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Maternal occupational exposure to polycyclic aromatic hydrocarbons and small for gestational age offspring

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Abstract

Objectives—While some of the highest maternal exposures to polycyclic aromatic hydrocarbons (PAHs) occur in the workplace, there is only one previous study of occupational PAH exposure and adverse pregnancy outcomes. We sought to extend this literature using interview data combined with detailed exposure assessment.

Methods—Data for 1997–2002 were analysed from mothers of infants without major birth defects in the National Birth Defects Prevention Study, a large population-based case-control study in the USA. Maternal telephone interviews yielded information on jobs held in the month before conception through delivery. From 6252 eligible control mothers, 2803 completed the interview, had a job, met other selection criteria, and were included in the analysis. Two industrial

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hygienists independently assessed occupational exposure to PAHs from the interview and reviewed results with a third to reach consensus. Small for gestational age (SGA) was the only adverse pregnancy outcome with enough exposed cases to yield meaningful results. Logistic regression estimated crude and adjusted ORs.

Results—Of the 2803 mothers, 221 (7.9%) had infants who were SGA. Occupational PAH exposure was found for 17 (7.7%) of the mothers with SGA offspring and 102 (4.0%) of the remaining mothers. Almost half the jobs with exposure were related to food preparation and serving. After adjustment for maternal age, there was a significant association of occupational exposure with SGA (OR=2.2, 95% CI 1.3 to 3.8).

Conclusions—Maternal occupational exposure to PAHs was found to be associated with increased risk of SGA offspring.

INTRODUCTION

Polycyclic aromatic hydrocarbons (PAHs) are lipophilic compounds formed during the incomplete burning of coal, tobacco or other organic substances. Humans are exposed by smoke from tobacco and other sources; by ambient air pollution; or by consuming PAHs in food, especially in charbroiled foods.¹ While environmental sources contribute to the total exposure burden, some of the highest exposure levels are found in the work-place.²³ Occupational exposures can occur in common workplace settings such as restaurants.⁴

PAHs and PAH-DNA adducts have been found in placental tissues of women, amniotic fluid samples and umbilical cord blood samples from newborns.⁵⁻¹⁰ PAH adducts can disrupt the cell's microenvironment,¹¹ to which the rapidly growing and differentiating cells of the fetus may be particularly vulnerable.¹² PAHs may also lead to periods of fetal hypoxia through reduced placental blood flow.¹³ PAHs have been shown in lab animals to be reproductive toxicants, causing fetal death and low fetal weight.¹⁴ Information on reproductive toxicity in humans is somewhat sparse. Maternal exposure to PAHs has been associated with low birth weight, preterm birth or intrauterine growth restriction, whether based on a job exposure matrix using job title and workplace,¹⁵ stationary air monitoring¹⁶ or personal air monitoring.¹¹⁷¹⁸ Newborns with high levels of PAH-DNA adducts in umbilical cord blood or placental samples had significantly decreased birth length, weight or head circumference,¹⁹²⁰ however the evidence for this association is equivocal.⁷²¹

Occupational exposures are often higher than environmental exposures and may be more amenable to intervention. However, only one study was found that specifically examined the association of occupational exposure to PAHs and adverse birth outcomes; it reported a significant decrease in fetal weight but not fetal head circumference or fetal length.¹⁵ The objective of the current study was to extend current knowledge by examining small for gestational age (SGA) among controls from a large ongoing case-control study of birth defects. Although preterm birth and term low birth weight were also initially considered as outcomes, their exposed sample size was too small.

