Preconception Maternal and Paternal Exposure to Persistent Organic Pollutants and Birth Size: The LIFE Study

Candace A. Robledo, National Institutes of Health
Edwina Yeung, National Institutes of Health
Pauline Mendola, National Institutes of Health
Rajeshwari Sundaram, National Institutes of Health
Jose Maisog, National Institutes of Health
Anne M. Sweeney, Texas A&M Health Sciences Center
Dana Barr, Emory University
Germaine M. Buck Louis, National Institutes of Health

Journal Title: Environmental Health Perspectives
Volume: Volume 123, Number 1
Publisher: National Institute of Environmental Health Sciences (NIEHS) | 2015-01-01, Pages 88-94
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1289/ehp.1308016
Permanent URL: https://pid.emory.edu/ark:/25593/s2d3k

Final published version: http://dx.doi.org/10.1289/ehp.1308016

Copyright information:
Publication of EHP lies in the public domain and is therefore without copyright.

Accessed September 15, 2017 2:56 AM EDT
Preconception Maternal and Paternal Exposure to Persistent Organic Pollutants and Birth Size: The LIFE Study

Candace A. Robledo,1 Edwina Yeung,1 Pauline Mendola,1 Rajeshwari Sundaram,1 Jose Maisog,1 Anne M. Sweeney,2 Dana Boyd Barr,3 and Germaine M. Buck Louis1

1Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services, Rockville, Maryland, USA; 2Department of Epidemiology and Biostatistics, School of Rural Public Health, Texas A&M Health Sciences Center, College Station, Texas, USA; 3Rollins School of Public Health, Emory University, Atlanta, Georgia, USA

BACKGROUND: Persistent organic pollutants (POPs) are developmental toxicants, but the impact of both maternal and paternal exposures on offspring birth size is largely unexplored.

OBJECTIVE: We examined associations between maternal and paternal serum concentrations of 63 POPs, comprising five major classes of pollutants, with birth size measures.

METHODS: Parental serum concentrations of 9 organochlorine pesticides, 1 polybrominated biphenyl (PBB), 7 perfluorinated chemicals (PFCs), 10 polybrominated diphenyl ethers (PBDEs), and 36 polychlorinated biphenyls (PCBs) were measured before conception for 234 couples. Differences in birth weight, length, head circumference, and ponderal index were estimated using multiple linear regression per 1-SD increase in natural log-transformed (ln-transformed) chemicals. Models were estimated separately for each parent and adjusted for maternal age, maternal prepregnancy body mass index (kilograms per meter squared) and other confounders, and all models included an interaction term between infant sex and each chemical.

RESULTS: Among girls (n = 117), birth weight was significantly lower (range, 84–195 g) in association with a 1-SD increase in ln-transformed maternal serum concentrations of DDT, PBDE congeners 28 and 183, and paternal serum concentrations of PBDE-183 and PCB-167. Among boys (n = 113), maternal (PCBs 138, 153, 167, 170, 195, and 209 and perfluorooctane sulfonamide) and paternal (PCBs 172 and 193) serum concentrations of several POPs were statistically associated with lower birth weight (range, 98–170 g), whereas paternal concentrations of PBDEs (66, 99) were associated with higher birth weight. Differences in offspring head circumference, length, and ponderal index were also associated with parental exposures.

CONCLUSIONS: Preconceptional maternal and paternal concentrations of several POPs were associated with statistically significant differences in birth size among offspring.


Introduction

The presence of persistent organic pollutants (POPs) in maternal blood (Llop et al. 2010; Rodríguez-Dozal et al. 2012; Rudge et al. 2012; Wang et al. 2009), umbilical cord blood (Aruckle et al. 2013; Foster et al. 2011), and breast milk (Miké et al. 2012; Pan et al. 2009; Tanabe and Kunisu 2007) documenting in utero and lactational exposure has prompted epidemiological studies to examine the relationship between exposure to these compounds and fetal growth and development (Mattison 2010; Windham and Fenster 2008). Research in this area has generally focused on outcomes such as birth weight and length of gestation, strong indicators of neonatal health. Epidemiological studies have shown a decrease in birth weight in relation to exposure to POPs that include polychlorinated biphenyls (PCBs) (Govarts et al. 2012; Karmas and Zhu 2004; Murphy et al. 2010), polychlorinated diphenyl ethers (PBDEs) (Harley et al. 2011), perfluoralkyl chemicals (PFCs) (Washino et al. 2009), and organochlorine pesticides (OCPs) (Wolff et al. 2007). Although the previous studies have demonstrated an association between POPs and reduced birth size, proxied by birth weight, findings are inconsistent and studies have also reported null associations (Farhang et al. 2005; Givens et al. 2007; Karmas and Zhu 2004; Kezios et al. 2012; Longnecker et al. 2005; Mazdai et al. 2003; Olsen et al. 2009; Pan et al. 2009; Sweeney andSymanski 2007; Tan et al. 2009; Wu et al. 2010).

