across countries, and remained after adjustment for factors associated with reduced birth weight. Maternal consumption of foods rich in acrylamide, such as fried potatoes, was associated with cord blood acrylamide adduct levels and with reduced birth weight.

Conclusions: Dietary exposure to acrylamide was associated with reduced birth weight and head circumference. Consumption of specific foods during pregnancy was associated with higher acrylamide exposure *in utero*. If confirmed, these findings suggest that dietary intake of acrylamide should be reduced among pregnant women.

» NEWS | SCIENCE SELECTION

Crispy Cravings May Affect Baby's Health: Prenatal Acrylamide Exposure Is Associated with Reduced Birth Weight

Julia R. Barrett | A475 (December 2012)

http://dx.doi.org/10.1289/ehp.120-A475b

Airborne $PM_{2.5}$ Chemical Components and Low Birth Weight in the Northeastern and Mid-Atlantic Regions of the United States

Keita Ebisu and Michelle L. Bell

120:1746–1752 (2012) | http://dx.doi.org/10.1289/ehp.1104763

Background: Previous studies on air pollutants and birth outcomes have reported inconsistent results. Chemical components of particulate matter ≤ 2.5 μm ($PM_{2.5}$) composition are spatially heterogeneous, which might contribute to discrepancies across $PM_{2.5}$ studies.

Objectives: We explored whether birth weight at term is affected by $PM_{2.5}$, PM_{10} (PM ≤ 10 μm), and gaseous pollutants.

Methods: We calculated exposures during gestation and each trimester for $PM_{2.5}$ chemical components, PM_{10}, $PM_{2.5}$, carbon monoxide, nitrogen dioxide, ozone, and sulfur dioxide for births in 2000–2007 for states in the northeastern and mid-Atlantic United States. Associations between exposures and risk of low birth weight (LBW) were adjusted by family and individual characteristics and region. Interaction terms were used to investigate whether risk differs by race or sex.

Results: Several $PM_{2.5}$ chemical components were associated with LBW. Risk increased 4.9% (95% CI: 3.4, 6.5%), 4.7% (3.2, 6.2%), 5.7% (2.7, 8.8%), and 5.0% (3.1, 7.0%) per interquartile range increase of $PM_{2.5}$ aluminum, elemental carbon, nickel, and titanium, respectively. Other $PM_{2.5}$ chemical components and gaseous pollutants showed associations, but were not statistically significant in multipollutant models. The trimester associated with the highest relative risk differed among pollutants. Effect estimates for $PM_{2.5}$ elemental carbon and nickel were higher for infants of white mothers than for those of African-American mothers, and for males than females.

Conclusions: Most exposure levels in our study area were in compliance with U.S. Environmental Protection Agency air pollution standards; however, we identified associations between $PM_{2.5}$ components and LBW. Findings suggest that some $PM_{2.5}$ components may be more harmful than others, and that some groups may be particularly susceptible.

Persistent Environmental Pollutants and Couple Fecundity: The LIFE Study

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121:231–236 (2013) | http://dx.doi.org/10.1289/ehp.1205301

Background: Evidence suggesting that persistent environmental pollutants may be reproductive toxicants underscores the need for prospective studies of couples for whom exposures are measured.

Objectives: We examined the relationship between selected persistent pollutants and couple fecundity as measured by time to pregnancy.

Methods: A cohort of 501 couples who discontinued contraception to become pregnant was prospectively followed for 12 months of trying to conceive or until a human chorionic gonadotrophin (hCG) test confirmed pregnancy. Couples completed daily journals on lifestyle and provided biospecimens for the quantification of 9 organochlorine pesticides, 1 polybrominated biphenyl, 10 polybrominated diphenyl ethers, 36 polychlorinated biphenyls (PCBs), and 7 perfluorochemicals (PFCs) in serum. Using Cox models for discrete time, we estimated fecundability odds ratios (FORs) and 95% CIs separately for each partner's concentrations adjusting for age, body mass index, serum cotinine, serum lipids (except for PFCs), and study site (Michigan or Texas); sensitivity models were further adjusted for left truncation or time off of contraception (≤ 2 months) before enrollment.

Results: The adjusted reduction in fecundability associated with standard deviation increases in log-transformed serum concentrations ranged between 18% and 21% for PCB congeners 118, 167, 209, and perfluorooctane sulfonamide in females; and between 17% and 29% for *p,p´*-DDE and PCB congeners 138, 156, 157, 167, 170, 172, and 209 in males. The strongest associations were observed for PCB 167 (FOR 0.79; 95% CI: 0.64, 0.97) in females and PCB 138 (FOR = 0.71; 95% CI: 0.52, 0.98) in males.

Conclusions: In this couple-based prospective cohort study with preconception enrollment and quantification of exposures in both female and male partners, we observed that a subset of persistent environmental chemicals were associated with reduced fecundity.

Maternal Exposure to Particulate Air Pollution and Term Birth Weight: A Multi-Country Evaluation of Effect and Heterogeneity

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121:367–373 (2013) | http://dx.doi.org/10.1289/ehp.1205575

Background: A growing body of evidence has associated maternal exposure to air pollution with adverse effects on fetal growth; however, the existing literature is inconsistent.

Objectives: We aimed to quantify the association between maternal exposure to particulate air pollution and term birth weight and low birth weight (LBW) across 14 centers from 9 countries, and to explore the influence of site characteristics and exposure assessment methods on between-center heterogeneity in this association.

Methods: Using a common analytical protocol, International Collaboration on Air Pollution and Pregnancy Outcomes (ICAPPO) centers generated effect estimates for term LBW and continuous birth weight associated with PM_{10} and $PM_{2.5}$ (particulate matter ≤ 10 and 2.5 μm). We used meta-analysis to combine the estimates of effect across centers (~ 3 million births) and used meta-regression to evaluate the influence of center characteristics and exposure assessment methods on between-center heterogeneity in reported effect estimates.

Results: In random-effects meta-analyses, term LBW was positively associated with a 10-μg/m^3 increase in PM_{10} [odds ratio (OR) = 1.03; 95% CI: 1.01, 1.05] and $PM_{2.5}$ (OR = 1.10; 95% CI: 1.03, 1.18) exposure during the entire pregnancy, adjusted for maternal socioeconomic status. A 10-μg/m^3 increase in PM_{10} exposure was also negatively associated with term birth weight as a continuous outcome in the fully adjusted random-effects meta-analyses (–8.9 g; 95% CI: –13.2, –4.6 g). Meta-regressions revealed that centers with higher median $PM_{2.5}$ levels and $PM_{2.5}$:PM_{10} ratios, and centers that used a temporal exposure assessment (compared with spatiotemporal), tended to report stronger associations.

Conclusion: Maternal exposure to particulate pollution was associated with LBW at term across study populations. We detected three site characteristics and aspects of exposure assessment methodology that appeared to contribute to the variation in associations reported by centers.

» NEWS | SCIENCE SELECTION

Global Push: Multicontinent Project Assesses Particulate Matter and Birth Weight

Tanya Tillett | A94 (March 2013)

http://dx.doi.org/10.1289/ehp.121-A94

Dietary Acrylamide Intake during Pregnancy and Fetal Growth—Results from the Norwegian Mother and Child Cohort Study (MoBa)

Talita Duarte-Salles, Hans von Stedingk, Berit Granum, Kristine B. Gützkow, Per Rydberg, Margareta Törnqvist, Michelle A. Mendez, Gunnar Brunborg, Anne Lise Brantsæter, Helle Margrete Meltzer, Jan Alexander, and Margaretha Haugen

121:374–379 (2013) | http://dx.doi.org/10.1289/ehp.1205396

Background: Acrylamide has shown developmental and reproductive toxicity in animals, as well as neurotoxic effects in humans with occupational exposures. Because it is widespread in food and can pass through the human placenta, concerns have been raised about potential developmental effects of dietary exposures in humans.

Objectives: We assessed associations of prenatal exposure to dietary acrylamide with small for gestational age (SGA) and birth weight.

Methods: This study included 50,651 women in the Norwegian Mother and Child Cohort Study (MoBa). Acrylamide exposure assessment was based on intake estimates obtained from a food frequency questionnaire (FFQ), which were compared with hemoglobin (Hb) adduct measurements reflecting acrylamide exposure in a subset of samples (n = 79). Data on infant birth weight and gestational age were obtained from the Medical Birth Registry of Norway. Multivariable regression was used to estimate associations between prenatal acrylamide and birth outcomes.

Results: Acrylamide intake during pregnancy was negatively associated with fetal growth. When women in the highest quartile of acrylamide intake were compared with women in the lowest quartile, the multivariable-adjusted odds ratio (OR) for SGA was 1.11 (95% CI: 1.02, 1.21) and the coefficient for birth weight was –25.7 g (95% CI: –35.9, –15.4). Results were similar after excluding mothers who smoked during pregnancy. Maternal acrylamide– and glycidamide–Hb adduct levels were correlated with estimated dietary acrylamide intakes (Spearman correlations = 0.24; 95% CI: 0.02, 0.44; and 0.48; 95% CI: 0.29, 0.63, respectively).

Conclusions: Lowering dietary acrylamide intake during pregnancy may improve fetal growth.

Fetal Growth and Prenatal Exposure to Bisphenol A: The Generation R Study

Claudia A. Snijder, Dick Heederik, Frank H. Pierik, Albert Hofman, Vincent W. Jaddoe, Holger M. Koch, Matthew P. Longnecker, and Alex Burdorf

121:393–398 (2013) | http://dx.doi.org/10.1289/ehp.1205296

Background: Prenatal exposure to bisphenol A (BPA) has been associated with adverse birth outcomes, but findings of previous studies have been inconsistent.

Objective: We investigated the relation of prenatal BPA exposure with intrauterine growth and evaluated the effect of the number of measurements per subject on observed associations.

Methods: This study was embedded in a Dutch population-based prospective cohort study, with urine samples collected during early, mid-, and late pregnancy. The study comprised 219 women, of whom 99 had one measurement, 40 had two measurements, and 80 had three measurements of urinary BPA. Fetal growth characteristics were repeatedly measured by ultrasound during pregnancy and combined with measurements at birth. Linear regression models for repeated measurements of both BPA and fetal growth were used to estimate associations between urinary concentrations of creatinine-based BPA (BPA_{CB}) and intrauterine growth.

Results: The relationship between BPA_{CB} and fetal growth was sensitive to the number of BPA measurements per woman. Among 80 women with three BPA measurements, women with BPA_{CB} > 4.22 µg/g crea (creatinine) had lower growth rates for fetal weight and head circumference than did women with BPA_{CB} < 1.54 µg/g crea, with estimated differences in mean values at birth of –683 g (20.3% of mean) and –3.9 cm (11.5% of mean), respectively. When fewer measurements were available per woman, the exposure–response relationship became progressively attenuated and statistically nonsignificant.

Conclusion: Our findings suggest that maternal urinary BPA may impair fetal growth. Because previous studies have shown contradictory findings, further evidence is needed to corroborate these findings in the general population.

INFECTIONS

Acute Lower Respiratory Infection in Childhood and Household Fuel Use in Bhaktapur, Nepal

Michael N. Bates, Ram K. Chandyo, Palle Valentiner-Branth, Amod K. Pokhrel, Maria Mathisen, Sudha Basnet, Prakash S. Shrestha, Tor A. Strand, and Kirk R. Smith

121:637–642 (2013) | http://dx.doi.org/10.1289/ehp.1205491

Background: Globally, solid fuels are used by about 3 billion people for cooking. These fuels have been associated with many health effects, including acute lower respiratory infection (ALRI) in young children. Nepal has a high prevalence of use of biomass for cooking and heating.

Objective: This case–control study was conducted among a population in the Bhaktapur municipality, Nepal, to investigate the relationship of cookfuel type to ALRI in young children.

Methods: Cases with ALRI and age-matched controls were enrolled from an open cohort of children 2–35 months old, under active monthly surveillance for ALRI. A questionnaire was used to obtain information on family characteristics, including household cooking and heating appliances and fuels. The main analysis was carried out using conditional logistic regression. Population-attributable fractions (PAF) for stove types were calculated.

Results: A total of 917 children (452 cases and 465 controls) were recruited into the study. Relative to use of electricity for cooking, ALRI was increased in association with any use of biomass stoves [odds ratio (OR) = 1.93; 95% CI: 1.24, 2.98], kerosene stoves (OR = 1.87; 95% CI: 1.24, 2.83), and gas stoves (OR = 1.62; 95% CI: 1.05, 2.50). Use of wood, kerosene, or coal heating was also associated with ALRI (OR = 1.45; 95% CI: 0.97, 2.14), compared with no heating or electricity or gas heating. PAFs for ALRI were 18.0% (95% CI: 8.1, 26.9%) and 18.7% (95% CI: 8.4%–27.8%), for biomass and kerosene stoves, respectively.

Conclusions: The study supports previous reports indicating that use of biomass as a household fuel is a risk factor for ALRI, and provides new evidence that use of kerosene for cooking may also be a risk factor for ALRI in young children.

FETAL OR EARLY-LIFE EXPOSURES CONTRIBUTING TO ADULT DISEASE

Predicting Later-Life Outcomes of Early-Life Exposures

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120:1353–1361 (2012) | http://dx.doi.org/10.1289/ehp.1204934

Background: *In utero* exposure of the fetus to a stressor can lead to disease in later life. Epigenetic mechanisms are likely mediators of later-life expression of early-life events.

Objectives: We examined the current state of understanding of later-life diseases resulting from early-life exposures in order to identify *in utero* and postnatal indicators of later-life diseases, develop an agenda for future research, and consider the risk assessment implications of this emerging knowledge.

Methods: This review was developed based on our participation in a National Research Council workshop titled "Use of *in Utero* and Postnatal Indicators to Predict Health Outcomes Later in Life: State of the Science and Research Recommendations." We used a case study approach to highlight the later-life consequences of early-life malnutrition and arsenic exposure.

Discussion: The environmental sensitivity of the epigenome is viewed as an adaptive mechanism by which the developing organism adjusts its metabolic and homeostatic systems to suit the anticipated extrauterine environment. Inappropriate adaptation may produce a mismatch resulting in subsequent increased susceptibility to disease. A nutritional mismatch between the prenatal and postnatal environments, or early-life obesogen exposure, may explain at least some of the recent rapid increases in the rates of obesity, type 2 diabetes, and cardiovascular diseases. Early-life arsenic exposure is also associated with later-life diseases, including cardiovascular disease and cancer.

Conclusions: With mounting evidence connecting early-life exposures and later-life disease, new strategies are needed to incorporate this emerging knowledge into health protective practices.

» NEWS | SCIENCE SELECTION

Asking the Right Questions: How Early-Life Exposures Influence Later Development of Disease

Julia R. Barrett | A403 (October 2012)

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Mortality in Young Adults following *in Utero* and Childhood Exposure to Arsenic in Drinking Water

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120:1527–1531 (2012) | http://dx.doi.org/10.1289/ehp.1104867

Background: Beginning in 1958, the city of Antofagasta in northern Chile was exposed to high arsenic concentrations (870 µg/L) when it switched water sources. The exposure abruptly stopped in 1970 when an arsenic-removal plant commenced operations. A unique exposure scenario like this—with an abrupt start, clear end, and large population (125,000 in 1970), all with essentially the same exposure—is rare in environmental epidemiology. Evidence of increased mortality from lung cancer, bronchiectasis, myocardial infarction, and kidney cancer has been reported among young adults who were *in utero* or children during the high-exposure period.