METHODS

Study population

This analysis used data from the National Birth Defects Prevention Study (NBDPS), an ongoing, population-based, case-control study of structural birth defects. Detailed study methods have been published elsewhere.²² Only control infants (without major structural birth defects) were used for this analysis. They were live-born, and were selected at random from birth certificates or birth hospital records in eight sites (Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York and Texas). More precisely, they were selected using software to randomly identify a subset of births from lists (of birth certificate numbers or projected deliveries in hospitals) that would reflect the number of births in that facility and month. If a selected birth turned out to have any birth defect, the next immediately following birth was selected instead. All mothers participated in a computer-assisted telephone interview (CATI) in English or Spanish, administered from 6 weeks through 24 months after their estimated due dates. Mothers were asked questions on a variety of topics including demographics, maternal illnesses and medication use, vitamin intake, tobacco use and information about jobs held for 1 month or more during preconception and pregnancy. The NBDPS and its informed consent procedures were approved by the Office of Management and Budget, and the appropriate institutional review boards at the Centers for Disease Control and Prevention (CDC) and at each participating site.

The study population for the current analysis started with 6252 mothers of NBDPS control infants with estimated dates of delivery from October 1, 1997 through December 31, 2002, since that was the period for which the exposure assessment described below had been conducted. Of those, 4139 completed all or part of the interview, leading to a participation rate of 66.2%. Selecting mothers who held a job for at least 1 month during the pregnancy and the month before conception narrowed the number to 2937. From that total, 134 subjects were excluded using the following criteria: (A) infants from plural births; with gestational ages greater than 42 weeks; or with missing gestational age, birth weight or sex; (B) mothers with missing parity information or with prepregnancy diabetes. That resulted in 2803 mothers.

We applied published sex-specific, race/ethnic-specific and parity-specific growth curves (Zhang and Bowes,²³ and Overpeck *et al*²⁴) to our study population and defined infants as SGA if their birth weight for gestational age was less than the 10th centile for the corresponding stratified growth curve. SGA infants were compared with all other infants.

Exposure assessment

For each job reported during the CATI, the mother was asked to provide the employer's name, job title, descriptions of the company's product/service, main job activities/duties, chemicals/substances handled and machines used on the job. Mothers also provided job start and end dates and the usual number of days worked per week and hours worked per day. Each self-reported job was then assigned standard codes corresponding to its occupation using the 2000 Standard Occupational Classification System,²⁵ and its industry using the 1997 North American Industry Classification System.²⁶

Using the CATI data, exposure classification was conducted by two industrial hygienists (raters), blinded to NBDPS case/control status. For jobs considered possibly exposed to PAHs, the industrial hygienists independently assigned the following characteristics: (1) whether inhalation exposure was direct, indirect or both; (2) whether the inhalation exposure was continuous, intermittent or both; (3) the fraction of total hours worked when exposure was direct; (4) the fraction of total hours worked when exposure was indirect; (5) the intensity of any direct inhalation exposure during the period of direct exposure; (6) the intensity of any indirect inhalation exposure during the period of indirect exposure. Discrepancies between the two hygienists were resolved at a consensus conference with a third industrial hygienist. This expert review strategy was based on an approach that had been previously developed and used for other occupational exposures (eg, solvents, lead, radiation) in the Baltimore-Washington Infant Study.²⁷²⁸

As part of the exposure assessment, a dichotomous yes/no rating of occupational exposure to PAHs was determined for each 'relevant' job (jobs considered relevant for SGA were those held in the period of 1 month before conception through delivery). A woman was classified as exposed if one or more of her relevant jobs was rated as exposed, whether part-time or full-time jobs. She was considered unexposed if all her relevant jobs were rated as unexposed.

In addition to the dichotomous rating, cumulative PAH exposure (unit-hours) was estimated by the industrial hygienists using: (weighted intensity in $\mu\text{g}/\text{m}^3$) \times ((hours worked per week)/(7 days per week)) \times (number of days worked in the relevant period). The resulting cumulative exposure value was job-specific rather than woman-specific; a woman's total occupational PAH exposure was calculated as the sum of the job-specific cumulative exposures in the relevant period.