Inconsistencies may be attributed to several key limitations of prior studies. Past research has focused on pre- and postnatal exposures to POPs, despite evidence that the preconception period may be a critical window of exposure for fetal growth and development (Chapin et al. 2004). Given the metabolic and physiological changes that occur during pregnancy, preconception levels may be more accurate in capturing the dose to the fetus. Regardless of their long half-lives and persistent nature, the concentrations of pollutants may vary across critical windows of development, as seen with PCBs (Bloom et al. 2007) and other selected POPs (Wang et al. 2009). Finally, prior studies have focused on elucidating the impact of maternal exposure to POPs on birth size, regardless of the fact that pregnancy is a couple-dependent outcome. Consequently, the impacts of paternally mediated factors on birth size have been largely unstudied (Cordier 2008; Shah and Knowledge Synthesis Group on Determinants of Preterm/Low Birthweight Births 2010). Limited to occupational studies, little is known about the impact of paternal POP exposures on birth size (Lawson et al. 2004; Michalek et al. 1998).

We aim to address these gaps in knowledge by estimating the associations of maternal and paternal preconceptional serum concentrations of POPs on birth size. We hypothesize that preconception serum concentrations of both maternal and paternal persistent environmental chemicals are associated with reduced birth size measures (i.e., birth weight, head circumference, length, and ponderal index).

Methods

Study population. The Longitudinal Investigation of Fertility and the Environment (LIFE) Study was a prospective cohort study conducted between 2005 and 2009 to assess the impact of persistent environmental chemicals on reproductive outcomes (Buck Louis et al. 2011). Briefly, LIFE recruited couples (n = 501) who resided in Michigan and
Persistent organic pollutants and birth size

Texas with reported or presumed exposure to persistent environmental chemicals. Married couples or those in a committed relationship who were planning a pregnancy in the subsequent 6 months were targeted for recruitment. Couples were ineligible to participate if either partner was medically/surgically sterile; they had discontinued contraception for > 2 months; the female’s menstrual cycle was not between 21 and 42 days or she had received injectable contraceptives within the previous 12 months; they were not of reproductive age (females < 18 or > 40 years, and males < 18 years); or they could not communicate in English or Spanish. Couples were followed until a positive human chorionic gonadotropin (hCG) pregnancy test or through 12 months of attempting pregnancy.

Following conception, women were followed daily for 8 weeks and then monthly until a pregnancy loss or delivery. Analyses were restricted to couples for whom a singleton pregnancy was observed (n = 247), regardless of a previous loss, and for whose child birth weight was reported (n = 234). In doing so, we excluded data for two sets of twin births.

Institutional review board approval was obtained from all collaborating institutions, and informed written consent was obtained from all couples before their participation.

Assessment of fetal growth outcomes and covariates. Couples were asked to report birth size characteristics for the index birth using standardized birth announcements specifically designed for the LIFE study that were included in the pregnancy diary (available on request). Women were trained in their use and completed them after delivery. Information recorded on the delivery cards included infant sex, birth weight (in grams or pounds and ounces) (n = 230), length (in centimeters or inches) (n = 229), and head circumference (in centimeters or inches) (n = 181). Ponderal index (n = 229), a marker of asymmetrical growth retardation thought to be a result of fetal insult, was defined as 100 x [birth weight (grams)/length (cubic centimeters)] (Sparks et al. 1998). Analyses did not include infants whose birth weight (n = 2) or head circumference (n = 2) exceeded the 99th percentile.