Objective: We investigated other causes of mortality in Antofagasta among 30- to 49-year-old adults who were *in utero* or ≤ 18 years of age during the high-exposure period.

Methods: We compared mortality data between Antofagasta and the rest of Chile for people 30–49 years of age during 1989–2000. We estimated expected deaths from mortality rates in all of Chile, excluding Region II where Antofagasta is located, and calculated standardized mortality ratios (SMRs).

Results: We found evidence of increased mortality from bladder cancer [SMR = 18.1; 95% confidence interval (CI): 11.3, 27.4], laryngeal cancer (SMR = 8.1; 95% CI: 3.5, 16.0), liver cancer (SMR = 2.5; 95% CI: 1.6, 3.7), and chronic renal disease (SMR = 2.0; 95% CI: 1.5, 2.8).

Conclusions: Taking together our findings in the present study and previous evidence of increased mortality from other causes of death, we conclude that arsenic in Antofagasta drinking water has resulted in the greatest increases in mortality in adults < 50 years of age ever associated with early-life environmental exposure.

Exposure to Tobacco Smoke *in Utero* and Subsequent Plasma Lipids, ApoB, and CRP among Adult Women in the MoBa Cohort

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120:1532–1537 (2012) | http://dx.doi.org/10.1289/ehp.1104563

Background: Recent findings suggest that maternal smoking during pregnancy may play a role in the development of metabolic alterations in offspring during childhood. However, whether such exposure increases the risk of developing similar metabolic alterations during adulthood is uncertain.

Objective: We evaluated the association of *in utero* exposure to maternal tobacco smoke with plasma lipids, apolipoprotein B (apoB), and C-reactive protein (CRP) in adulthood.

Methods: The study was based on a subsample of the Norwegian Mother and Child Cohort Study (MoBa) and included 479 pregnant women with plasma lipids, apoB, and CRP measurements. Information on *in utero* exposure to tobacco smoke, personal smoking, and other factors were obtained from the women by a self-completed questionnaire at enrollment, at approximately 17 weeks of gestation.

Results: Women exposed to tobacco smoke *in utero* had higher triglycerides [10.7% higher; 95% confidence interval (CI): 3.9, 17.9] and lower high-density lipoprotein cholesterol (HDL) (–1.9 mg/dL; 95% CI: –4.3, 0.5) compared with unexposed women, after adjusting for age, physical activity, education, personal smoking, and current body mass index (BMI). Exposed women were also more likely to have triglycerides ≥ 200 mg/dL [adjusted odds ratio (aOR) = 2.5; 95% CI: 1.3, 5.1] and HDL < 50 mg/dL (aOR = 2.3; 95% CI: 1.1, 5.0). Low-density lipoprotein cholesterol, total cholesterol, and apoB were not associated with the exposure. CRP was increased among exposed women; however, after adjustment for BMI, the association was completely attenuated.

Conclusions: In this population, *in utero* exposure to tobacco smoke was associated with high triglycerides and low HDL in adulthood, 18–44 years after exposure.

Childhood Thyroid Radioiodine Exposure and Subsequent Infertility in the Intermountain Fallout Cohort

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121:79–84 (2013) | http://dx.doi.org/10.1289/ehp.1104231

Background: Above-ground and underground nuclear weapon detonation at the Nevada Test Site (1951–1992) has resulted in radioiodine exposure for nearby populations. Although the long-term effect of environmental radioiodine exposure on thyroid disease has been well studied, little is known regarding the effect of childhood radioiodine exposure on subsequent fertility.

Objectives: We investigated early childhood thyroid radiation exposure from nuclear testing fallout (supplied predominantly by radioactive isotopes of iodine) and self-reported lifetime incidence of male or female infertility or sterility.

Methods: Participants were members of the 1965 Intermountain Fallout Cohort, schoolchildren at the time of exposure who were reexamined during two subsequent study phases to collect dietary and reproductive histories. Thyroid radiation exposure was calculated via an updated dosimetry model. We used multivariable logistic regression with robust sandwich estimators to estimate odds ratios for infertility, adjusted for potential confounders and (in separate models) for a medically confirmed history of thyroid disease.

Results: Of 1,389 participants with dosimetry and known fertility history, 274 were classified as infertile, including 30 classified as sterile. Childhood thyroid radiation dose was possibly associated with infertility [adjusted odds ratio (AOR) = 1.17; 95% CI: 0.82, 1.67 and AOR = 1.35; 95% CI: 0.96, 1.90 for the middle and upper tertiles vs. the first tertile of exposure, respectively]. The odds ratios were attenuated (AOR = 1.08; 95% CI: 0.75, 1.55 and AOR = 1.29; 95% CI: 0.91, 1.83 for the middle and upper tertiles, respectively) after adjusting for thyroid disease. There was no association of childhood radiation dose and sterility.

Conclusion: Our findings suggest that childhood radioiodine exposure from nuclear testing may be related to subsequent adult infertility. Further research is required to confirm this.

Associations of *in Utero* Exposure to Perfluorinated Alkyl Acids with Human Semen Quality and Reproductive Hormones in Adult Men

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121:453–458 (2013) | http://dx.doi.org/10.1289/ehp.1205118

Background: Perfluorinated alkyl acids (PFAAs), persistent chemicals with unique water-, dirt-, and oil-repellent properties, are suspected of having endocrine-disrupting activity. The PFAA compounds perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) are found globally in humans; because they readily cross the placental barrier, *in utero* exposure may be a cause for concern.

Objectives: We investigated whether *in utero* exposure to PFOA and PFOS affects semen quality, testicular volume, and reproductive hormone levels.

Methods: We recruited 169 male offspring (19–21 years of age) from a pregnancy cohort established in Aarhus, Denmark, in 1988–1989, corresponding to 37.6% of the eligible sons. Each man provided a semen sample and a blood sample. Semen samples were analyzed for sperm concentration, total sperm count, motility, and morphology, and blood samples were used to measure reproductive hormones. As a proxy for *in utero* exposure, PFOA and PFOS were measured in maternal blood samples from pregnancy week 30.

Results: Multivariable linear regression analysis suggested that *in utero* exposure to PFOA was associated with lower adjusted sperm concentration ($p_{trend} = 0.01$) and total sperm count ($p_{trend} = 0.001$) and with higher adjusted levels of luteinizing hormone ($p_{trend} = 0.03$) and follicle-stimulating hormone ($p_{trend} = 0.01$). PFOS did not appear to be associated with any of the outcomes assessed, before or after adjustment.

Conclusions: The results suggest that *in utero* exposure to PFOA may affect adult human male semen quality and reproductive hormone levels.

Prenatal Exposure to the Pesticide DDT and Hypertension Diagnosed in Women before Age 50: A Longitudinal Birth Cohort Study

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121:594–599 (2013) | http://dx.doi.org/10.1289/ehp.1205921

Background: Elevated levels of the pesticide DDT (dichlorodiphenyltrichloroethane) have been positively associated with blood pressure and hypertension in studies among adults. Accumulating epidemiologic and toxicologic evidence suggests that hypertension during adulthood may also be affected by earlier life and possibly the prenatal environment.

Objectives: We assessed whether prenatal exposure to the pesticide DDT increases risk of adult hypertension.

Methods: We examined concentrations of DDT (*p,p´*- and *o,p´*-) and its metabolite *p,p´*-DDE (dichlorodiphenyldichloroethylene) in prenatal serum samples from a subset of women ($n = 527$) who had participated in the prospective Child Health and Development Studies birth cohort in the San Francisco Bay area while they were pregnant between 1959 and 1967. We surveyed daughters 39–47 years of age by telephone interview from 2005 to 2008 to obtain information on self-reported physician-diagnosed hypertension and use of hypertensive medication. We used multivariable regression analysis of time to hypertension based on the Cox proportional hazards model to estimate relative rates for the association between prenatal DDT exposures and hypertension treated with medication in adulthood, with adjustment for potential confounding by maternal, early-life, and adult exposures.

Results: Prenatal *p,p´*-DDT exposure was associated with hypertension [adjusted hazard ratio (aHR) = 3.6; 95% CI: 1.8, 7.2 and aHR = 2.5; 95% CI: 1.2, 5.3 for middle and high tertiles of *p,p´*-DDT relative to the lowest tertile, respectively]. These associations between *p,p´*-DDT and hypertension were robust to adjustment for independent hypertension risk factors as well as sensitivity analyses.

Conclusions: These findings suggest that the association between DDT exposure and hypertension may have its origins early in development.

Diabetes, Metabolic Syndrome, and Obesity in Relation to Serum Dioxin Concentrations: The Seveso Women's Health Study

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121:906–911 (2013) | http://dx.doi.org/10.1289/ehp.1206113

Background: In animal studies, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) alters glucose transport and increases serum lipid levels and blood pressure. Epidemiologic evidence suggests an association between TCDD and metabolic disease.

Objectives: On 10 July 1976, a chemical explosion in Seveso, Italy, resulted in the highest known residential exposure to TCDD. Using data from the Seveso Women's Health Study (SWHS), a cohort study of the health of the women, we examined the relation of serum TCDD to diabetes, metabolic syndrome, and obesity > 30 years later.

Methods: In 1996, we enrolled 981 women who were newborn to 40 years of age in 1976 and resided in the most contaminated areas. Individual TCDD concentration was measured in archived serum that had been collected soon after the explosion. In 2008, 833 women participated in a follow-up study. Diabetes was classified based on self-report or fasting serum glucose and glycated hemoglobin levels. Metabolic syndrome was defined by International Diabetes Federation criteria. Obesity was defined as body mass index ≥ 30 kg/m^2.

Results: A 10-fold increase in serum TCDD ($\log_{10}$TCDD) was not associated with diabetes (adjusted hazard ratio = 0.76; 95% CI: 0.45, 1.28) or obesity [adjusted odds ratio (OR) = 0.80; 95% CI: 0.58, 1.10]. $\log_{10}$TCDD was associated with metabolic syndrome, but only among women who were ≤ 12 years of age at the time of the explosion (adjusted OR = 2.03; 95% CI: 1.25, 3.29; $p_{\text{interaction}} = 0.01$).

Conclusions: We found an increased prevalence of metabolic syndrome associated with TCDD, but only among women who were the youngest at the time of the explosion. Continued follow-up of the SWHS cohort will be informative.

OBESITY

Evaluation of the Association between Maternal Smoking, Childhood Obesity, and Metabolic Disorders: A National Toxicology Program Workshop Review

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121:170–180 (2013) | http://dx.doi.org/10.1289/ehp.1205404

Background: An emerging literature suggests that environmental chemicals may play a role in the development of childhood obesity and metabolic disorders, especially when exposure occurs early in life.

Objective: Here we assess the association between these health outcomes and exposure to maternal smoking during pregnancy as part of a broader effort to develop a research agenda to better understand the role of environmental chemicals as potential risk factors for obesity and metabolic disorders.

Methods: PubMed was searched up to 8 March 2012 for epidemiological and experimental animal studies related to maternal smoking or nicotine exposure during pregnancy and childhood obesity or metabolic disorders at any age. A total of 101 studies—83 in humans and 18 in animals—were identified as the primary literature.

Discussion: Current epidemiological data support a positive association between maternal smoking and increased risk of obesity or overweight in offspring. The data strongly suggest a causal relation, although the possibility that the association is attributable to unmeasured residual confounding cannot be completely ruled out. This conclusion is supported by findings from laboratory animals exposed to nicotine during development. The existing literature on human exposures does not support an association between maternal smoking during pregnancy and type 1 diabetes in offspring. Too few human studies have assessed outcomes related to type 2 diabetes or metabolic syndrome to reach conclusions based on patterns of findings. There may be a number of mechanistic pathways important for the development of aberrant metabolic outcomes following perinatal exposure to cigarette smoke, which remain largely unexplored.

Conclusions: From a toxicological perspective, the linkages between maternal smoking during pregnancy and childhood overweight/obesity provide proof-of-concept of how early-life exposure to an environmental toxicant can be a risk factor for childhood obesity.

In Utero DDT and DDE Exposure and Obesity Status of 7-Year-Old Mexican-American Children in the CHAMACOS Cohort

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121:631–636 (2013) | http://dx.doi.org/10.1289/ehp.1205656

Background: *In utero* exposure to endocrine disrupting compounds including dichlorodiphenyltrichloroethane (DDT) and dichlorodiphenyldichloroethylene (DDE) has been hypothesized to increase risk of obesity later in life.

Objectives: The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study is a longitudinal birth cohort of low-income Latinas living in a California agricultural community. We examined the relation of *in utero* DDT and DDE exposure to child obesity at 7 years of age. We also examined the trend with age (2, 3.5, 5, and 7 years) in the exposure–obesity relation.

Methods: We included 270 children with *o,p´*-DDT, *p,p´*-DDT, and *p,p´*-DDE concentrations measured in maternal serum during pregnancy (nanograms per gram lipid) and complete 7-year follow-up data including weight (kilograms) and height (centimeters). Body mass index (BMI; kilograms per meter squared) was calculated and obesity was defined as ≥ 95th percentile on the sex-specific BMI-for-age Centers for Disease Control and Prevention 2000 growth charts.

Results: At 7 years, 96 (35.6%) children were obese. A 10-fold increase in *o,p´*-DDT, *p,p´*-DDT, or *p,p´*-DDE, was nonsignificantly associated with increased odds (OR) of obesity [*o,p´*-DDT adjusted (adj-) OR = 1.17, 95% CI: 0.75, 1.82; *p,p´*-DDT adj-OR = 1.19, 95% CI: 0.81, 1.74; *p,p´*-DDE adj-OR = 1.22, 95% CI: 0.72, 2.06]. With increasing age at follow-up, we observed a significant trend toward a positive association between DDT and DDE exposure and odds of obesity.

Conclusion: We did not find a significant positive relation between *in utero* DDT and DDE exposure and obesity status of 7-year-old children. However, given the observed trend with age, continued follow-up will be informative.

Prenatal Exposure to Persistent Organochlorines and Childhood Obesity in the U.S. Collaborative Perinatal Project

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121:1103–1109 (2013) | http://dx.doi.org/10.1289/ehp.1205901

Background: In some previous studies, prenatal exposure to persistent organochlorines such as 1,1,-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (*p,p´*-DDE), polychlorinated biphenyls (PCBs), and hexachlorobenzene (HCB) has been associated with higher body mass index (BMI) in children.

Objective: Our goal was to evaluate the association of maternal serum levels of β-hexachlorocyclohexane (β-HCH), *p,p´*-DDE, dichlorodiphenyltrichloroethane (*p,p´*-DDT), dieldrin, heptachlor epoxide, HCB, *trans*-nonachlor, oxychlordane, and PCBs with offspring obesity during childhood.

Methods: The analysis was based on a subsample of 1,915 children followed until 7 years of age as part of the U.S. Collaborative Perinatal Project (CPP). The CPP enrolled pregnant women in 1959–1965; exposure levels were measured in third-trimester maternal serum that was collected before these organochlorines were banned in the United States. Childhood overweight and obesity were defined using age- and sex-specific cut points for BMI as recommended by the International Obesity Task Force.

Results: Adjusted results did not show clear evidence for an association between organochlorine exposure and obesity; however, a suggestive finding emerged for dieldrin. Compared with those in the lowest quintile (dieldrin, < 0.57 μg/L), odds of obesity were 3.6 (95% CI: 1.3, 10.5) for the fourth and 2.3 (95% CI: 0.8, 7.1) for the highest quintile. Overweight and BMI were unrelated to organochlorine exposure.

Conclusions: In this population with relatively high levels of exposure to organochlorines, no clear associations with obesity or BMI emerged.