'Occupational exposure' refers here to inhalation exposures inherent in the job or workplace aside from secondhand smoke, and did not consider exposure through skin or ingestion. Other sources of potential PAH exposure obtained from the interview included maternal smoking, secondhand smoke at home and secondhand smoke at work. Six women were excluded whose occupational PAH exposure could not be assigned for one or more of the jobs due to insufficient information.

Covariates

Several covariates were considered as potential confounders or effect measure modifiers based on associations either with SGA or with PAH exposure as reported in the literature. The CATI yielded data on the following maternal characteristics of interest as potential confounders (categories shown in table 1): age at delivery; race/ethnicity (based on standard CDC classification); education; number of previous live births; prepregnancy body mass index (categorised according to the National Heart, Lung, and Blood Institute cut-offs as underweight ($<18.5 \text{ kg}/\text{m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg}/\text{m}^2$), overweight ($25.0\text{--}29.9 \text{ kg}/\text{m}^2$) and obese ($\geq 30.0 \text{ kg}/\text{m}^2$)). Data on the following additional maternal characteristics also obtained during the CATI pertained to exposure in the period from 1 month before conception through delivery: use of folate antagonist medications (trimetrex-ate, methotrexate, carbamazepine, valproic acid, dilantin); consumption of folic acid

supplements; cigarette smoking; secondhand smoke exposure at home; secondhand smoke exposure at work; and consumption of alcohol. The following were also considered as potential confounders: infant sex; annual household income; and study site. In the analysis, all covariates were treated as categorical variables.

Statistical analysis

The association between each potential covariate and (A) SGA and (B) PAH exposure (yes/no) was examined using a χ^2 test or Fisher's exact test when cell sizes were less than 5 subjects. The number of jobs falling into the 23 Standard Occupational Classification-based major job groups were tabulated over all subjects, stratified by occupational PAH exposure status (yes/no).

Mothers of SGA infants were compared with mothers of all remaining infants. Using unconditional logistic regression, crude and adjusted ORs and 95% CIs were estimated to evaluate the association of maternal occupational exposure to PAHs with SGA in offspring. All the potential covariates described in the above section were included in a full model and submitted to manual backward stepwise logistic regression, removing the covariate with the highest p value. That covariate was retained if its removal resulted in a change of 10% in the effect measure estimate for PAHs and SGA. Then the next covariate with the highest p value was removed and checked for the 10% change, and so on. This continued until all remaining covariates exhibited the 10% change.

Several subanalyses were conducted: (1) To evaluate the independent effect of occupational PAHs, the first subanalysis adjusted for the most common source of human PAH exposure: active smoking and secondhand smoke exposure at home or at work. (2) Subjects were stratified by prepregnancy body mass index (obese/overweight mothers vs all others), as body fat may influence the storage and transformation of PAHs,¹ and stratified ORs were calculated to check for effect measure modification. Mothers were also stratified by age, race/ethnic group, education, folic acid supplement use, active smoking and any smoking exposure to examine possible effect measure modification. (3) To evaluate a possible exposure-response relationship, cumulative exposure level was categorised into none, low and high based on the frequency distribution among exposed mothers of non-SGA infants. The two-sided Cochran-Armitage trend test was used to test for trend. Estimated cumulative exposure was also analysed as a continuous variable, crude and adjusted for maternal age. (4) The largest number of PAH-exposed mothers was in food services. In order to control for possible residual confounding by socioeconomic status and to consider the possibility that exposures might be industry-specific, the PAH exposure (yes/no) analysis was stratified into women who worked in food services versus all other women. (5) To more closely replicate the previous study on occupational PAH exposure and birth outcomes,¹⁵ birth weight was analysed in a linear model adjusted for gestational age. As in that study, customised growth curves for the entire study population were constructed, SD scores for each birth were calculated as a deviation from the 'overall' average at that gestational week, and represented as the equivalent Z-scores.²⁹ The linear model initially contained terms for exposure, gestational week, and exposure \times gestational week, and non-significant terms were dropped.