Baseline questionnaires were administered to each partner separately and were used to collect medical and reproductive histories. Information on lifestyle factors such as the use of alcohol and tobacco in the previous 4 weeks was collected from each partner separately and were used to measure concentrations of environmental chemicals. For quality control, blood collection equipment was tested and determined to be free from contaminants under study. Quantity of serum toxicants was conducted by the Division of Laboratory Sciences in the National Center for Environmental Health at the Centers for Disease Control and Prevention (CDC). A list of all congeners measured and their abbreviations can be found in Table 1. Established protocols using isotope dilution gas chromatography–high resolution mass spectrometry or high performance liquid chromatography–tandem mass spectrometry (Barr et al. 2003; Kuklenyik et al. 2005; Sandau et al. 2003) were used to estimate serum concentrations of 1 polybrominated biphenyl (PBB), 9 OCPOs, 10 PBDEs, 36 PCBs, and 7 PFCs. Liquid chromatography–isotope dilution tandem mass spectrometry (Bennert et al. 1997) was used to quantify serum concentrations of cotinine (nanograms per milliliter), as a measure of tobacco exposure. Enzymatic methods were used to estimate total cholesterol, nonesterified cholesterol, triglycerides, and phospholipids (Akins et al. 1989). Total serum lipids (nanograms per gram serum) were calculated using established summation methods (Bennert et al. 2007; Phillips et al. 1989). Serum lipid concentrations were included in models as a covariate, and pollutant concentrations are reported in nanograms per gram serum, except for PFCs and cotinine, which are reported in nanograms per milliliter.

Statistical analyses. We assessed the distributions of all exposures and relevant covariates. Normality of continuous variables was assessed using Kolmogorov–Smirnov tests. Missing covariate values and missing chemical, cotinine, and lipid data (< 4%), due to insufficient blood for analysis, were imputed under the missing at random assumption, using Markov chain Monte Carlo methods (Rubin 1996) detailed elsewhere (Buck Louis et al. 2013). Machine-read values for chemical concentrations were used, and values below the limit of detection were not substituted to avoid introducing bias (Schisterman et al. 2006). To account for skewed distribution and for ease of interpretation, chemical concentrations were natural log-transformed (ln) and rescaled by their standard deviation. Geometric means (GMs) and 95% confidence intervals (CIs) were calculated for all chemicals. See Supplemental Material, Table S1, for a list of SDs and GMs for this study population. The outcome variables, birth weight (grams), head circumference (centimeters), length (centimeters), and ponderal index (grams per cubic centimeter) were not In-transformed. Each outcome and chemical concentration was modeled as a continuous variable.

We used multiple linear regression to estimate the mean difference in each outcome per 1-SD increase for all In-transformed chemicals. The mean differences in growth outcomes for each chemical and parent were estimated separately. Models were adjusted a priori for maternal age, the difference between maternal and paternal age, maternal prepregnancy BMI, infant sex, serum lipids (except PFCs), and serum cotinine concentrations (Cliver et al. 1995; Cogswell and Yip 1995; Shah and Knowledge Synthesis Group on Determinants of Preterm/Low Birthweight Births 2010). The sum of the remaining chemical concentrations (In-transformed and scaled by their respective standard deviation) in each chemical’s respective class was included in models to account for the mean level of individual concentrations. To account

<table>
<thead>
<tr>
<th>Table 1. Persistent organic pollutants (POPs) measured in study population, LIFE Study, 2005–2008.</th>
</tr>
</thead>
<tbody>
<tr>
<td>POPs</td>
</tr>
<tr>
<td>Polybrominated biphenyls (PBB)</td>
</tr>
<tr>
<td>Organochlorine pesticides (OCPs)</td>
</tr>
<tr>
<td>Polybrominated diphenyl ethers (PBDEs)</td>
</tr>
<tr>
<td>Perfluorooalkyl chemicals (PFCs)</td>
</tr>
</tbody>
</table>

Environmental Health Perspectives • VOLUME 123 | NUMBER 1 | January 2015
for the partner’s exposure, each model also included the total sum of partner’s serum concentrations in the respective class for the chemical being evaluated. Interaction between each pollutant and infant sex was evaluated by examining the statistical significance of their product term in each model ($p < 0.05$). Evidence of interaction between chemical exposures and birth outcomes by infant sex was observed for some chemicals and models by significant interaction term ($p$-interaction < 0.05), so all associations were estimated stratified by sex for consistency. We report associations for chemicals for which at least one statistically significant association was estimated with birth size measures. Statistical significance was set at $p < 0.05$.

We conducted a sensitivity analysis that excluded pregnancies complicated by gestational diabetes or hypertension because of their known effects on fetal growth (Mayer and Joseph 2013). Results and conclusions of the association between parental preconception exposure to persistent organic pollutants and birth size measures did not vary (data not shown). Therefore, model estimates that include all pregnancies are reported.