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

Mercury, Cadmium, and Lead Levels in Human Placenta: A Systematic Review

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120:1369–1377 (2012) | http://dx.doi.org/10.1289/ehp.1204952

Background: Placental tissue may furnish information on the exposure of both mother and fetus. Mercury (Hg), cadmium (Cd), and lead (Pb) are toxicants of interest in pregnancy because they are associated with alterations in child development.

Objectives: The aim of this study was to summarize the available information regarding total Hg, Cd, and Pb levels in human placenta and possible related factors.

Methods: We performed a systematic search of PubMed/MEDLINE, EMBASE, Lilacs, OSH, and Web of Science for original papers on total Hg, Cd, or Pb levels in human placenta that were published in English or Spanish (1976–2011). Data on study design, population characteristics, collection and analysis of placenta specimens, and main results were extracted using a standardized form.

Results: We found a total of 79 papers (73 different studies). Hg, Cd, and Pb levels were reported in 24, 46, and 46 studies, respectively. Most studies included small convenience samples of healthy pregnant women. Studies were heterogeneous regarding populations selected, processing of specimens, and presentation of results. Hg concentrations > 50 ng/g were found in China (Shanghai), Japan, and the Faroe Islands. Cd levels ranged from 1.2 ng/g to 53 ng/g and were highest in the United States, Japan, and Eastern Europe. Pb showed the greatest variability, with levels ranging from 1.18 ng/g in China (Shanghai) to 500 ng/g in a polluted area of Poland.

Conclusion: The use of the placenta as a biomarker to assess heavy metals exposure is not properly developed because of heterogeneity among the studies. International standardized protocols are needed to enhance comparability and increase the usefulness of this promising tissue in biomonitoring studies.

Rice Consumption and Urinary Arsenic Concentrations in U.S. Children

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120:1418–1424 (2012) | http://dx.doi.org/10.1289/ehp.1205014

Background: In adult populations, emerging evidence indicates that humans are exposed to arsenic by ingestion of contaminated foods such as rice, grains, and juice; yet little is known about arsenic exposure among children.

Objectives: Our goal was to determine whether rice consumption contributes to arsenic exposure in U.S. children.

Methods: We used data from the nationally representative National Health and Nutrition Examination Survey (NHANES) to examine the relationship between rice consumption (measured in 0.25 cups of cooked rice per day) over a 24-hr period and subsequent urinary arsenic concentration among the 2,323 children (6–17 years of age) who participated in NHANES from 2003 to 2008. We examined total urinary arsenic (excluding arsenobetaine and arsenocholine) and dimethylarsinic acid (DMA) concentrations overall and by age group: 6–11 years and 12–17 years.

Results: The median [interquartile range (IQR)] total urinary arsenic concentration among children who reported consuming rice was 8.9 µg/L (IQR: 5.3–15.6) compared with 5.5 µg/L (IQR: 3.1–8.4) among those who did not consume rice. After adjusting for potentially confounding factors, and restricting the study to participants who did not consume seafood in the preceding 24 hr, total urinary arsenic concentration increased 14.2% (95% confidence interval: 11.3, 17.1%) with each 0.25 cup increase in cooked rice consumption.

Conclusions: Our study suggests that rice consumption is a potential source of arsenic exposure in U.S. children.

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Element of Surprise? Rice as a Source of Arsenic in Children's Diets
Rebecca Kessler | A402 (October 2012)
http://dx.doi.org/10.1289/ehp.120-A402b

Childhood Lead Poisoning Associated with Gold Ore Processing: a Village-Level Investigation—Zamfara State, Nigeria, October–November 2010

Yi-Chun Lo, Carrie A. Dooyema, Antonio Neri, James Durant, Taran Jefferies, Andrew Medina-Marino, Lori de Ravello, Douglas Thoroughman, Lora Davis, Raymond S. Dankoli, Matthias Y. Samson, Luka M. Ibrahim, Ossai Okechukwu, Nasir T. Umar-Tsafe, Alhassan H. Dama, and Mary Jean Brown

120:1450–1455 (2012) | http://dx.doi.org/10.1289/ehp.1104793

Background: During May–June 2010, a childhood lead poisoning outbreak related to gold ore processing was confirmed in two villages in Zamfara State, Nigeria. During June–September of that year, villages with suspected or confirmed childhood lead poisoning continued to be identified in Zamfara State.

Objectives: We investigated the extent of childhood lead poisoning [≥ 1 child with a blood lead level (BLL) ≥ 10 µg/dL] and lead contamination (≥ 1 soil/dust sample with a lead level > 400 parts per million) among villages in Zamfara State and identified villages that should be prioritized for urgent interventions.

Methods: We used chain-referral sampling to identify villages of interest, defined as villages suspected of participation in gold ore processing during the previous 12 months. We interviewed villagers, determined BLLs among children < 5 years of age, and analyzed soil/dust from public areas and homes for lead.

Results: We identified 131 villages of interest and visited 74 (56%) villages in three local government areas. Fifty-four (77%) of 70 villages that completed the survey reported gold ore processing. Ore-processing villages were more likely to have ≥ 1 child < 5 years of age with lead poisoning (68% vs. 50%, $p = 0.17$) or death following convulsions (74% vs. 44%, $p = 0.02$). Soil/dust contamination and BLL ≥ 45 µg/dL were identified in ore-processing villages only [50% ($p < 0.001$) and 15% ($p = 0.22$), respectively]. The odds of childhood lead poisoning or lead contamination was 3.5 times as high in ore-processing villages than the other villages (95% confidence interval: 1.1, 11.3).

Conclusion: Childhood lead poisoning and lead contamination were widespread in surveyed areas, particularly among villages that had processed ore recently. Urgent interventions are required to reduce lead exposure, morbidity, and mortality in affected communities.

RELATED ARTICLES

NEWS | Unsafe Harbor? Elevated Blood Lead Levels in Refugee Children

Charles W. Schmidt | A190 (June 2013)
http://dx.doi.org/10.1289/ehp.121-A190

Refugee children in the United States have proven to be at particular risk for elevated blood lead. Some arrive in this country with high blood lead levels attributable not only to leaded gasoline and lead-based paint but also culture-specific routes of exposure, including artisanal pottery and traditional folk remedies. Others encounter lead hazards only after they immigrate, often a result of living in older housing with flaking lead-based paint. Educating refugees about lead hazards requires sensitivity to cultural mores and awareness of potential communication barriers.

EDITORIAL | Health Risks from Lead-Based Ammunition in the Environment

David C. Bellinger, Joanna Burger, Tom J. Cade, Deborah A. Cory-Slechta, Myra Finkelstein, Howard Hu, Michael Kosnett, Philip J. Landrigan, Bruce Lanphear, Mark A. Pokras, Patrick T. Redig, Bruce A. Rideout, Ellen Silbergeld, Robert Wright, and Donald R. Smith | A178
http://dx.doi.org/10.1289/ehp.1306945

Prenatal Methylmercury, Postnatal Lead Exposure, and Evidence of Attention Deficit/ Hyperactivity Disorder among Inuit Children in Arctic Québec

Olivier Boucher, Sandra W. Jacobson, Pierrich Plusquellec, Éric Dewailly, Pierre Ayotte, Nadine Forget-Dubois, Joseph L. Jacobson, and Gina Muckle

120:1456–1461 (2012) | http://dx.doi.org/10.1289/ehp.1204976

Background: Prenatal exposure to methylmercury (MeHg) and polychlorinated biphenyls (PCBs) has been associated with impaired performance on attention tasks in previous studies, but the extent to which these cognitive deficits translate into behavioral problems in the classroom and attention deficit/ hyperactivity disorder (ADHD) remains unknown. By contrast, lead (Pb) exposure in childhood has been associated with ADHD and disruptive behaviors in several studies.

Objectives: In this study we examined the relation of developmental exposure to MeHg, PCBs, and Pb to behavioral problems at school age in Inuit children exposed through their traditional diet.

Methods: In a prospective longitudinal study conducted in the Canadian Arctic, exposure to contaminants was measured at birth and at school age. An assessment of child behavior (n = 279; mean age = 11.3 years) was obtained from the child's classroom teacher on the Teacher Report Form (TRF) from the Child Behavior Checklist, and the Disruptive Behavior Disorders Rating Scale (DBD).

Results: Cord blood mercury concentrations were associated with higher TRF symptom scores for attention problems and DBD scores consistent with ADHD. Current blood Pb concentrations were associated with higher TRF symptom scores for externalizing problems and with symptoms of ADHD (hyperactive-impulsive type) based on the DBD.

Conclusions: To our knowledge, this study is the first to identify an association between prenatal MeHg and ADHD symptomatology in childhood and the first to replicate previously reported associations between low-level childhood Pb exposure and ADHD in a population exposed to Pb primarily from dietary sources.

Early-Life Cadmium Exposure and Child Development in 5-Year-Old Girls and Boys: A Cohort Study in Rural Bangladesh

Maria Kippler, Fahmida Tofail, Jena D. Hamadani, Renee M. Gardner, Sally M. Grantham-McGregor, Matteo Bottai, and Marie Vahter

120:1462–1468 (2012) | http://dx.doi.org/10.1289/ehp.1104431

Background: Cadmium is a commonly occurring toxic food contaminant, but health consequences of early-life exposure are poorly understood.

Objectives: We evaluated the associations between cadmium exposure and neurobehavioral development in preschool children.

Methods: In our population-based mother–child cohort study in rural Bangladesh, we assessed cadmium exposure in 1,305 women in early pregnancy and their children at 5 years of age by measuring concentrations in urine (U-Cd), using inductively coupled plasma mass spectrometry. Children's IQ at 5 years of age, including Verbal (VIQ), Performance (PIQ), and Full-Scale IQ (FSIQ), were measured by Wechsler Preschool and Primary Scale of Intelligence. Behavior was assessed by the Strengths and Difficulties Questionnaire (SDQ).

Results: In multiple linear regression models, adjusted for sex, home stimulation, socioeconomic status (SES), and maternal and child characteristics, a doubling of maternal U-Cd was inversely associated with VIQ (–0.84 points; 95% confidence interval: –1.3, –0.40), PIQ (–0.64 points; –1.1, –0.18), and FSIQ (–0.80 points; –1.2, –0.39). Concurrent child U-Cd showed somewhat weaker association with VIQ and FSIQ, but not PIQ. Stratification by sex and SES indicated slightly stronger associations with PIQ and FSIQ in girls than in boys and in higher-income compared with lower-income families. Concurrent U-Cd was inversely associated with SDQ-prosocial behavior and positively associated with SDQ-difficult behavior, but associations were close to the null after adjustment. Quantile regression analysis showed similar associations across the whole range of each developmental outcome.

Conclusion: Early-life low-level cadmium exposure was associated with lower child intelligence scores in our study cohort. Further research in this area is warranted.

Adverse Health Effects of Child Labor: High Exposure to Chromium and Oxidative DNA Damage in Children Manufacturing Surgical Instruments

Muhammad Sughis, Tim S. Nawrot, Vincent Haufroid, and Benoit Nemery

120:1469–1474 (2012) | http://dx.doi.org/10.1289/ehp.1104678

Background: A considerable part of the worldwide production of surgical instruments takes place in Sialkot, Pakistan. Many children work in hazardous conditions in this industry.

Objective: We investigated exposure to metals and possible health effects among children working in surgical instruments manufacturing units compared with schoolchildren from the same city.

Methods: In a cross-sectional study we studied a convenience sample of 104 male children (10–14 years of age) working in surgical instruments manufacturing units and 75 male children of similar age from a school in Sialkot, Pakistan. A respiratory questionnaire was administered, spirometry was performed, and blood pressure was measured. In a spot urine sample, concentrations of metals were measured by inductively coupled plasma mass spectrometry and 8-hydroxydeoxyguanosine (8OHdG, reflecting oxidative DNA damage) by ELISA.

Results: The working children reported more asthma (10% vs. 0%; $p = 0.005$) and dry cough at night (36% vs. 20%; $p = 0.02$) than did the schoolchildren, but there were no significant differences in pulmonary function or blood pressure. The urinary concentration of chromium was 35 times higher in working children [geometric mean, 23.0 µg/L; 25th–75th percentile, 8.38–58.6] than in schoolchildren [0.66 µg/L; 0.38–1.09)], and largely in excess of the occupational Biological Exposure Index for adult workers (25 µg/L). Urinary 8-OHdG concentrations were not significantly higher in working children than in schoolchildren (19.3 vs. 17.6 µg/g creatinine, $p = 0.4$), but were significantly correlated with urinary nickel ($r = 0.41$; $p < 0.0001$) and with a composite index of metal exposure ($r = 0.46$; $p < 0.0001$).

Conclusions: Children working in the surgical instruments manufacturing industry had substantial exposure to several metals, especially chromium and nickel, which are established carcinogens. Exposure to nickel was associated with evidence of increased oxidative DNA damage.

» NEWS | SCIENCE SELECTION

Metal Exposure in Child Workers: Assessing Hazards in Surgical Instrument Manufacturing Workshops

Tanya Tillett | A403 (October 2012)

http://dx.doi.org/10.1289/ehp.120-A403b

Thyroid Hormones in Relation to Lead, Mercury, and Cadmium Exposure in the National Health and Nutrition Examination Survey, 2007–2008

Aimin Chen, Stephani S. Kim, Ethan Chung, and Kim N. Dietrich

121:181–186 (2013) | http://dx.doi.org/10.1289/ehp.1205239

Background: Heavy metals, such as lead (Pb), mercury (Hg), and cadmium (Cd), are known toxicants, but their associations with the thyroid axis have not been well quantified at U.S. background levels.

Objectives: We investigated the relationships between thyroid hormones (total and free thyroxine [TT_4 and FT_4], total and free triiodothyronine [TT_3 and FT_3], thyroid-stimulating hormone [TSH], and thyroglobulin [Tg]) and levels of Pb, Hg, and Cd in blood and Cd in urine.

Methods: We separately analyzed a sample of 1,109 adolescents (12–19 years of age) and a sample of 4,409 adults from the U.S. National Health and Nutrition Examination Survey (NHANES) 2007–2008. We estimated associations after adjusting for age, sex, race, urinary iodine, body mass index, and serum cotinine.

Results: The geometric mean (GM) levels of blood Pb (BPb), total Hg, and Cd were 0.81 µg/dL, 0.47 µg/L, and 0.21 µg/L in adolescents and 1.43 µg/dL, 0.96 µg/L, and 0.38 µg/L in adults, respectively. The GMs of urinary Cd were 0.07 and 0.25 µg/g creatinine in adolescents and adults, respectively. No consistent pattern of metal and thyroid hormone associations was observed in adolescents. In adults, blood Hg was inversely related to TT_4, TT_3, and FT_3 and urinary Cd was positively associated with TT_4, TT_3, FT_3, and Tg, but there were no associations with Pb. Associations were relatively weak at an individual level, with about 1–4% change in thyroid hormones per interquartile-range increase in Hg or Cd.

Conclusions: Our analysis suggests an inverse association between Hg exposure and thyroid hormones, and a positive association between Cd exposure and thyroid hormones in adults.

Exposures

The Broad Scope of Health Effects from Chronic Arsenic Exposure: Update on a Worldwide Public Health Problem

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121:295–302 (2013) | http://dx.doi.org/10.1289/ehp.1205875

Background: Concerns for arsenic exposure are not limited to toxic waste sites and massive poisoning events. Chronic exposure continues to be a major public health problem worldwide, affecting hundreds of millions of persons.