RESULTS

Of the 2803 mothers included in the current study, 199 (7.1%) had preterm births, 35 (1.2%) had term deliveries that were low birth weight and 221 (7.9%) had offspring who were SGA. Mothers of SGA infants had a lower education, were more likely to smoke or report secondhand smoking at home, and to be underweight or normal weight compared with mothers of non-SGA infants (table 1). Other maternal characteristics that were checked but not significantly different were maternal age, race/ethnicity, parity, household income or NBDPS Center of residence, as well as the following exposures from 1 month before conception through delivery: secondhand smoke exposure at work, alcohol drinking, taking folic acid supplements. Sex was not significantly different between SGA and non-SGA infants.

Of the 2803 mothers, 119 (4.2%) had occupational PAH exposure in one or more jobs. Occupational PAH exposure was significantly more common among mothers who were younger, non-Hispanic Black or Hispanic, overweight or obese, had lower education, avoided drinking alcohol, smoked cigarettes, were exposed to secondhand smoking at home or work, or had lower income (data not shown). Among all jobs reported by mothers, almost half (45%) of those with occupational exposure to PAHs were in food preparation or serving related jobs (see online supplementary table). About 35% were in sales and related positions. Upon closer examination, it was found that most of the latter were (1) cashiers at fast food restaurants who worked the drive-through window, which is usually back in the kitchen area and very close to the grills/fryers, or (2) assistant managers, managers or floating staff in restaurants who work multiple positions, including sometimes cooking.

Occupational PAH exposure was found for 17 (7.7%) of the 221 mothers with SGA offspring and 102 (4.0%) of the remaining 2582 mothers. Maternal occupational PAH exposure was associated with having SGA offspring, whether crude or adjusted for maternal age (table 2); the adjusted OR was 2.2, with a 95% CI 1.3 to 3.8.

Statistically elevated ORs for SGA persisted whether adjusting for all smoking exposure (mother smoking or exposed to secondhand smoke at home or work) (OR 1.9, 95% CI 1.1 to 3.2), or for maternal age and all smoking exposure (OR 2.1, 95% CI 1.2 to 3.7). In our data, there was no evidence of statistically significant effect measure modification by any covariate of interest (data not shown). Even though the crude and adjusted models for SGA yielded a statistically significant trend with levels of estimated cumulative exposure ($p < 0.02$), the increases were not monotonic so evidence of a trend was lacking (table 2). Increases were similar after adjusting for maternal age, smoking (active and secondhand) and education; the ORs and 95% CIs were no PAH exposure=1.0 (ref), low PAH=2.2 (1.0, 4.6), high PAH=1.8 (0.8, 3.9). Analysing cumulative exposure as a continuous variable also did not provide conclusive evidence of a trend; crude and adjusted for maternal age, OR=1.1 per 100 $\mu\text{g}/\text{m}^3\text{-h}$, 95% CI 1.0 to 1.1. When stratified by type of occupation, 10 women in food services with SGA offspring were occupationally exposed to PAHs, yielding a crude OR of 2.2 (95% CI 0.9 to 5.2). Seven women in other job types with SGA offspring were exposed to PAHs, with a crude OR of 1.5 (95% CI 0.7 to 3.3). Treating birth weight as a continuous variable adjusted for gestational age (ie, using Z-scores as the outcome) yielded

non-significant terms for gestational age and the interaction which were dropped. The term for occupational PAH exposure was statistically significant, crude ($p=0.01$) and adjusted for maternal age ($p=0.01$).

DISCUSSION

This large population-based case-control study found that occupational exposure to PAHs was associated with an increased occurrence of SGA offspring. We did not observe a clear dose-dependent relationship in these analyses; the highest cumulative PAH exposure level showed a lower effect estimate with a CI that included 1.0. Occupational PAH exposure in food preparation and serving related jobs seemed to have a somewhat stronger association with SGA offspring than other occupations grouped together; however, the numbers were small.