**Results**

**Study population.** Partners for whom a singleton delivery occurred were very similar in their sociodemographic characteristics (Table 2). The majority of men and women were non-Hispanic white, had a college education, were insured, and did not smoke or drink alcohol. Compared with their female counterparts, males were approximately 2 years older and on average had a higher BMI (29.3 vs. 26.5 kg/m²). Women reported having gestational diabetes mellitus ($n = 27$), hypercholesterolemia ($n = 18$), and preexisting hypertension ($n = 7$). The majority of infants were girls (51%). The mean (± SD) postconception gestational age and birth weight of infants at delivery was 36.2 ± 2.2 weeks and 3382.3 ± 487.5 g, respectively.

Serum concentrations of most POPs among couples were similar for partners. However, geometric mean concentrations of pesticides such as $p,p^\prime$-DDE (dichlorodiphenyldichloroethylene) (0.580 ng/g; 95% CI: 0.534, 0.630 vs. 0.752 ng/g; 95% CI: 0.700, 0.808), mirex (0.007 ng/g; 95% CI: 0.007, 0.008 vs. 0.013 ng/g; 95% CI: 0.011, 0.014), and several PFCs were markedly higher among males (see Supplemental Material, Table S1). Preconceptional parental concentrations of POPs were found to be associated with changes in birth size measures.

**OCPs and PCBs.** Statistically significant differences in birth size measures were estimated in association with both maternal and paternal preconception serum concentrations of OCPs among girls, but virtually no significant associations were observed among boys (Table 3). See Supplemental Material, Tables S2–S5, for all estimated associations for birth size measures and chemicals evaluated in our study. Among girls, a 1-SD increase in ln-transformed maternal serum concentrations of $o,p^\prime$-DDT (dichlorodiphenyltrichloroethane) was associated with lower birth weight ($\beta =$ 195.39 g; 95% CI: –351.25, –39.52), driven perhaps by smaller head circumference ($\beta =$ –0.78 cm; 95% CI: –1.48, –0.09). Smaller head circumference was also seen with increasing maternal concentrations of $\beta$-HCH (hexachlorocyclohexane) ($\beta =$ 1.47 cm; 95% CI: –2.33, –0.61). Length among girls was inversely associated with maternal concentrations of $\gamma$-HCH (lindane) and subsequently higher ponderal index ($\beta =$ 0.09 g/cm²; 95% CI: 0.03, 0.16). Similarly, paternal concentrations of $\gamma$-HCH were associated with shorter length and higher ponderal index among girls, despite mutual adjustment for mean partner concentrations of other organochlorine exposure. A higher ponderal index among girls was also seen with increasing paternal concentrations of $p,p^\prime$-DDE. Except for larger head circumference observed with increasing maternal concentrations of HCB (hexachlorobenzene), preconceptional parental concentrations of OCPs were not associated with birth size among boys. Parental preconception concentrations of PBB-153 were not found to be associated with birth size measures.

**PCBs.** The mean birth weight of boys was 104.23 g lower (95% CI: –194.16, –14.30) for every 1-SD increase in ln-transformed maternal concentrations of PFOA (perfluorooctanoate sulfonamide). Maternal concentrations of the Et-PFOA-AcOH [2-(o-ethyl-perfluorooctanoate sulfonamide)] acetate metabolite were associated with a smaller mean ponderal index among girls ($\beta =$ –0.09 g/cm²; 95% CI: –0.16, –0.02). We did not observe associations between preconceptional paternal concentrations of PCFs and birth measures. Furthermore, preconceptional parental concentrations of PCBs were not associated with length or head circumference at birth.

**PBDEs.** Maternal concentrations of PBDEs were associated with significant differences in mean birth weight in boys and girls. Maternal concentrations of PBDE congeners 28 and 183 were associated with lower birth weight among girls; the largest negative association was estimated for PBDE-28 ($\beta =$ –151.33 g; 95% CI: –298.56, –4.10). Maternal concentrations of PBDE-28 were also statistically associated with smaller length and head circumference among girls. On the contrary, for every 1-SD increase in ln-transformed maternal concentrations of PBDEs 66 and 99, mean birth weight among boys was 125.04 g (95% CI: 18.16, 231.92) and 133.39 g (95% CI: 9.12, 257.37) higher, respectively. Among boys, PBDE congeners were also statistically associated with larger length (PBDE-99) and head circumference (PBDEs 66, 85, 99). As seen with maternal concentrations, paternal concentrations of PBDE-183 were also significantly associated with lower birth weight among girls ($\beta =$ –92.13 g; 95% CI: –173.44, –10.82).