Objectives: We reviewed recent information on worldwide concerns for arsenic exposures and public health to heighten awareness of the current scope of arsenic exposure and health outcomes and the importance of reducing exposure, particularly during pregnancy and early life.

Methods: We synthesized the large body of current research pertaining to arsenic exposure and health outcomes with an emphasis on recent publications.

Discussion: Locations of high arsenic exposure via drinking water span from Bangladesh, Chile, and Taiwan to the United States. The U.S. Environmental Protection Agency maximum contaminant level (MCL) in drinking water is 10 µg/L; however, concentrations of > 3,000 µg/L have been found in wells in the United States. In addition, exposure through diet is of growing concern. Knowledge of the scope of arsenic-associated health effects has broadened; arsenic leaves essentially no bodily system untouched. Arsenic is a known carcinogen associated with skin, lung, bladder, kidney, and liver cancer. Dermatological, developmental, neurological, respiratory, cardiovascular, immunological, and endocrine effects are also evident. Most remarkably, early-life exposure may be related to increased risks for several types of cancer and other diseases during adulthood.

Conclusions: These data call for heightened awareness of arsenic-related pathologies in broader contexts than previously perceived. Testing foods and drinking water for arsenic, including individual private wells, should be a top priority to reduce exposure, particularly for pregnant women and children, given the potential for life-long effects of developmental exposure.

Concentrations and Potential Health Risks of Metals in Lip Products

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121:705–710 (2013) | http://dx.doi.org/10.1289/ehp.1205518

Background: Metal content in lip products has been an issue of concern.

Objectives: We measured lead and eight other metals in a convenience sample of 32 lip products used by young Asian women in Oakland, California, and assessed potential health risks related to estimated intakes of these metals.

Methods: We analyzed lip products by inductively coupled plasma optical emission spectrometry and used previous estimates of lip product usage rates to determine daily oral intakes. We derived acceptable daily intakes (ADIs) based on information used to determine public health goals for exposure, and compared ADIs with estimated intakes to assess potential risks.

Results: Most of the tested lip products contained high concentrations of titanium and aluminum. All examined products had detectable manganese. Lead was detected in 24 products (75%), with an average concentration of 0.36 ± 0.39 ppm, including one sample with 1.32 ppm. When used at the estimated average daily rate, estimated intakes were > 20% of ADIs derived for aluminum, cadmium, chromium, and manganese. In addition, average daily use of 10 products tested would result in chromium intake exceeding our estimated ADI for chromium. For high rates of product use (above the 95th percentile), the percentages of samples with estimated metal intakes exceeding ADIs were 3% for aluminum, 68% for chromium, and 22% for manganese. Estimated intakes of lead were < 20% of ADIs for average and high use.

Conclusions: Cosmetics safety should be assessed not only by the presence of hazardous contents, but also by comparing estimated exposures with health-based standards. In addition to lead, metals such as aluminum, cadmium, chromium, and manganese require further investigation.

» NEWS | SCIENCE SELECTION

Metals in Lip Products: A Cause for Concern?
Valerie J. Brown | A196 (June 2013)
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Linking Geological and Health Sciences to Assess Childhood Lead Poisoning from Artisanal Gold Mining in Nigeria

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121:744–750 (2013) | http://dx.doi.org/10.1289/ehp.1206051

Background: In 2010, Médecins Sans Frontières discovered a lead poisoning outbreak linked to artisanal gold processing in northwestern Nigeria. The outbreak has killed approximately 400 young children and affected thousands more.

Objectives: Our aim was to undertake an interdisciplinary geological- and health-science assessment to clarify lead sources and exposure pathways, identify additional toxicants of concern and populations at risk, and examine potential for similar lead poisoning globally.

Methods: We applied diverse analytical methods to ore samples, soil and sweep samples from villages and family compounds, and plant foodstuff samples.

Results: Natural weathering of lead-rich gold ores before mining formed abundant, highly gastric-bioaccessible lead carbonates. The same fingerprint of lead minerals found in all sample types confirms that ore processing caused extreme contamination, with up to 185,000 ppm lead in soils/sweep samples and up to 145 ppm lead in plant foodstuffs. Incidental ingestion of soils via hand-to-mouth transmission and of dusts cleared from the respiratory tract is the dominant exposure pathway. Consumption of water and foodstuffs contaminated by the processing is likely lesser, but these are still significant exposure pathways. Although young children suffered the most immediate and severe consequences, results indicate that older children, adult workers, pregnant women, and breastfed infants are also at risk for lead poisoning. Mercury, arsenic, manganese, antimony, and crystalline silica exposures pose additional health threats.

Conclusions: Results inform ongoing efforts in Nigeria to assess lead contamination and poisoning, treat victims, mitigate exposures, and remediate contamination. Ore deposit geology, pre-mining weathering, and burgeoning artisanal mining may combine to cause similar lead poisoning disasters elsewhere globally.

RELATED ARTICLES

NEWS | Quicksilver and Gold: Mercury Pollution from Artisanal and Small-Scale Gold Mining

Charles W. Schmidt | A424–A429 (November 2012)
http://dx.doi.org/10.1289/ehp.120-A424

Mercury amalgamation has been used for centuries to process precious metals. Today, artisanal and small-scale gold mining is the world's second greatest source of atmospheric mercury pollution after coal combustion. Other mercury waste ends up in soils and waterways. And with gold prices now exceeding US$1,600 per ounce, artisanal and small-scale gold mining is on the rise along with its mercury problem.

Burden of Disease from Toxic Waste Sites in India, Indonesia, and the Philippines in 2010

Kevin Chatham-Stephens, Jack Caravanos, Bret Ericson, Jennifer Sunga-Amparo, Budi Susilorini, Promila Sharma, Philip J. Landrigan, and Richard Fuller

121:791–796 (2013) | http://dx.doi.org/10.1289/ehp.1206127

Background: Prior calculations of the burden of disease from toxic exposures have not included estimates of the burden from toxic waste sites due to the absence of exposure data.

Objective: We developed a disability-adjusted life year (DALY)-based estimate of the disease burden attributable to toxic waste sites. We focused on three low- and middle-income countries (LMICs): India, Indonesia, and the Philippines.

Methods: Sites were identified through the Blacksmith Institute's Toxic Sites Identification Program, a global effort to identify waste sites in LMICs. At least one of eight toxic chemicals was sampled in environmental media at each site, and the population at risk estimated. By combining estimates of disease incidence from these exposures with population data, we calculated the DALYs attributable to exposures at each site.

Results: We estimated that in 2010, 8,629,750 persons were at risk of exposure to industrial pollutants at 373 toxic waste sites in the three countries, and that these exposures resulted in 828,722 DALYs, with a range of 814,934–1,557,121 DALYs, depending on the weighting factor used. This disease burden is comparable to estimated burdens for outdoor air pollution (1,448,612 DALYs) and malaria (725,000 DALYs) in these countries. Lead and hexavalent chromium collectively accounted for 99.2% of the total DALYs for the chemicals evaluated.

Conclusions: Toxic waste sites are responsible for a significant burden of disease in LMICs. Although some factors, such as unidentified and unscreened sites, may cause our estimate to be an underestimate of the actual burden of disease, other factors, such as extrapolation of environmental sampling to the entire exposed population, may result in an overestimate of the burden of disease attributable to these sites. Toxic waste sites are a major, and heretofore underrecognized, global health problem.

Blood Lead Levels and Serum Insulin-Like Growth Factor 1 Concentrations in Peripubertal Boys

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121:854–858 (2013) | http://dx.doi.org/10.1289/ehp.1206105

Background: Childhood lead exposure has been associated with growth delay. However, the association between blood lead levels (BLLs) and insulin-like growth factor 1 (IGF-1) has not been characterized in a large cohort with low-level lead exposure.

Methods: We recruited 394 boys 8–9 years of age from an industrial Russian town in 2003–2005 and followed them annually thereafter. We used linear regression models to estimate the association of baseline BLLs with serum IGF-1 concentration at two follow-up visits (ages 10–11 and 12–13 years), adjusting for demographic and socioeconomic covariates.

Results: At study entry, median BLL was 3 μg/dL (range, < 0.5–31 μg/dL), most boys (86%) were prepubertal, and mean ± SD height and BMI *z*-scores were 0.14 ± 1.0 and –0.2 ± 1.3, respectively. After adjustment for covariates, the mean follow-up IGF-1 concentration was 29.2 ng/mL lower (95% CI: –43.8, –14.5) for boys with high versus low BLL (≥ 5 μg/dL or < 5 μg/dL); this difference persisted after further adjustment for pubertal status. The association of BLL with IGF-1 was stronger for mid-pubertal than prepubertal boys ($p = 0.04$). Relative to boys with BLLs < 2 μg/dL, adjusted mean IGF-1 concentrations decreased by 12.8 ng/mL (95% CI: –29.9, 4.4) for boys with BLLs of 3–4 μg/dL; 34.5 ng/mL (95% CI: –53.1, –16.0) for BLLs 5–9 μg/dL; and 60.4 ng/mL (95% CI: –90.9, –29.9) for BLLs ≥ 10 μg/dL.

Conclusions: In peripubertal boys with low-level lead exposure, higher BLLs were associated with lower serum IGF-1. Inhibition of the hypothalamic–pituitary–growth axis may be one possible pathway by which lead exposure leads to growth delay.

Blood Lead Level and Measured Glomerular Filtration Rate in Children with Chronic Kidney Disease

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121:965–970 (2013) | http://dx.doi.org/10.1289/ehp.1205164

Background: The role of environmental exposure to lead as a risk factor for chronic kidney disease (CKD) and its progression remains controversial, and most studies have been limited by a lack of direct glomerular filtration rate (GFR) measurement.

Objective: We evaluated the association between lead exposure and GFR in children with CKD.

Methods: In this cross-sectional study, we examined the association between blood lead levels (BLLs) and GFR measured by the plasma disappearance of iohexol among 391 participants in the Chronic Kidney Disease in Children (CKiD) prospective cohort study.

Results: Median BLL and GFR were 1.2 µg/dL and 44.4 mL/min per 1.73 m^2, respectively. The average percent change in GFR for each 1-µg/dL increase in BLL was –2.1 (95% CI: –6.0, 1.8). In analyses stratified by CKD diagnosis, the association between BLL and GFR was stronger among children with glomerular disease underlying CKD; in this group, each 1-µg/dL increase in BLL was associated with a –12.1 (95% CI: –22.2, –1.9) percent change in GFR. In analyses stratified by anemia status, each 1-µg/dL increase in BLL among those with and without anemia was associated with a –0.3 (95% CI: –7.2, 6.6) and –4.6 (95% CI: –8.9, –0.3) percent change in GFR, respectively.

Conclusions: There was no significant association between BLL and directly measured GFR in this relatively large cohort of children with CKD, although associations were observed in some subgroups. Longitudinal analyses are needed to examine the temporal relationship between lead and GFR decline, and to further examine the impact of underlying cause of CKD and anemia/hemoglobin status among patients with CKD.

Associations of Urinary Cadmium with Age and Urinary Proteins: Further Evidence of Physiological Variations Unrelated to Metal Accumulation and Toxicity

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121:1047–1053 (2013) | http://dx.doi.org/10.1289/ehp.1306607

Background: The current risk assessment for environmental cadmium (Cd) largely relies on the assumption that urinary Cd (U-Cd) is a reliable biomarker of the Cd body burden. Recent studies have questioned the validity of this assumption.

Objectives: We studied the lifetime trend of U-Cd as a function of diuresis, gender, smoking status, and protein tubular reabsorption. We also analyzed the associations between U-Cd and urinary proteins.

Methods: Cd, retinol-binding protein, and albumin were measured in the urine of six cohorts of the general population of Belgium, with a mean age ranging from 5.7 to 88.1 years (n = 1,567). Variations of U-Cd with age were modeled using natural cubic splines.

Results: In both genders, U-Cd decreased to a minimum (~ 0.20 µg/L) at the end of adolescence, then increased until 60–70 years of age (~ 0.60 µg/L in never-smokers) before leveling off or decreasing. When U-Cd was expressed in micrograms per gram of creatinine, these variations were amplified (minimum, 0.15 µg/g creatinine; maximum, 0.70 µg/g creatinine) and much higher U-Cd values were observed in women. We observed no difference in U-Cd levels between never-smokers and former smokers, and the difference with current smokers did not increase over time. Lifetime curves of U-Cd were higher with increasing urinary retinol-binding protein or albumin, a consequence of the coexcretion of Cd with proteins.

Conclusions: At low Cd exposure levels, U-Cd and age are associated through nonlinear and nonmonotonic relationships that appear to be driven mainly by recent Cd intake and physiological variations in the excretion of creatinine and proteins.

Carotid Intima-Media Thickness and Plasma Asymmetric Dimethylarginine in Mexican Children Exposed to Inorganic Arsenic

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121:1090–1096 (2013) | http://dx.doi.org/10.1289/ehp.1205994

Background: Arsenic exposure is a risk factor for atherosclerosis in adults, but there is little information on arsenic and early risk biomarkers for atherosclerosis in children. Carotid intima-media thickness (cIMT) is an indicator of subclinical atherosclerotic burden that has been associated with plasma asymmetric dimethylarginine (ADMA), a predictor of cardiovascular disease risk.

Objectives: The aim of this study was to investigate associations of arsenic exposure with cIMT, ADMA, and endothelial adhesion molecules [soluble intercellular cell adhesion molecule-1 (sICAM-1); soluble vascular cell adhesion molecule-1 (sVCAM-1)] in children who had been exposed to environmental inorganic arsenic (iAs).

Methods: We conducted a cross-sectional study in 199 children 3–14 years of age who were residents of Zimapan, México. We evaluated cIMT using ultrasonography, and plasma lipid profiles by standard methods. We analyzed ADMA, sICAM-1, and sVCAM-1 by ELISA, and measured the concentrations of total speciated arsenic (tAs) in urine using hydride generation cryotrapping atomic absorption spectrometry.

Results: In the multiple linear regression model for cIMT, tAs categories were positively associated with cIMT increase. The estimated cIMT diameter was greater in 35- to 70-ng/mL and > 70-ng/mL groups (0.035 mm and 0.058 mm per 1-ng/mL increase in urinary tAs, respectively), compared with the < 35-ng/mL group. In addition to tAs level, plasma ADMA was a significant predictor of cIMT. In the adjusted regression model, cIMT, percent iAs, and plasma sVCAM-1 were significant predictors of ADMA levels (e.g., 0.419-μmol/L increase in ADMA per 1-mm increase in cIMT).

Conclusions: Arsenic exposure and plasma ADMA levels were positively associated with cIMT in a population of Mexican children with environmental arsenic exposure through drinking water.

Economic Costs of Childhood Lead Exposure in Low- and Middle-Income Countries

Teresa M. Attina and Leonardo Trasande

121:1097–1102 (2013) | http://dx.doi.org/10.1289/ehp.1206424

Background: Children's blood lead levels have declined worldwide, especially after the removal of lead in gasoline. However, significant exposure remains, particularly in low- and middle-income countries. To date, there have been no global estimates of the costs related to lead exposure in children in developing countries.

Objective: Our main aim was to estimate the economic costs attributable to childhood lead exposure in low- and middle-income countries.

Methods: We developed a regression model to estimate mean blood lead levels in our population of interest, represented by each 1-year cohort of children < 5 years of age. We used an environmentally attributable fraction model to estimate lead-attributable economic costs and limited our analysis to the neurodevelopmental impacts of lead, assessed as decrements in IQ points. Our main outcome was lost lifetime economic productivity due to early childhood exposure.