**PBDEs.** Among girls, maternal concentrations of PBDEs were not associated with significant differences in birth weight. However, for every 1-SD increase in ln-transformed concentrations of paternal concentrations of PCB-167, the mean birth weight among girls was 97.49 g lower (95% CI: –187.45, –7.54), and mean length ($\beta =$ –0.57 cm; 95% CI: –1.12, –0.02) and head circumference ($\beta =$ –0.45 cm; 95% CI: –0.86, –0.03) were smaller. Significant associations between parental concentrations of PCBs and birth size were more frequent among boys. Birth weight among boys was lower by 99–170 g per 1-SD increase in ln-transformed maternal concentrations of PBDEs 66, 85, 99, 153, 167, 170, 195, and 209 and paternal (PCBs 172, 195) concentrations. Maternal concentrations of PCBs were statistically associated with smaller head circumference. The majority of infants were girls (51%), the mean (± SD) postconception gestational age and birth weight of infants at delivery was 36.2 ± 2.2 weeks and 3382.3 ± 487.5 g, respectively.

**Table 2.** Description of study cohort by partner among those with a singleton delivery ($n = 234$), LIFE Study, 2005–2009 [n (%) or mean ± SD].

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mother</th>
<th>Father</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>194 (84)</td>
<td>189 (85)</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>2 (1)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>20 (9)</td>
<td>20 (9)</td>
</tr>
<tr>
<td>Other</td>
<td>16 (7)</td>
<td>12 (5)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; High school</td>
<td>0 (0)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>High school/ equivalent</td>
<td>9 (4)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>College</td>
<td>223 (98)</td>
<td>225 (97)</td>
</tr>
<tr>
<td><strong>Health insurance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5 (2)</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Yes</td>
<td>227 (98)</td>
<td>223 (96)</td>
</tr>
<tr>
<td><strong>Smoking status at baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active (cotinine ≥ 100 ng/mL)</td>
<td>11 (5)</td>
<td>24 (10)</td>
</tr>
<tr>
<td>Passive (cotinine &lt; 100 ng/mL)</td>
<td>219 (95)</td>
<td>205 (90)</td>
</tr>
<tr>
<td><strong>Cigarettes smoked (9–12 weeks)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>227 (98.8)</td>
<td>—</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>2 (0.8)</td>
<td>—</td>
</tr>
<tr>
<td>≥ 10</td>
<td>1 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td><strong>Alcohol use at baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>52 (22)</td>
<td>31 (13)</td>
</tr>
<tr>
<td>Yes</td>
<td>182 (78)</td>
<td>203 (87)</td>
</tr>
<tr>
<td><strong>Alcohol use (9–12 weeks)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>229 (99.6)</td>
<td>—</td>
</tr>
<tr>
<td>1 drink/week</td>
<td>1 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>29 ± 3.7</td>
<td>31.5 ± 4.6</td>
</tr>
<tr>
<td>Body mass index (kg/m²)*</td>
<td>26 ± 6.5</td>
<td>29 ± 5.3</td>
</tr>
<tr>
<td>Parity</td>
<td>1.1 ± 2.0</td>
<td>1.0 ± 1.1</td>
</tr>
<tr>
<td>Parity</td>
<td>0.7 ± 0.8</td>
<td>0.69 ± 0.8</td>
</tr>
</tbody>
</table>

All characteristics are self-reported except for body mass index. Missing covariate data was not included in table.

*At baseline, participants reported whether they had consumed alcohol in the last 12 months. *Chi-square test $p < 0.05$.  

90
Persistent organic pollutants and birth size

circumference in girls (PCB-138) and boys (PCBs 128, 138, 153). Paternal concentrations of PCBs were also significantly associated with smaller head circumference among girls (PCB-167) and boys (PCBs 128, 157). Maternal concentrations of PCBs 201 and 206 were associated with larger head circumference. Maternal concentrations of PCB-138 were associated with lower mean birth weight among boys and smaller mean head circumference and ponderal index among boys and girls. Paternal concentrations of PCB-138 were estimated to be associated with smaller mean ponderal index among boys. Additionally, in girls, paternal concentrations of PCB-156 and in boys maternal (PCBs 170, 172) and paternal (PCBs 156, 157) PCB concentrations were associated with smaller ponderal index (range, 0.08–0.13 g/cm³).

Persistent organic pollutants associated with multiple birth size outcomes. Both maternal and paternal concentrations of several persistent organic pollutants were associated with statistical differences in the same birth size measure among their offspring. The statistical differences associated with increasing parental concentrations of these pollutants were often of similar magnitude and direction. We briefly highlight these compounds here.

Lower mean birth weight was observed in association with increasing preconception maternal and paternal concentrations of PBDE-183 among girls and PCBs 128 and 195 among boys. Maternal concentrations of PCB-167 were associated with lower mean birth weight among girls only, but paternal concentrations were associated with lower birth weight in boys. Increasing maternal and paternal concentrations of γ-HCH were associated with smaller head circumference and higher ponderal index among girls.

Discussion
In this prospective pregnancy study with preconception enrollment of couples, we demonstrated that both preconception maternal and paternal serum concentrations of persistent organic pollutants were...
significantly associated with birth size measures among their offspring, even after taking into account their partner’s serum concentrations. In addition, we also report several statistically significant differences in birth size measures by infant sex and between and within classes of pollutants. We observed decreases in infant birth weight between 85 and 195 g with 1-SD increases in preconception maternal and paternal serum concentrations of POPs.

This reduction is similar in magnitude to what has been reported for other prenatal maternal environmental exposures. Compared with nonsmokers, lower mean birth weight has been reported for infants born to women who reported cigarette smoking during the first trimester or throughout pregnancy (range, 55–189 g) (Olive et al. 1995). Meta-analyses have reported lower birth weight among infants born to nonsmoking women exposed to environmental tobacco smoke (33 g: 95% CI: 16, 51) (Leonardi-Bee et al. 2011) and in association with increasing cord serum concentrations of PCP-153 (150 g: 95% CI: 50, 250) (Govarts et al. 2012). Last, a meta-analysis reported that when compared with lower exposure groups, women exposed to higher mean levels of indoor air pollution from solid fuel use had infants whose birth weight was approximately 96.6 g lower (95% CI: 68.5, 124.7) (Pope et al. 2010).

Our findings underscore the importance of designing epidemiological studies that ascertain preconception parental exposures in relation to birth size measures. In addition, given that paternal environmental exposures are often overlooked when examining the associations between parental exposures and fetal growth, there is a need for more comprehensive investigations of the associations between preconception paternal exposures and fetal growth and development. Both maternal and paternal serum concentrations of several pollutants (PBDE-183, PCBs 128, 138, 167, and 195, and γ-HCH) were associated with birth size measures, but more research is needed to investigate whether associations that are specific to parental serum concentrations are relevant and can be confirmed in other populations.

Few prospective pregnancy studies report parental preconception serum concentrations of POPs, making it difficult to further evaluate our findings. The only known study to examine the association between preconception maternal PCB levels and birth weight was conducted using data obtained from a prospective cohort of New York women and their partners planning a pregnancy within the next 6 months (Murphy et al. 2010). After adjustment for maternal height, smoking, and infant sex, the birth weight of infants (n = 50) born to mothers with the highest concentrations of antiestrogenic PCBs [interquartile range (IQR): 0.23–0.33 ng/g serum] was approximately 471 g (95% CI: –890.2, –51.3) lighter than infants born to mothers with the lowest concentrations (IQR: 0.13–0.15 ng/g serum). This study also examined the association between infant birth weight and maternal antiestrogenic PCB concentrations from serum measured during the prenatal period (median, 6 weeks gestation). The mean difference in infant birth weight between women with the highest (IQR: 0.15–0.21 ng/g serum) and lowest (IQR: 0.07–0.09 ng/g serum) prenatal concentrations of maternal antiestrogenic PCBs was approximately 260 g less (β = –260.5; 95% CI: –667.4, 146.5) than what was reported for preconception levels (Murphy et al. 2010)

Given the debate about classifying chemicals by their action, which may also be a function of dose, we decided to examine each individually. By doing so, we did not make any assumptions regarding their hypothesized biologic activity or how compounds might interact with each other in mixture form. However, in our present study we report statistically significant associations between birth size measures and two PCB congeners. For one previously shown to be estrogenic (PCB-153), we found that maternal concentrations were significantly associated with lower birth weight and head circumference in boys; for another, shown to be antiestrogenic (PCB-156), we found paternal concentrations to be associated with lower ponderal index in both boys and girls (Cooke et al. 2001). We also observed associations between birth weight and lower serum concentrations of PCBs than what has been previously published in a study of New Yorkers and their partners planning a pregnancy, mentioned above (Murphy et al. 2010). It has been shown that serum concentrations of POPs in the LIFE study population (Buck Louis et al. 2013) are lower than reported for the U.S. population (CDC 2014). This difference is not surprising given that concentrations of persistent chemicals increase with age and the LIFE cohort is comprised of couples of reproductive age, unlike the NHANES population that comprises women 12–85 years of age.