Results: We estimated a total cost of $977 billions of international dollars in low- and middle-income countries, with economic losses equal to $134.7 billion in Africa [4.03% of gross domestic product (GDP)], $142.3 billion in Latin America and the Caribbean (2.04% of GDP), and $699.9 billion in Asia (1.88% of GDP). Our sensitivity analysis indicates a total economic loss in the range of $728.6–1162.5 billion.

Conclusions: We estimated that, in low- and middle-income countries, the burden associated with childhood lead exposure amounts to 1.20% of world GDP in 2011. For comparison, in the United States and Europe lead-attributable economic costs have been estimated at $50.9 and $55 billion, respectively, suggesting that the largest burden of lead exposure is now borne by low- and middle-income countries.

PESTICIDES AND OTHER CHEMICALS/COMPOUNDS (E.G., BPA, PCBs, PBDEs, PFCs, PHTHALATES, ENDOCRINE DISRUPTORS)

Maternal Concentrations of Polyfluoroalkyl Compounds during Pregnancy and Fetal and Postnatal Growth in British Girls

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120:1432–1437 (2012) | http://dx.doi.org/10.1289/ehp.1003096

Background: Prenatal exposures to polyfluoroalkyl compounds (PFCs) may be associated with adverse changes in fetal and postnatal growth.

Objective: We explored associations of prenatal serum concentrations of perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), and perfluorohexane sulfonate (PFHxS) with fetal and postnatal growth in girls.

Methods: We studied a sample of 447 singleton girls and their mothers participating in the Avon Longitudinal Study of Parents and Children (ALSPAC). Data on weight and length were obtained at birth and at 2, 9, and 20 months. Serum samples were obtained in 1991–1992, from mothers during pregnancy. We explored associations between prenatal PFC concentrations and weight at birth as well as longitudinal changes in weight-for-age SD scores between birth and 20 months.

Results: PFOS (median, 19.6 ng/mL), PFOA (median, 3.7 ng/mL), and PFHxS (median, 1.6 ng/mL) were detected in 100% of samples. On average, girls born to mothers with prenatal concentrations of PFOS in the upper tertile weighed 140 g less [95% confidence interval (CI): –238, –42] at birth than girls born to mothers with concentrations in the lower tertile in adjusted models. Similar patterns were seen for PFOA (–133 g; 95% CI: –237, –30) and PFHxS (–108 g; 95% CI: –206, –10). At 20 months, however, girls born to mothers with prenatal concentrations of PFOS in the upper tertile weighed 580 g more (95% CI: 301, 858) when compared with those in the lower tertile. No differences in weight were found for PFOA and PFHxS.

Conclusions: Girls with higher prenatal exposure to each of the PFCs examined were smaller at birth than those with lower exposure. In addition, those with higher exposure to PFOS were larger at 20 months.

Lactational Exposure to Polybrominated Diphenyl Ethers and Its Relation to Social and Emotional Development among Toddlers

Kate Hoffman, Margaret Adgent, Barbara Davis Goldman, Andreas Sjödin, and Julie L. Daniels

120:1438–1442 (2012) | http://dx.doi.org/10.1289/ehp.1205100

Background: Polybrominated diphenyl ethers (PBDEs) have been widely used as flame retardants and are ubiquitous environmental contaminants. PBDEs have been linked to adverse neurodevelopment in animals and humans.

Objectives: We investigated the association between breast milk PBDE levels and social and emotional development in toddlers.

Methods: The Pregnancy Infection and Nutrition (PIN) and PIN Babies studies followed a cohort of North Carolina pregnant women and their children through 36 months of age. Breast milk samples obtained at 3 months postpartum were analyzed for PBDEs. The Infant–Toddler Social and Emotional Assessment (ITSEA) was completed by mothers when children were approximately 30 months of age ($n = 222$). We assessed the relationship between breast milk concentrations of five PBDE congeners—BDEs 28, 47, 99, 100, and 153—and children's social and emotional development, adjusting for other factors.

Results: A small, imprecise, yet consistent positive association was apparent between BDEs 47, 99, and 100 and increased externalizing behaviors, specifically activity/impulsivity behaviors. Externalizing domain *T*-scores ranged from 30 to 87 with a mean of 47.8. Compared with those with BDE-47 concentrations below the median, adjusted externalizing behavior domain scores were 1.6 [95% confidence interval (CI): –1.2, 4.4] and 2.8 (95% CI: –0.1, 5.7) points higher for children born to women with breast milk concentrations in the 3rd and 4th quartiles, respectively. PBDEs were not associated with other social and emotional developmental domains.

Conclusions: Our results, although imprecise, suggest a subtle association between early-life PBDE exposure and increased activity/impulsivity behaviors in early childhood. Confirmation of these results is needed in other longitudinal studies.

Prenatal Exposure to Butylbenzyl Phthalate and Early Eczema in an Urban Cohort

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120:1475–1480 (2012) | http://dx.doi.org/10.1289/ehp.1104544

Background: Recent cross-sectional studies suggest a link between butylbenzyl phthalate (BBzP) in house dust and childhood eczema.

Objectives: We aimed to evaluate whether concentrations of monobenzyl phthalate (MBzP), the main BBzP metabolite in urine, during pregnancy are associated prospectively with eczema in young children, and whether this association varies by the child's sensitization to indoor allergens or serological evidence of any allergies.

Methods: MBzP was measured in spot urine samples during the third trimester of pregnancy from 407 African-American and Dominican women residing in New York City in 1999–2006. Repeated questionnaires asked mothers whether their doctor ever said their child had eczema. Child blood samples at 24, 36, and 60 months of age were analyzed for total, anti-cockroach, dust mite, and mouse IgE. Relative risks (RR) were estimated with multivariable modified Poisson regression. Analyses included a multinomial logistic regression model for early- and late-onset eczema versus no eczema through 60 months of age.

Results: MBzP was detected in > 99% of samples (geometric mean = 13.6; interquartile range: 5.7–31.1 ng/mL). By 24 months, 30% of children developed eczema, with the proportion higher among African Americans (48%) than among Dominicans (21%) ($p < 0.001$). An interquartile range increase in log MBzP concentration was associated positively with early-onset eczema (RR = 1.52 for eczema by 24 months; 95% confidence interval: 1.21, 1.91, $p = 0.0003$, $n = 113$ reporting eczema/376 total sample), adjusting for urine specific gravity, sex, and race/ethnicity. MBzP was not associated with allergic sensitization, nor did seroatopy modify consistently the MBzP and eczema association.

Conclusions: Prenatal exposure to BBzP may influence the risk of developing eczema in early childhood.

Exposures to Endocrine-Disrupting Chemicals and Age of Menarche in Adolescent Girls in NHANES (2003–2008)

Danielle E. Buttke, Kanta Sircar, and Colleen Martin

120:1613–1618 (2012) | http://dx.doi.org/10.1289/ehp.1104748

Background: The observed age of menarche has fallen, which may have important adverse social and health consequences. Increased exposure to endocrine-disrupting compounds (EDCs) has been associated with adverse reproductive outcomes.

Objective: Our objective was to assess the relationship between EDC exposure and the age of menarche in adolescent girls.

Methods: We used data from female participants 12–16 years of age who had completed the reproductive health questionnaire and laboratory examination for the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) for years 2003–2008 (2005–2008 for analyses of phthalates and parabens). Exposures were assessed based on creatinine-corrected natural log urine concentrations of selected environmental chemicals and metabolites found in at least 75% of samples in our study sample. We used Cox proportional hazards analysis in SAS 9.2 survey procedures to estimate associations after accounting for censored data among participants who had not reached menarche. We evaluated body mass index (BMI; kilograms per meter squared), family income-to-poverty ratio, race/ethnicity, mother's smoking status during pregnancy, and birth weight as potential confounders.

Results: The weighted mean age of menarche was 12.0 years of age. Among 440 girls with both reproductive health and laboratory data, after accounting for BMI and race/ethnicity, we found that 2,5-dichlorophenol (2,5-DCP) and summed environmental phenols (2,5-DCP and 2,4-DCP) were inversely associated with age of menarche [hazard ratios of 1.10; 95% confidence interval (CI): 1.01, 1.19 and 1.09; 95% CI: 1.01, 1.19, respectively]. Other exposures (total parabens, bisphenol A, triclosan, benzophenone-3, total phthalates, and 2,4-DCP) were not significantly associated with age of menarche.

Conclusions: Our findings suggest an association between 2,5-DCP, a potential EDC, and earlier age of menarche in the general U.S. population.

Polybrominated Diphenyl Ethers (PBDEs) in Breast Milk and Neuropsychological Development in Infants

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120:1760–1765 (2012) | http://dx.doi.org/10.1289/ehp.1205266

Background: There is increasing interest in the potential effects of polybrominated diphenyl ethers (PBDEs) on children's neuropsychological development, but only a few small studies have evaluated such effects.

Objectives: Our goal was to examine the association between PBDE concentrations in colostrum and infant neuropsychological development and to assess the influence of other persistent organic pollutants (POPs) on such association.

Methods: We measured concentrations of PBDEs and other POPs in colostrum samples of 290 women recruited in a Spanish birth cohort. We tested children for mental and psychomotor development with the Bayley Scales of Infant Development at 12–18 months of age. We analyzed the sum of the seven most common PBDE congeners (BDEs 47, 99, 100, 153, 154, 183, 209) and each congener separately.

Results: Increasing Σ_7PBDEs concentrations showed an association of borderline statistical significance with decreasing mental development scores (β per log ng/g lipid = –2.25; 95% CI: –4.75, 0.26). BDE-209, the congener present in highest concentrations, appeared to be the main congener responsible for this association (β = –2.40, 95% CI: –4.79, –0.01). There was little evidence for an association with psychomotor development. After adjustment for other POPs, the BDE-209 association with mental development score became slightly weaker (β = –2.10, 95% CI: –4.66, 0.46).

Conclusions: Our findings suggest an association between increasing PBDE concentrations in colostrum and a worse infant mental development, particularly for BDE-209, but require confirmation in larger studies. The association, if causal, may be due to unmeasured BDE-209 metabolites, including OH-PBDEs (hydroxylated PBDEs), which are more toxic, more stable, and more likely to cross the placenta and to easily reach the brain than BDE-209.

Genetic Modification of the Association between Peripubertal Dioxin Exposure and Pubertal Onset in a Cohort of Russian Boys

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121:111–117 (2013) | http://dx.doi.org/10.1289/ehp.1205278

Background: Exposure to dioxins has been associated with delayed pubertal onset in both epidemiologic and animal studies. Whether genetic polymorphisms may modify this association is currently unknown. Identifying such genes could provide insight into mechanistic pathways. This is one of the first studies to assess genetic susceptibility to dioxins.

Objectives: We evaluated whether common polymorphisms in genes affecting either molecular responses to dioxin exposure or pubertal onset influence the association between peripubertal serum dioxin concentration and male pubertal onset.

Methods: In this prospective cohort of Russian adolescent boys (n = 392), we assessed gene–environment interactions for 337 tagging single-nucleotide polymorphisms (SNPs) from 46 candidate genes and two intergenic regions. Dioxins were measured in the boys' serum at age 8–9 years. Pubertal onset was based on testicular volume and on genitalia staging. Statistical approaches for controlling for multiple testing were used, both with and without prescreening for marginal genetic associations.

Results: After accounting for multiple testing, two tag SNPs in the glucocorticoid receptor (*GR/NR3C1*) gene and one in the estrogen receptor-α (*ESR1*) gene were significant ($q < 0.2$) modifiers of the association between peripubertal serum dioxin concentration and male pubertal onset defined by genitalia staging, although not by testicular volume. The results were sensitive to whether multiple comparison adjustment was applied to all gene–environment tests or only to those with marginal genetic associations.

Conclusions: Common genetic polymorphisms in the glucocorticoid receptor and estrogen receptor-α genes may modify the association between peripubertal serum dioxin concentration and pubertal onset. Further studies are warranted to confirm these findings.

» NEWS | SCIENCE SELECTION

Gene–Dioxin Interactions and Pubertal Onset in Boys: Findings from the Russian Children's Study

Julia R. Barrett | A30 (January 2013)

http://dx.doi.org/10.1289/ehp.121-A30

Variability of Organophosphorous Pesticide Metabolite Levels in Spot and 24-hr Urine Samples Collected from Young Children during 1 Week

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121:118–124 (2013) | http://dx.doi.org/10.1289/ehp.1104808

Background: Dialkyl phosphate (DAP) metabolites in spot urine samples are frequently used to characterize children's exposures to organophosphorous (OP) pesticides. However, variable exposure and short biological half-lives of OP pesticides could result in highly variable measurements, leading to exposure misclassification.

Objective: We examined within- and between-child variability in DAP metabolites in urine samples collected during 1 week.

Methods: We collected spot urine samples over 7 consecutive days from 25 children (3–6 years of age). On two of the days, we collected 24-hr voids. We assessed the reproducibility of urinary DAP metabolite concentrations and evaluated the sensitivity and specificity of spot urine samples as predictors of high (top 20%) or elevated (top 40%) weekly average DAP metabolite concentrations.

Results: Within-child variance exceeded between-child variance by a factor of two to eight, depending on metabolite grouping. Although total DAP concentrations in single spot urine samples were moderately to strongly associated with concentrations in same-day 24-hr samples ($r \approx 0.6–0.8$, $p < 0.01$), concentrations in spot samples collected > 1 day apart and in 24-hr samples collected 3 days apart were weakly correlated ($r \approx –0.21$ to 0.38). Single spot samples predicted high (top 20%) and elevated (top 40%) full-week average total DAP excretion with only moderate sensitivity (≈ 0.52 and ≈ 0.67, respectively) but relatively high specificity (≈ 0.88 and ≈ 0.78, respectively).

Conclusions: The high variability we observed in children's DAP metabolite concentrations suggests that single-day urine samples provide only a brief snapshot of exposure. Sensitivity analyses suggest that classification of cumulative OP exposure based on spot samples is prone to type 2 classification errors.

Maternal Urinary Bisphenol A during Pregnancy and Maternal and Neonatal Thyroid Function in the CHAMACOS Study

Jonathan Chevrier, Robert B. Gunier, Asa Bradman, Nina T. Holland, Antonia M. Calafat, Brenda Eskenazi, and Kim G. Harley

121:138–144 (2013) | http://dx.doi.org/10.1289/ehp.1205092

Background: Bisphenol A (BPA) is widely used in the manufacture of polycarbonate plastic bottles, food and beverage can linings, thermal receipts, and dental sealants. Animal and human studies suggest that BPA may disrupt thyroid function. Although thyroid hormones play a determinant role in human growth and brain development, no studies have investigated relations between BPA exposure and thyroid function in pregnant women or neonates.

Objective: Our goal was to evaluate whether exposure to BPA during pregnancy is related to thyroid hormone levels in pregnant women and neonates.

Methods: We measured BPA concentration in urine samples collected during the first and second half of pregnancy in 476 women participating in the CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas) study. We also measured free thyroxine (T_4), total T_4, and thyroid-stimulating hormone (TSH) in women during pregnancy, and TSH in neonates.

Results: Associations between the average of the two BPA measurements and maternal thyroid hormone levels were not statistically significant. Of the two BPA measurements, only the one taken closest in time to the TH measurement was significantly associated with a reduction in total T_4 ($\beta = –0.13$ µg/dL per $\log_2$ unit; 95% CI: –0.25, 0.00). The average of the maternal BPA concentrations was associated with reduced TSH in boys (–9.9% per $\log_2$ unit; 95% CI: –15.9%, –3.5%) but not in girls. Among boys, the relation was stronger when BPA was measured in the third trimester of pregnancy and decreased with time between BPA and TH measurements.