Our study also reports several positive associations between pollutants and birth size measures. Maternal concentrations of PBDEs 66 and 99 were associated with increased mean birth weight, length, and head circumference among boys only. Maternal concentrations of PCBs 201 and 206 and maternal and paternal concentrations of OCPs were associated with increased mean head circumference and ponderal index among girls only. Although they are not comparable to our study, other studies have reported positive associations between maternal prenatal levels of environmental chemicals. Maternal prenatal concentrations of total PCBs and PBBs (congener specific information not available) have been associated with higher birth weight (Sweeney and Symanski 2007). Positive associations between head circumference and length have also been reported for maternal prenatal levels of organophosphate pesticides not evaluated in this study (Eskenazi et al. 2004). Associations reported by these studies also differed by sex. We are unable to explain these findings, but posit that they may reflect differing structural activity or biological activity of individual congeners, particularly given that associations differed by infant sex. Also, the windows of vulnerability for a fetus’s growth and development may differ by congener. We also speculate that these positive associations may be confounded by healthy behaviors such as the consumption of fish or antioxidant-rich foods. These healthy behaviors, although potential sources of parental POP exposure, may also positively influence fetal growth and development.

Our study addressed several key limitations of prior studies with equivocal findings of the association between prenatal exposure to POPs and birth size. For one, many studies ascertainment prenatal exposure to POPs during late pregnancy using maternal serum concentrations at the time of delivery or using umbilical cord serum concentrations. These studies may not be capturing exposure during relevant windows of fetal growth and development. Prospective pregnancy cohort studies that recruit couples discontinuing contraception to become pregnant are rare, and this is the only way to examine the association between preconceptional exposures to POPs and human birth size. Despite their long half-lives, maternal serum concentrations of PCBs and selected POPs can vary across critical windows of human reproduction and development during pregnancy (Bloom et al. 2007; Wang et al. 2009). Preconception maternal serum concentrations are not influenced by the expansion of blood volume and changes in metabolism associated with normal pregnancy. Thus, we can explore associations with birth size measures in relation to exposure that reflects preconception and early pregnancy, a key window for these effects.

Prior studies have focused on maternal exposures and how they impact developmental health. Paternal exposures to POPs have been largely unstudied, and little is known about their potential impact on fetal development and growth. Environmental chemical exposures that occur during spermatogenesis may affect the quality of a father’s gametes, and therefore may affect the susceptibility and health of his offspring in utero or after birth (Olshen and Faustman...
Persistent organic pollutants and birth size

References

Adegoye AR, Heitmann B. 2008. Accuracy and corre-
lates of maternal recall of birthweight and gesta-
tional age. BJOG 115:886–893.

Akins JR, Waldrep K, Bernert JT Jr. 1989. The estima-
tion of total serum lipids by a completely enzymatic

Anderson D. 2005. Male-mediated developmental toxi-

Aruckle TE, Kubwabo C, Walker M, Davis K, Lalonde K,
Kosarac I, et al. 2013. Umbilical cord blood levels of
perfluoroalkyl acids and polybrominated flame

Barr JR, Maggio VL, Barr DB, Turner WE, Sjödin A,
Sandau CD, et al. 2003. New high-resolution mass-
 spectrometric approach for the measurement of
polychlorinated biphenyls and organochlorine
pesticides in human serum. J Chromatogr B Analyst

Bat-Erdene U, Mercatella A, McDonald SW, Tough SC.
2013. Validation of Canadian mothers’ recall of
events in labour and delivery with electronic health
records. BMC Pregnancy Childbirth 13(suppl 1):S3;

Bernert JT, Turner WE, Patterson DG Jr, Needham LL.
2007. Calculation of serum “total lipid” concen-
trations for the adjustment of persistent organo-
halogen toxicant measurements in human samples.
Chemosphere 68:824–831.

Bernert JT Jr, Turner WE, Pirkle JL, Sosnoff CS, Akins JR,
tion of sensitive method for determination of
serum cotinine in smokers and nonsmokers by liquid
chromatography/atmospheric pressure ionization

Bloom MS, Buck Louis GM, Schisterman EF, Liu A,
Kostyniak PJ. 2007. Maternal serum polychlorinated
biphenyl concentrations across critical windows
of human development. Environ Health Perspect
115:1320–1324; doi:10.1289/ehp.10086.

Buck Louis GM, Schisterman EF, Sweeney AM,
2011. Designing prospective cohort studies for
assessing reproductive and developmental effects
during sensitive windows of human reproduction
and development—the LIFE Study. Paediatr Perinat

Buck Louis GM, Sundaram R, Schisterman EF,
2013. Persistent environmental pollutants and
family feecundity: the LIFE Study. Environ Health
Perspect 121:231–236; doi:10.1289/ehp.1205301.

The retrospective measurement of prenatal and peri-
natal events: accuracy of maternal recall. Schizophr

CDC (Centers for Disease Control and Prevention).
2014. Fourth National Report on Human Exposure to
Environmental Chemicals. Updated Tables, Tables,
September 2013. Atlanta, GA:National Center for
Environmental Health; Division of Laboratory
exposurerreport/ [accessed 12 December 2014].

Chapin RE, Robbins WA, Scheije H, Schiller SA.,
Tabacova SA, Tomakose MKM. 2004. Off to a good
start: the influence of pre- and periconceptional
exposures, parental fertility, and nutrition on chil-
dren’s health. Environ Health Perspect 112:89–78.

Chen SP, Goldstein JM, Rite CR, Hoffman DJ, Davis RD,
Nelson KG. 1995. The effect of cigarette
smoking on neonatal anthropometric measurements.

Coggswell ME, Yip R. 1995. The influence of fetal and
maternal factors on the distribution of birthweight.
Semin Perinatal 19:222–227.

Cooke PS, Sato T, Buchanan DL. 2001. Disruption of
steroid hormone signaling by PCBs. In: PCBs:
Recent Advances in Environmental Toxicology
and Health Effects (Robertson LW, Hansen LG, eds).
Lexington, KY:University of Kentucky, 257–263.

Corder S. 2008. Evidence for a role of paternal expo-
sures in developmental toxicity. Basic Clin Phar-

Curley JP, Mashed R, Champagne FA. 2011. Epigenetics
and the origins of paternal effects. Horm

Eskenazi B, Harley K, Bradman A, Wolkoff E, Jewell NP,
Barr DB, et al. 2004. Association of in utero organo-
phosphate pesticide exposure and fetal growth and
length of gestation in an agricultural population.
Environ Health Perspect 121:1116–1124; doi:10.1289/
ehp.7689.

Farhang L, Weintraub JM, Petreas M, Eskenazi B,
Bhatia R. 2005. Association of DDT and DDE with
birth weight and length of gestation in the Child

Foster KG, Gregorovich S, Morrison KM, Atkinson SA,
and umbilical cord blood concentrations of
polybrominated diphenyl ethers. Chemosphere
64:1300–1307.

Fullston T, Ohlsson Teague EM, Palmer NO, DeBlasio
obesity initiates metabolic disturbances in two
generations of mice with incomplete pene-
tration to the F2 generation and alters the transcrip-
tional profile of testis and sperm microRNA content.
FASEB J 27:4226–4234.

Givens ML, Small CM, Terrell ML, Cameron LL,
Michels Blanck H, Tolbert PE, et al. 2007. Maternal
exposure to polybrominated and polybrominated:
infant birth weight and gestational age.

Govarts E, Nieuwenhuisen M, Schoeters G, Ballester F,
Bloemen K, de Boer M, et al. 2012. Birth weight and
prenatal exposure to polychlorinated biphenyls
(PCBs) and dichlorodiphenyldichloroethylene (DDE):
a meta-analysis within 12 European birth cohorts.
Environ Health Perspect 120:162–170; doi:10.1289/
ehp.1102767.

Hey KG, Chevrier J, Aguilar Schall R, Sjödin A,
exposure to polybrominated diphenyl ethers and

Karmaus W, Zhu X. 2004. Maternal concentration of
polybrominated biphenyls and dichlorodiphenyl
dichloroethylene and birth weight in Michigan
fish eaters: a cohort study. Environ Health 3:1;

Kezios KL, Liu X, Cirillo PM, Kalantzi OI, Wang Y,
biphenyl exposure is associated with decreased
gestational length but not birth weight: archived
samples from the Child Health and Development
Studies pregnancy cohort. Environ Health 11:49;

Measurement of 18 perfluorinated organic acids
and amides in human serum using on-line solid-

Lawson CC, Schnorr TM, Whelan EA, Deddens JA,
occupational exposure to 2,3,7,8-tetrachlorodibenzo-
p-dioxin and birth outcomes of offspring: birth
weight, preterm delivery, and birth defects.
Environ Health Perspect 112:1403–1406; doi:10.1289/
ehp.7051.