Conclusion: Results suggest that exposure to BPA during pregnancy is related to reduced total T_4 in pregnant women and decreased TSH in male neonates. Findings may have implications for fetal and neonatal development.

In Utero and Childhood Polybrominated Diphenyl Ether (PBDE) Exposures and Neurodevelopment in the CHAMACOS Study

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121:257–262 (2013) | http://dx.doi.org/10.1289/ehp.1205597

Background: California children's exposures to polybrominated diphenyl ether flame retardants (PBDEs) are among the highest worldwide. PBDEs are known endocrine disruptors and neurotoxicants in animals.

Objective: Here we investigate the relation of *in utero* and child PBDE exposure to neurobehavioral development among participants in CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas), a California birth cohort.

Methods: We measured PBDEs in maternal prenatal and child serum samples and examined the association of PBDE concentrations with children's attention, motor functioning, and cognition at 5 ($n = 310$) and 7 years of age ($n = 323$).

Results: Maternal prenatal PBDE concentrations were associated with impaired attention as measured by a continuous performance task at 5 years and maternal report at 5 and 7 years of age, with poorer fine motor coordination—particularly in the nondominant—at both age points, and with decrements in Verbal and Full-Scale IQ at 7 years. PBDE concentrations in children 7 years of age were significantly or marginally associated with concurrent teacher reports of attention problems and decrements in Processing Speed, Perceptual Reasoning, Verbal Comprehension, and Full-Scale IQ. These associations were not altered by adjustment for birth weight, gestational age, or maternal thyroid hormone levels.

Conclusions: Both prenatal and childhood PBDE exposures were associated with poorer attention, fine motor coordination, and cognition in the CHAMACOS cohort of school-age children. This study, the largest to date, contributes to growing evidence suggesting that PBDEs have adverse impacts on child neurobehavioral development.

RELATED ARTICLES

NEWS | Thermal Reaction: The Spread of Bisphenol S via Paper Products
Lindsey Konkel | A76 (March 2013)
http://dx.doi.org/10.1289/ehp.121-A76

NEWS | Exposure to TDCPP Appears Widespread
Kellyn S. Betts | A150 (May 2013)
http://dx.doi.org/10.1289/ehp.121-A150

FOCUS | Breaking the Mold: New Strategies for Fighting Aflatoxins
Charles W. Schmidt | A270 (September 2013)
http://dx.doi.org/10.1289/ehp.121-A270

Aflatoxin B1, the most potent naturally occurring liver carcinogen ever identified, is produced by *Aspergillus* fungi that infect crops during periods of drought stress and intense heat. Although found around the world, aflatoxins pose a human health threat primarily in developing countries. Researchers and development groups are investigating a variety of new methods to keep these agents out of food supplies.

Human Health Effects of Trichloroethylene: Key Findings and Scientific Issues

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121:303–311 (2013) | http://dx.doi.org/10.1289/ehp.1205879

Background: In support of the Integrated Risk Information System (IRIS), the U.S. Environmental Protection Agency (EPA) completed a toxicological review of trichloroethylene (TCE) in September 2011, which was the result of an effort spanning > 20 years.

Objectives: We summarized the key findings and scientific issues regarding the human health effects of TCE in the U.S. EPA's toxicological review.

Methods: In this assessment we synthesized and characterized thousands of epidemiologic, experimental animal, and mechanistic studies, and addressed several key scientific issues through modeling of TCE toxicokinetics, meta-analyses of epidemiologic studies, and analyses of mechanistic data.

Discussion: Toxicokinetic modeling aided in characterizing the toxicological role of the complex metabolism and multiple metabolites of TCE. Meta-analyses of the epidemiologic data strongly supported the conclusions that TCE causes kidney cancer in humans and that TCE may also cause liver cancer and non-Hodgkin lymphoma. Mechanistic analyses support a key role for mutagenicity in TCE-induced kidney carcinogenicity. Recent evidence from studies in both humans and experimental animals point to the involvement of TCE exposure in autoimmune disease and hypersensitivity. Recent avian and *in vitro* mechanistic studies provided biological plausibility that TCE plays a role in developmental cardiac toxicity, the subject of substantial debate due to mixed results from epidemiologic and rodent studies.

Conclusions: TCE is carcinogenic to humans by all routes of exposure and poses a potential human health hazard for noncancer toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and the developing embryo/fetus.

Race/Ethnicity–Specific Associations of Urinary Phthalates with Childhood Body Mass in a Nationally Representative Sample

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121:501–506 (2013) | http://dx.doi.org/10.1289/ehp.1205526

Background: Phthalates have antiandrogenic effects and may disrupt lipid and carbohydrate metabolism. Racial/ethnic subpopulations have been documented to have varying urinary phthalate concentrations and prevalences of childhood obesity.

Objective: We examined associations between urinary phthalate metabolites and body mass outcomes in a nationally representative sample of U.S. children and adolescents.

Methods: We performed stratified and whole-sample cross-sectional analyses of 2,884 children 6–19 years of age who participated in the 2003–2008 National Health and Nutrition Examination Survey. Multivariable linear and logistic analyses of body mass index *z*-score, overweight, and obesity were performed against molar concentrations of low-molecular-weight (LMW), high-molecular-weight (HMW), and di-2-ethylhexylphthalate (DEHP) metabolites, controlling for sex, television watching, caregiver education, caloric intake, poverty–income ratio, race/ethnicity, serum cotinine, and age group. We used sensitivity analysis to examine robustness of results to removing sample weighting, normalizing phthalate concentrations for molecular weight, and examining different dietary intake covariates.

Results: In stratified, multivariable models, each log unit (roughly 3-fold) increase in LMW metabolites was associated with 21% and 22% increases in odds (95% CI: 1.05–1.39 and 1.07–1.39, respectively) of overweight and obesity, and a 0.090-SD unit increase in BMI *z*-score (95% CI: 0.003–0.18), among non-Hispanic blacks. Significant associations were not identified in any other racial/ethnic subgroup or in the study sample as a whole after controlling for potential confounders, associations were not significant for HMW or DEHP metabolites, and results did not change substantially with sensitivity analysis.

Conclusions: We identified a race/ethnicity–specific association of phthalates with childhood obesity in a nationally representative sample. Further study is needed to corroborate the association and evaluate genetic/epigenomic predisposition and/or increased phthalate exposure as possible explanations for differences among racial/ethnic subgroups.

Prenatal and Postnatal Bisphenol A Exposure and Body Mass Index in Childhood in the CHAMACOS Cohort

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121:514–520 (2013) | http://dx.doi.org/10.1289/ehp.1205548

Background: Bisphenol A (BPA), a widely used endocrine-disrupting chemical, has been associated with increased body weight and fat deposition in rodents.

Objectives: We examined whether prenatal and postnatal urinary BPA concentrations were associated with body mass index (BMI), waist circumference, percent body fat, and obesity in 9-year-old children ($n = 311$) in the CHAMACOS longitudinal cohort study.

Methods: BPA was measured in spot urine samples collected from mothers twice during pregnancy and from children at 5 and 9 years of age.

Results: Prenatal urinary BPA concentrations were associated with decreased BMI at 9 years of age in girls but not boys. Among girls, being in the highest tertile of prenatal BPA concentrations was associated with decreased BMI *z*-score ($\beta = -0.47$, 95% CI: −0.87, −0.07) and percent body fat ($\beta = -4.36$, 95% CI: −8.37, −0.34) and decreased odds of overweight/obesity [odds ratio (OR) = 0.37, 95% CI: 0.16, 0.91] compared with girls in the lowest tertile. These findings were strongest in prepubertal girls. Urinary BPA concentrations at 5 years of age were not associated with any anthropometric parameters at 5 or 9 years, but BPA concentrations at 9 years were positively associated with BMI, waist circumference, fat mass, and overweight/obesity at 9 years in boys and girls.

Conclusions: Consistent with other cross-sectional studies, higher urinary BPA concentrations at 9 years of age were associated with increased adiposity at 9 years. However, increasing BPA concentrations in mothers during pregnancy were associated with decreased BMI, body fat, and overweight/obesity among their daughters at 9 years of age.

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Unclear Relationship: Prenatal but Not Concurrent Bisphenol A Exposure Linked to Lower Weight and Less Fat

Kellyn S. Betts | A135 (April 2013)

http://dx.doi.org/10.1289/ehp.121-A135

Polycyclic Aromatic Hydrocarbons in Residential Dust: Sources of Variability

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121:543–550 (2013) | http://dx.doi.org/10.1289/ehp.1205821

Background: There is interest in using residential dust to estimate human exposure to environmental contaminants.

Objectives: We aimed to characterize the sources of variability for polycyclic aromatic hydrocarbons (PAHs) in residential dust and provide guidance for investigators who plan to use residential dust to assess exposure to PAHs.

Methods: We collected repeat dust samples from 293 households in the Northern California Childhood Leukemia Study during two sampling rounds (from 2001 through 2007 and during 2010) using household vacuum cleaners, and measured 12 PAHs using gas chromatography–mass spectrometry. We used a random- and a mixed-effects model for each PAH to apportion observed variance into four components and to identify sources of variability.

Results: Median concentrations for individual PAHs ranged from 10 to 190 ng/g of dust. For each PAH, total variance was apportioned into regional variability (1–9%), intraregional between-household variability (24–48%), within-household variability over time (41–57%), and within-sample analytical variability (2–33%). Regional differences in PAH dust levels were associated with estimated ambient air concentrations of PAH. Intraregional differences between households were associated with the residential construction date and the smoking habits of residents. For some PAHs, a decreasing time trend explained a modest fraction of the within-household variability; however, most of the within-household variability was unaccounted for by our mixed-effects models. Within-household differences between sampling rounds were largest when the interval between dust sample collections was at least 6 years in duration.

Conclusions: Our findings indicate that it may be feasible to use residential dust for retrospective assessment of PAH exposures in studies of health effects.

Acetylcholinesterase Activity, Cohabitation with Floricultural Workers, and Blood Pressure in Ecuadorian Children

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121:619–624 (2013) | http://dx.doi.org/10.1289/ehp.1205431

Background: Acetylcholinesterase (AChE) inhibitors are commonly used pesticides that can effect hemodynamic changes through increased cholinergic stimulation. Children of agricultural workers are likely to have paraoccupational exposures to pesticides, but the potential physiological impact of such exposures is unclear.

Objectives: We investigated whether secondary pesticide exposures were associated with blood pressure and heart rate among children living in agricultural Ecuadorian communities.

Methods: This cross-sectional study included 271 children 4–9 years of age [51% cohabited with one or more flower plantation workers (mean duration, 5.2 years)]. Erythrocyte AChE activity was measured using the EQM Test-mate system. Linear regression models were used to estimate associations of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate with AChE activity, living with flower workers, duration of cohabitation with a flower worker, number of flower workers in the child's home, and number of practices that might increase children's exposure to pesticides.

Results: Mean (± SD) AChE activity was 3.14 ± 0.49 U/mL. A 1-U/mL decrease in AChE activity was associated with a 2.86-mmHg decrease in SBP (95% CI: –5.20, –0.53) and a 2.89-mmHg decrease in DBP (95% CI: –5.00, –0.78), after adjustment for potential confounders. Children living with flower workers had lower SBP (–1.72 mmHg; 95% CI: –3.53, 0.08) than other children, and practices that might increase exposure also were associated with lower SBP. No significant associations were found between exposures and heart rate.

Conclusions: Our findings suggest that subclinical secondary exposures to pesticides may affect vascular reactivity in children. Additional research is needed to confirm these findings.

Exposure to Perfluoroalkyl Acids and Markers of Kidney Function among Children and Adolescents Living near a Chemical Plant

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121:625–630 (2013) | http://dx.doi.org/10.1289/ehp.1205838

Background: Serum levels of perfluorooctanoic acid (PFOA) have been associated with decreased renal function in cross-sectional analyses, but the direction of the association is unclear.

Objectives: We examined the association of measured and model-predicted serum PFOA concentrations with estimated glomerular filtration rate (eGFR), a marker of kidney function, in a highly exposed population (median serum PFOA, 28.3 ng/mL).

Methods: We measured serum creatinine, PFOA, perfluorooctane sulfonate (PFOS), perfluorononanoic acid (PFNA), and perfluorohexane sulfonate (PFHxS) and calculated eGFR in 9,660 children 1 to < 18 years of age at study enrollment. We predicted concurrent and historical serum PFOA concentrations using a validated environmental, exposure, and pharmacokinetic model based on individual residential histories, and used linear regression to estimate the association between eGFR and measured and predicted serum PFOA concentrations. We hypothesized that predicted serum PFOA levels would be less susceptible to reverse causation than measured levels.

Results: An interquartile range increase in measured serum PFOA concentrations [IQR ln(PFOA) = 1.63] was associated with a decrease in eGFR of 0.75 mL/min/1.73 m^2 (95% CI: –1.41, –0.10; $p = 0.02$). Measured serum levels of PFOS, PFNA, and PFHxS were also cross-sectionally associated with decreased eGFR. In contrast, predicted serum PFOA concentrations at the time of enrollment were not associated with eGFR (–0.10; 95% CI: –0.80, 0.60; $p = 0.78$). Additionally, predicted serum PFOA levels at birth and during the first ten years of life were not related to eGFR.

Conclusions: Our findings suggest that the cross-sectional association between eGFR and serum PFOA observed in this and prior studies may be a consequence of, rather than a cause of, decreased kidney function.

Exposures

Residential Proximity to Methyl Bromide Use and Birth Outcomes in an Agricultural Population in California

Alison Gemmill, Robert B. Gunier, Asa Bradman, Brenda Eskenazi, and Kim G. Harley

121:737–743 (2013) | http://dx.doi.org/10.1289/ehp.1205682

Background: Methyl bromide, a fungicide often used in strawberry cultivation, is of concern for residents who live near agricultural applications because of its toxicity and potential for drift. Little is known about the effects of methyl bromide exposure during pregnancy.

Objective: We investigated the relationship between residential proximity to methyl bromide use and birth outcomes.

Methods: Participants were from the CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas) study (n = 442), a longitudinal cohort study examining the health effects of environmental exposures on pregnant women and their children in an agricultural community in northern California. Using data from the California Pesticide Use Reporting system, we employed a geographic information system to estimate the amount of methyl bromide applied within 5 km of a woman's residence during pregnancy. Multiple linear regression models were used to estimate associations between trimester-specific proximity to use and birth weight, length, head circumference, and gestational age.

Results: High methyl bromide use (vs. no use) within 5 km of the home during the second trimester was negatively associated with birth weight (β = –113.1 g; CI: –218.1, –8.1), birth length (β = –0.85 cm; CI: –1.44, –0.27), and head circumference (β = –0.33 cm; CI: –0.67, 0.01). These outcomes were also associated with moderate methyl bromide use during the second trimester. Negative associations with fetal growth parameters were stronger when larger (5 km and 8 km) versus smaller (1 km and 3 km) buffer zones were used to estimate exposure.

Conclusions: Residential proximity to methyl bromide use during the second trimester was associated with markers of restricted fetal growth in our study.

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Getting the Drift: Methyl Bromide Application and Adverse Birth Outcomes in an Agricultural Area

Julia R. Barrett | A198 (June 2013)

http://dx.doi.org/10.1289/ehp.121-A198

Evaluation of the Association between Persistent Organic Pollutants (POPs) and Diabetes in Epidemiological Studies: A National Toxicology Program Workshop Review

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121:774–783 (2013) | http://dx.doi.org/10.1289/ehp.1205502

Background: Diabetes is a major threat to public health in the United States and worldwide. Understanding the role of environmental chemicals in the development or progression of diabetes is an emerging issue in environmental health.

Objective: We assessed the epidemiologic literature for evidence of associations between persistent organic pollutants (POPs) and type 2 diabetes.

Methods: Using a PubMed search and reference lists from relevant studies or review articles, we identified 72 epidemiological studies that investigated associations of persistent organic pollutants (POPs) with diabetes. We evaluated these studies for consistency, strengths and weaknesses of study design (including power and statistical methods), clinical diagnosis, exposure assessment, study population characteristics, and identification of data gaps and areas for future research.

Conclusions: Heterogeneity of the studies precluded conducting a meta-analysis, but the overall evidence is sufficient for a positive association of some organochlorine POPs with type 2 diabetes. Collectively, these data are not sufficient to establish causality. Initial data mining revealed that the strongest positive correlation of diabetes with POPs occurred with organochlorine compounds, such as *trans*-nonachlor, dichlorodiphenyldichloroethylene (DDE), polychlorinated biphenyls (PCBs), and dioxins and dioxin-like chemicals. There is less indication of an association between other nonorganochlorine POPs, such as perfluoroalkyl acids and brominated compounds, and type 2 diabetes. Experimental data are needed to confirm the causality of these POPs, which will shed new light on the pathogenesis of diabetes. This new information should be considered by governmental bodies involved in the regulation of environmental contaminants.

AIR POLLUTION: PARTICULATE MATTER/SMOKE/INDOOR AIR

Research Opportunities for Cancer Associated with Indoor Air Pollution from Solid-Fuel Combustion

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120:1495–1498 (2012) | http://dx.doi.org/10.1289/ehp.1204962

Background: Indoor air pollution (IAP) derived largely from the use of solid fuels for cooking and heating affects about 3 billion people worldwide, resulting in substantial adverse health outcomes, including cancer. Women and children from developing countries are the most exposed populations. A workshop was held in Arlington, Virginia, 9–11 May 2011, to better understand women's and children's potential health effects from IAP in developing countries. Workshop participants included international scientists, manufacturers, policy and regulatory officials, community leaders, and advocates who held extensive discussions to help identify future research needs.

Objectives: Our objective was to identify research opportunities regarding IAP and cancer, including research questions that could be incorporated into studies of interventions to reduce IAP exposure. In this commentary, we describe the state of the science in understanding IAP and its associations with cancer and suggest research opportunities for improving our understanding of the issues.

Discussion: Opportunities for research on IAP and cancer include studies of the effect of IAP on cancers other than lung cancer; studies of genetic factors that modify susceptibility; studies to determine whether the effects of IAP are mediated via germline, somatic, and/or epigenetic changes; and studies of the effects of IAP exposure via dermal and/or oral routes.

Conclusions: IAP from indoor coal use increases the risk of lung cancer. Installing chimneys can reduce risk, and some genotypes, including *GSTM1*-null, can increase risk. Additional research is needed regarding the effects of IAP on other cancers and the effects of different types of solid fuels, oral and dermal routes of IAP exposure, genetic and epigenetic mechanisms, and genetic susceptibility.

Air Pollution Exposure and Markers of Placental Growth and Function: The Generation R Study

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120:1753–1759 (2012) | http://dx.doi.org/10.1289/ehp.1204918

Background: Air pollution exposure during pregnancy might affect placental growth and function, perhaps leading to pregnancy complications.

Objective: We prospectively evaluated the associations of maternal air pollution exposure with markers of placental growth and function among 7,801 pregnant women in the Netherlands.

Methods: We estimated levels of particulate matter ≤ 10 μm in aerodynamic diameter (PM_{10}) and nitrogen dioxide (NO_2) at the home address for different periods during pregnancy using dispersion modeling techniques. Pro- and anti-angiogenic factors [placental growth factor (PlGF) and soluble fms-like tyrosine kinase 1 (sFlt-1), respectively] were measured in first- and second-trimester maternal blood and in fetal cord blood samples at delivery. Pulsatility index of the uterine and umbilical arteries was measured by Doppler ultrasound in second and third trimester, and notching was assessed in third trimester. Placenta weight and birth weight were obtained from medical records.

Results: Higher PM_{10} and NO_2 exposure levels were associated with lower second-trimester maternal sFlt-1 and PlGF levels. PM_{10} and NO_2 exposures averaged over total pregnancy were associated with higher sFlt-1 and lower PlGF levels in fetal cord blood, consistent with an anti-angiogenic state. PM_{10} and NO_2 exposures were not consistently associated with second- or third-trimester placental resistance indices. NO_2 exposure was associated with third-trimester notching (odds ratio 1.33; 95% CI: 0.99, 1.78 per 10-μg/m^3 increase in the prior 2 months). PM_{10} and NO_2 exposures were associated with lower placenta weight (–11.8 g; 95% CI: –20.9, –2.7, and –10.7 g; 95% CI: –19.0, –2.4, respectively, per 10-μg/m^3 increase in the prior 2 months), but not with placenta to birth weight ratio.

Conclusions: Our results suggest that maternal air pollution exposure may influence markers of placental growth and function. Future studies are needed to confirm these findings and explore the maternal and fetal consequences.

Early-Life Exposure to Outdoor Air Pollution and Respiratory Health, Ear Infections, and Eczema in Infants from the INMA Study

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121:387–392 (2013) | http://dx.doi.org/10.1289/ehp.1205281

Background: Prenatal and early-life periods may be critical windows for harmful effects of air pollution on infant health.

Objectives: We studied the association of air pollution exposure during pregnancy and the first year of life with respiratory illnesses, ear infections, and eczema during the first 12–18 months of age in a Spanish birth cohort of 2,199 infants.

Methods: We obtained parentally reported information on doctor-diagnosed lower respiratory tract infections (LRTI) and parental reports of wheezing, eczema, and ear infections. We estimated individual exposures to nitrogen dioxide (NO_2) and benzene with temporally adjusted land use regression models. We used log-binomial regression models and a combined random-effects meta-analysis to estimate the effects of air pollution exposure on health outcomes across the four study locations.

Results: A 10-μg/m^3 increase in average NO_2 during pregnancy was associated with LRTI [relative risk (RR) = 1.05; 95% CI: 0.98, 1.12] and ear infections (RR = 1.18; 95% CI: 0.98, 1.41). The RRs for an interquartile range (IQR) increase in NO_2 were 1.08 (95% CI: 0.97, 1.21) for LRTI and 1.31 (95% CI: 0.97, 1.76) for ear infections. Compared with NO_2, the association for an IQR increase in average benzene exposure was similar for LRTI (RR = 1.06; 95% CI: 0.94, 1.19) and slightly lower for ear infections (RR = 1.17; 95% CI: 0.93, 1.46). Associations were slightly stronger among infants whose mothers spent more time at home during pregnancy. Air pollution exposure during the first year was highly correlated with prenatal exposure, so we were unable to discern the relative importance of each exposure period.

Conclusions: Our findings support the hypothesis that early-life exposure to ambient air pollution may increase the risk of upper and lower respiratory tract infections in infants.

RELATED ARTICLES

SPHERES OF INFLUENCE | Environmental Exposures in the Context of Child Care

Nate Seltenrich | A160 (May 2013)
http://dx.doi.org/10.1289/ehp.121-A160

NEWS | Organic Food Conclusions Don't Tell the Whole Story

David C. Holzman | A458 (December 2012)
http://dx.doi.org/10.1289/ehp.120-A458

Gestational Diabetes and Preeclampsia in Association with Air Pollution at Levels below Current Air Quality Guidelines

Ebba Malmqvist, Kristina Jakobsson, Håkan Tinnerberg, Anna Rignell-Hydbom, and Lars Rylander

121:488–493 (2013) | http://dx.doi.org/10.1289/ehp.1205736

Background: Several studies have estimated associations between air pollution and birth outcomes, but few have evaluated potential effects on pregnancy complications.

Objective: We investigated whether low-level exposure to air pollution is associated with gestational diabetes and preeclampsia.

Methods: High-quality registry information on 81,110 singleton pregnancy outcomes in southern Sweden during 1999–2005 was linked to individual-level exposure estimates with high spatial resolution. Modeled exposure to nitrogen oxides (NO_x), expressed as mean concentrations per trimester, and proximity to roads of different traffic densities were used as proxy indicators of exposure to combustion-related air pollution. The data were analyzed by logistic regression, with and without adjusting for potential confounders.

Results: The prevalence of gestational diabetes increased with each NO_x quartile, with an adjusted odds ratio (OR) of 1.69 (95% CI: 1.41, 2.03) for the highest (> 22.7 μg/m^3) compared with the lowest quartile (2.5–8.9 μg/m^3) of exposure during the second trimester. The adjusted OR for acquiring preeclampsia after exposure during the third trimester was 1.51 (1.32, 1.73) in the highest quartile of NO_x compared with the lowest. Both outcomes were associated with high traffic density, but ORs were significant for gestational diabetes only.

Conclusion: NO_x exposure during pregnancy was associated with gestational diabetes and preeclampsia in an area with air pollution levels below current air quality guidelines.

» NEWS | SCIENCE SELECTION

When Blood Meets Nitrogen Oxides: Pregnancy Complications and Air Pollution Exposure

Tanya Tillett | A136 (April 2013)

http://dx.doi.org/10.1289/ehp.121-A136

Reducing Health Risks from Indoor Exposures in Rapidly Developing Urban China

Yinping Zhang, Jinhan Mo, and Charles J. Weschler

121:751–755 (2013) | http://dx.doi.org/10.1289/ehp.1205983

Background: Over the past two decades there has been a large migration of China's population from rural to urban regions. At the same time, residences in cities have changed in character from single-story or low-rise buildings to high-rise structures constructed and furnished with many synthetic materials. As a consequence, indoor exposures (to pollutants with outdoor and indoor sources) have changed significantly.

Objectives: We briefly discuss the inferred impact that urbanization and modernization have had on indoor exposures and public health in China. We argue that growing adverse health costs associated with these changes are not inevitable, and we present steps that could be taken to reduce indoor exposures to harmful pollutants.

Discussion: As documented by China's Ministry of Health, there have been significant increases in morbidity and mortality among urban residents over the past 20 years. Evidence suggests that the population's exposure to air pollutants has contributed to increases in lung cancer, cardiovascular disease, pulmonary disease, and birth defects. Whether a pollutant has an outdoor or an indoor source, most exposure to the pollutant occurs indoors. Going forward, indoor exposures can be reduced by limiting the ingress of outdoor pollutants (while providing adequate ventilation with clean air), minimizing indoor sources of pollutants, updating government policies related to indoor pollution, and addressing indoor air quality during a building's initial design.

Conclusions: Taking the suggested steps could lead to significant reductions in morbidity and mortality, greatly reducing the societal costs associated with pollutant derived ill health.

RADIATION

Measures of Thyroid Function among Belarusian Children and Adolescents Exposed to Iodine-131 from the Accident at the Chernobyl Nuclear Plant

Evgenia Ostroumova, Alexander Rozhko, Maureen Hatch, Kyoji Furukawa, Olga Polyanskaya, Robert J. McConnell, Eldar Nadyrov, Sergey Petrenko, George Romanov, Vasilina Yauseyenka, Vladimir Drozdovitch, Viktor Minenko, Alexander Prokopovich, Irina Savasteeva, Lydia B. Zablotska, Kiyohiko Mabuchi, and Alina V. Brenner

121:865–871 (2013) | http://dx.doi.org/10.1289/ehp.1205783

Background: Thyroid dysfunction after exposure to low or moderate doses of radioactive iodine-131 (^{131}I) at a young age is a public health concern. However, quantitative data are sparse concerning ^{131}I-related risk of these common diseases.

Objective: Our goal was to assess the prevalence of thyroid dysfunction in association with ^{131}I exposure during childhood (≤ 18 years) due to fallout from the Chernobyl accident.

Methods: We conducted a cross-sectional analysis of hypothyroidism, hyperthyroidism, autoimmune thyroiditis (AIT), serum concentrations of thyroid-stimulating hormone (TSH), and autoantibodies to thyroperoxidase (ATPO) in relation to measurement-based ^{131}I dose estimates in a Belarusian cohort of 10,827 individuals screened for various thyroid diseases.

Results: Mean age at exposure (± SD) was 8.2 ± 5.0 years. Mean (median) estimated ^{131}I thyroid dose was 0.54 (0.23) Gy (range, 0.001–26.6 Gy). We found significant positive associations of ^{131}I dose with hypothyroidism (mainly subclinical and antibody-negative) and serum TSH concentration. The excess odds ratio per 1 Gy for hypothyroidism was 0.34 (95% CI: 0.15, 0.62) and varied significantly by age at exposure and at examination, presence of goiter, and urban/rural residency. We found no evidence of positive associations with antibody-positive hypothyroidism, hyperthyroidism, AIT, or elevated ATPO.

Conclusions: The association between ^{131}I dose and hypothyroidism in the Belarusian cohort is consistent with that previously reported for a Ukrainian cohort and strengthens evidence of the effect of environmental ^{131}I exposure during childhood on hypothyroidism, but not other thyroid outcomes.

FOOD SAFETY/INSECURITY, NUTRITION

Climate Change and Food Security: Health Impacts in Developed Countries

Iain R. Lake, Lee Hooper, Asmaa Abdelhamid, Graham Bentham, Alistair B.A. Boxall, Alizon Draper, Susan Fairweather-Tait, Mike Hulme, Paul R. Hunter, Gordon Nichols, and Keith W. Waldron

120:1520–1526 (2012) | http://dx.doi.org/10.1289/ehp.1104424

Background: Anthropogenic climate change will affect global food production, with uncertain consequences for human health in developed countries.

Objectives: We investigated the potential impact of climate change on food security (nutrition and food safety) and the implications for human health in developed countries.

Methods: Expert input and structured literature searches were conducted and synthesized to produce overall assessments of the likely impacts of climate change on global food production and recommendations for future research and policy changes.

Results: Increasing food prices may lower the nutritional quality of dietary intakes, exacerbate obesity, and amplify health inequalities. Altered conditions for food production may result in emerging pathogens, new crop and livestock species, and altered use of pesticides and veterinary medicines, and affect the main transfer mechanisms through which contaminants move from the environment into food. All these have implications for food safety and the nutritional content of food. Climate change mitigation may increase consumption of foods whose production reduces greenhouse gas emissions. Impacts may include reduced red meat consumption (with positive effects on saturated fat, but negative impacts on zinc and iron intake) and reduced winter fruit and vegetable consumption. Developed countries have complex structures in place that may be used to adapt to the food safety consequences of climate change, although their effectiveness will vary between countries, and the ability to respond to nutritional challenges is less certain.

Conclusions: Climate change will have notable impacts upon nutrition and food safety in developed countries, but further research is necessary to accurately quantify these impacts. Uncertainty about future impacts, coupled with evidence that climate change may lead to more variable food quality, emphasizes the need to maintain and strengthen existing structures and policies to regulate food production, monitor food quality and safety, and respond to nutritional and safety issues that arise.

Methodologies *and* Populations

COMMUNITY-BASED PARTICIPATORY RESEARCH AND TRANSLATION/ENVIRONMENTAL JUSTICE

Indigenous Peoples of North America: Environmental Exposures and Reproductive Justice

Elizabeth Hoover, Katsi Cook, Ron Plain, Kathy Sanchez, Vi Waghiyi, Pamela Miller, Renee Dufault, Caitlin Sislin, and David O. Carpenter

120:1645–1649 (2012) | http://dx.doi.org/10.1289/ehp.1205422

Background: Indigenous American communities face disproportionate health burdens and environmental health risks compared with the average North American population. These health impacts are issues of both environmental and reproductive justice.

Objectives: In this commentary, we review five indigenous communities in various stages of environmental health research and discuss the intersection of environmental health and reproductive justice issues in these communities as well as the limitations of legal recourse.

Discussion: The health disparities impacting life expectancy and reproductive capabilities in indigenous communities are due to a combination of social, economic, and environmental factors. The system of federal environmental and Indian law is insufficient to protect indigenous communities from environmental contamination. Many communities are interested in developing appropriate research partnerships in order to discern the full impact of environmental contamination and prevent further damage.

Conclusions: Continued research involving collaborative partnerships among scientific researchers, community members, and health care providers is needed to determine the impacts of this contamination and to develop approaches for remediation and policy interventions.

Environmental Inequality in Exposures to Airborne Particulate Matter Components in the United States

Michelle L. Bell and Keita Ebisu

120:1699–1704 (2012) | http://dx.doi.org/10.1289/ehp.1205201

Background: Growing evidence indicates that toxicity of fine particulate matter ≤ 2.5 μm in diameter ($PM_{2.5}$) differs by chemical component. Exposure to components may differ by population.

Objectives: We investigated whether exposures to $PM_{2.5}$ components differ by race/ethnicity, age, and socioeconomic status (SES).

Methods: Long-term exposures (2000 through 2006) were estimated for 215 U.S. census tracts for $PM_{2.5}$ and for 14 $PM_{2.5}$ components. Population-weighted exposures were combined to generate overall estimated exposures by race/ethnicity, education, poverty status, employment, age, and earnings. We compared population characteristics for tracts with and without $PM_{2.5}$ component monitors.

Results: Larger disparities in estimated exposures were observed for components than for $PM_{2.5}$ total mass. For race/ethnicity, whites generally had the lowest exposures. Non-Hispanic blacks had higher exposures than did whites for 13 of the 14 components. Hispanics generally had the highest exposures (e.g., 152% higher than whites for chlorine, 94% higher for aluminum). Young persons (0–19 years of age) had levels as high as or higher than other ages for all exposures except sulfate. Persons with lower SES had higher estimated exposures, with some exceptions. For example, a 10% increase in the proportion unemployed was associated with a 20.0% increase in vanadium and an 18.3% increase in elemental carbon. Census tracts with monitors had more non-Hispanic blacks, lower education and earnings, and higher unemployment and poverty than did tracts without monitors.

Conclusions: Exposures to $PM_{2.5}$ components differed by race/ethnicity, age, and SES. If some components are more toxic than others, certain populations are likely to suffer higher health burdens. Demographics differed between populations covered and not covered by monitors.

Methodologies *and* Populations

EPIGENETICS

450K Epigenome-Wide Scan Identifies Differential DNA Methylation in Newborns Related to Maternal Smoking during Pregnancy

Bonnie R. Joubert, Siri E. Håberg, Roy M. Nilsen, Xuting Wang, Stein E. Vollset, Susan K. Murphy, Zhiqing Huang, Cathrine Hoyo,Øivind Midttun, Lea A. Cupul-Uicab, Per M. Ueland, Michael C. Wu, Wenche Nystad, Douglas A. Bell, Shyamal D. Peddada, and Stephanie J. London

120:1425–1431 (2012) | http://dx.doi.org/10.1289/ehp.1205412

Background: Epigenetic modifications, such as DNA methylation, due to *in utero* exposures may play a critical role in early programming for childhood and adult illness. Maternal smoking is a major risk factor for multiple adverse health outcomes in children, but the underlying mechanisms are unclear.

Objective: We investigated epigenome-wide methylation in cord blood of newborns in relation to maternal smoking during pregnancy.

Methods: We examined maternal plasma cotinine (an objective biomarker of smoking) measured during pregnancy in relation to DNA methylation at 473,844 CpG sites (CpGs) in 1,062 newborn cord blood samples from the Norwegian Mother and Child Cohort Study (MoBa) using the Infinium HumanMethylation450 BeadChip (450K).

Results: We found differential DNA methylation at epigenome-wide statistical significance (p-value < 1.06×10^{-7}) for 26 CpGs mapped to 10 genes. We replicated findings for CpGs in *AHRR*, *CYP1A1*, and *GFI1* at strict Bonferroni-corrected statistical significance in a U.S. birth cohort. *AHRR* and *CYP1A1* play a key role in the aryl hydrocarbon receptor signaling pathway, which mediates the detoxification of the components of tobacco smoke. *GFI1* is involved in diverse developmental processes but has not previously been implicated in responses to tobacco smoke.

Conclusions: We identified a set of genes with methylation changes present at birth in children whose mothers smoked during pregnancy. This is the first study of differential methylation across the genome in relation to maternal smoking during pregnancy using the 450K platform. Our findings implicate epigenetic mechanisms in the pathogenesis of the adverse health outcomes associated with this important *in utero* exposure.

» NEWS | SCIENCE SELECTION

Pattern of Clues: Evidence of Distinct DNA Methylation in Newborns of Smoking Women

Wendee Nicole | A402 (October 2012)

http://dx.doi.org/10.1289/ehp.120-A402a

RELATED ARTICLES

EDITORIAL | The Public Health and Policy Implications of Epigenetics and Pediatric Health Research

Nsedu Obot Witherspoon, Kristie Trousdale, Cynthia F. Bearer, Rachel L. Miller | A380–A381 (October 2012)

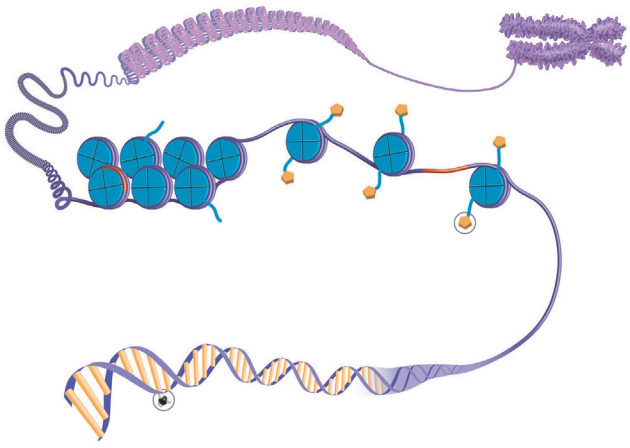
http://dx.doi.org/10.1289/ehp.1205956

NEWS | A Steep Learning Curve: Decoding Epigenetic Influence on Behavior and Mental Health

Bob Weinhold | A396–A401 (October 2012)

http://dx.doi.org/10.1289/ehp.120-A396

Research on epigenetics has surged in the past two decades as it has become apparent that changes in gene function aside from those related to DNA mutations or natural variations may be integral factors in numerous perplexing health disorders. Although much remains unknown about this relatively new field, early results in the niche field of behavioral epigenetics suggest such studies could provide insights into behavioral and mental health conditions such as autism spectrum disorders, attention deficit/hyperactivity disorder, schizophrenia, bipolar disorder, depression, and anxiety.



FOCUS | The Environment Within: Exploring the Role of the Gut Microbiome in Health and Disease

Lindsey Konkel | A276 (September 2013)

http://dx.doi.org/10.1289/ehp.121-A276

A growing body of research suggests that part of what determines how the human body responds to external stimuli may be not only our own genes but also the genes of the trillions of microorganisms that reside on and in the human body. New studies are shedding light on the ways that microorganisms in the gut influence biological functions and play a role in diseases throughout the body.

Methodologies *and* Populations

Differential DNA Methylation in Umbilical Cord Blood of Infants Exposed to Low Levels of Arsenic *in Utero*

Devin C. Koestler, Michele Avissar-Whiting, E. Andres Houseman, Margaret R. Karagas, and Carmen J. Marsit

121:971–977 (2013) | http://dx.doi.org/10.1289/ehp.1205925

Background: There is increasing epidemiologic evidence that arsenic exposure *in utero*, even at low levels found throughout much of the world, is associated with adverse reproductive outcomes and may contribute to long-term health effects. Animal models, *in vitro* studies, and human cancer data suggest that arsenic may induce epigenetic alterations, specifically by altering patterns of DNA methylation.

Objectives: In this study we aimed to identify differences in DNA methylation in cord blood samples of infants with *in utero*, low-level arsenic exposure.

Methods: DNA methylation of cord-blood derived DNA from 134 infants involved in a prospective birth cohort in New Hampshire was profiled using the Illumina Infinium Methylation450K array. *In utero* arsenic exposure was estimated using maternal urine samples collected at 24–28 weeks gestation. We used a novel cell mixture deconvolution methodology for examining the association between inferred white blood cell mixtures in infant cord blood and *in utero* arsenic exposure; we also examined the association between methylation at individual CpG loci and arsenic exposure levels.

Results: We found an association between urinary inorganic arsenic concentration and the estimated proportion of $CD8^+$ T lymphocytes (1.18; 95% CI: 0.12, 2.23). Among the top 100 CpG loci with the lowest *p*-values based on their association with urinary arsenic levels, there was a statistically significant enrichment of these loci in CpG islands ($p = 0.009$). Of those in CpG islands ($n = 44$), most (75%) exhibited higher methylation levels in the highest exposed group compared with the lowest exposed group. Also, several CpG loci exhibited a linear dose-dependent relationship between methylation and arsenic exposure.

Conclusions: Our findings suggest that *in utero* exposure to low levels of arsenic may affect the epigenome. Long-term follow-up is planned to determine whether the observed changes are associated with health outcomes.

METHODOLOGIES

Toxicokinetic Modeling of Persistent Organic Pollutant Levels in Blood from Birth to 45 Months of Age in Longitudinal Birth Cohort Studies

Marc-André Verner, Dean Sonneborn, Kinga Lancz, Gina Muckle, Pierre Ayotte, Éric Dewailly, Anton Kocan, Lubica Palkovicová, Tomas Trnovec, Sami Haddad, Irva Hertz-Picciotto, and Merete Eggesbø

121:131–137 (2013) | http://dx.doi.org/10.1289/ehp.1205552

Background: Despite experimental evidence that lactational exposure to persistent organic pollutants (POPs) can impact health, results from epidemiologic studies are inconclusive. Inconsistency across studies may reflect the inability of current methods to estimate children's blood levels during specific periods of susceptibility.

Objectives: We developed a toxicokinetic model to simulate blood POP levels in children from two longitudinal birth cohorts and aimed to validate it against blood levels measured at 6, 16, and 45 months of age.

Methods: The model consisted of a maternal and a child lipid compartment connected through placental diffusion and breastfeeding. Simulations were carried out based on individual physiologic parameters; duration of breastfeeding; and levels of POPs measured in maternal blood at delivery, cord blood, or breast milk. Model validity was assessed through regression analyses of simulated against measured blood levels.

Results: Simulated levels explained between 10% and 83% of measured blood levels depending on the cohort, the compound, the sample used to simulate children's blood levels, and child's age when blood levels were measured. Model accuracy was highest for estimated blood POP levels at 6 months based on maternal or cord blood levels. However, loss in model precision between the 6th and the 45th month was small for most compounds.

Conclusions: Our validated toxicokinetic model can be used to estimate children's blood POP levels in early to mid-childhood. Estimates can be used in epidemiologic studies to evaluate the impact of exposure during hypothesized postnatal periods of susceptibility on health.

Methodologies *and* Populations

Systems Biology and Birth Defects Prevention: Blockade of the Glucocorticoid Receptor Prevents Arsenic-Induced Birth Defects

Bhavesh K. Ahir, Alison P. Sanders, Julia E. Rager, and Rebecca C. Fry

121:332–338 (2013) | http://dx.doi.org/10.1289/ehp.1205659

Background: The biological mechanisms by which environmental metals are associated with birth defects are largely unknown. Systems biology–based approaches may help to identify key pathways that mediate metal-induced birth defects as well as potential targets for prevention.

Objectives: First, we applied a novel computational approach to identify a prioritized biological pathway that associates metals with birth defects. Second, in a laboratory setting, we sought to determine whether inhibition of the identified pathway prevents developmental defects.

Methods: Seven environmental metals were selected for inclusion in the computational analysis: arsenic, cadmium, chromium, lead, mercury, nickel, and selenium. We used an *in silico* strategy to predict genes and pathways associated with both metal exposure and developmental defects. The most significant pathway was identified and tested using an *in ovo* whole chick embryo culture assay. We further evaluated the role of the pathway as a mediator of metal-induced toxicity using the *in vitro* midbrain micromass culture assay.

Results: The glucocorticoid receptor pathway was computationally predicted to be a key mediator of multiple metal-induced birth defects. In the chick embryo model, structural malformations induced by inorganic arsenic (iAs) were prevented when signaling of the glucocorticoid receptor pathway was inhibited. Further, glucocorticoid receptor inhibition demonstrated partial to complete protection from both iAs- and cadmium-induced neurodevelopmental toxicity *in vitro*.

Conclusions: Our findings highlight a novel approach to computationally identify a targeted biological pathway for examining birth defects prevention.

» NEWS | SCIENCE SELECTION

A Systems-Level Approach to Studying Birth Defects: Novel Method Identifies Potential Key Pathway

Kellyn S. Betts | A95 (March 2013)

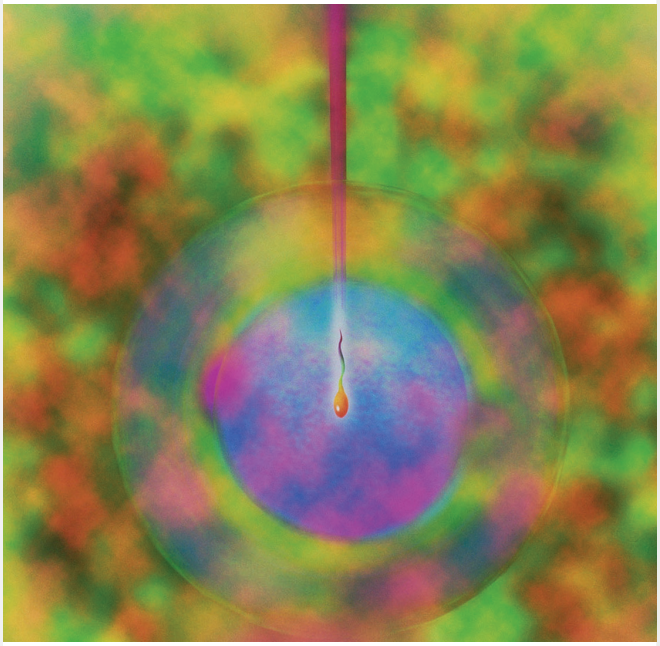
http://dx.doi.org/10.1289/ehp.121-A95

RELATED ARTICLES

NEWS | Altering The Primal Environment: Health Effects Associated with Assisted Reproductive Technologies

Julie Halpert | A390–A395 (October 2012)
http://dx.doi.org/10.1289/ehp.120-A390

Assisted reproductive technologies (ART) have made it possible for couples to have children who otherwise would not have been able to. What influence might ART procedures, as well as underlying infertility, have on the health of children conceived using these methods? Investigators are studying whether introducing fertility drugs and manipulating eggs and sperm in a laboratory setting—in essence, altering the primal environment—sets the stage for adverse health effects in children.



NEWS | Gut Bacteria and Melamine Toxicity

Bob Weinhold | A149 (May 2013)
http://dx.doi.org/10.1289/ehp.121-A149

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