Our observations were generally consistent with the only study we found that examined occupational exposure to PAHs and adverse birth outcomes, though the primary effect measures were different.¹⁵ Their exposure information was gathered by a questionnaire completed in mid-pregnancy by Dutch women; exposure assessment involved using a job exposure matrix followed by consensus of three experts, yielding 1.3% of the women exposed to PAHs compared with 4.2% in the current analysis. Their outcomes (including fetal weight) were measured during pregnancy, while ours were at the end. Their study reported that fetal weight adjusted for gestational age (crude and adjusted for confounders) significantly decreased with maternal occupational PAH exposure. Our supplemental analysis of fetal weight adjusted for gestational age also found a statistically significant association with occupational PAH exposure. However, the estimated levels of exposure were not reported in the Dutch study, so those could not be compared with the current paper. The previous study found no statistically significant association of PAH exposure with fetal head circumference or length.

The current study was also consistent with a report of intra-uterine growth restriction and environmental PAH exposure using stationary air monitoring.¹⁶ It was partly consistent with two studies^{17,18} that reported a statistically significant decrease in birth weight (adjusted for gestational age) with PAH exposure measured through personal monitoring in Krakow Caucasians and New York City (NYC) African Americans. A later analysis from the same study¹¹ specifically examined SGA, and also found a significant association with PAH exposure among NYC African Americans.

A causal relationship between occupational PAH exposure and SGA is biologically plausible. PAHs cross the placenta⁷ and have been found in cord blood.⁵ They have been shown to form bulky DNA adducts in mothers and offspring.³⁰ Workers exposed to PAHs have higher levels of PAH-DNA adducts compared with the general population.²³¹ If not repaired, these adducts can disrupt the cell's microenvironment, leading to inhibition of important enzymes, cell death and alteration of other cells.¹¹¹ The fetus is particularly vulnerable due to its rapid growth, the process of cellular differentiation, the immaturity of its metabolic pathways and the stage of development of vital organs.¹² Another possible mechanism is if PAH exposure leads to periods of fetal hypoxia through reduced placental

blood flow.¹³ Future research with a greater sample size might start to clarify possible mechanisms by examining different exposure periods during pregnancy.

PAHs occur in complex and dynamic mixtures that may contain hundreds of separate chemicals; the individual components of these mixtures vary widely. For example, the PAH composition of a cigarette depends on the brand and its proprietary additives, and on the batch of tobacco (and where that batch was grown) and the batch of paper (and the species of trees, and where the trees grew, that were used in making the paper). This makes evaluating specific types of PAHs, rather than PAHs as a group, very difficult. Assessing PAHs as a group is sensible, in that it allows us to move beyond assessment by job title to begin zeroing in on a group of related chemicals that co-occur.

A limitation of this study was the potential for exposure mis-classification. The three industrial hygienists had several years of experience and working knowledge, but the maternal occupational information reported during the CATI was limited and did not include potentially important exposure-modifying factors such as use of personal protective equipment and ventilation practices. However, the expert rater approach used was superior to relying exclusively on maternal self-report of PAH exposure, which is likely to be limited and could introduce recall bias.³² In our dichotomised exposure analyses (any/none), non-differential errors in exposure misclassification would be expected to bias the ORs towards the null.

Another limitation was that in using these data, there was little information about other sources of PAH exposure. For example, subjects came from different areas of the country (highly industrialised to rural), and PAH levels are associated with certain industries and exposure to traffic.¹¹⁰ The main source of ingested PAHs are some foods such as grilled, fried or smoked meat products which might partly explain the apparent higher OR for mothers in food service industries (although that might also have been due to residual confounding by socioeconomic status). Also, exposure assessment had not been conducted for paternal occupational exposure to PAHs. However, smoking is an important source of PAHs,¹ and we were able to account for personal tobacco use and exposure to secondhand tobacco smoke at home or at work. Further, since levels of occupational PAH exposure are generally higher than environmental sources,²³ it is important to consider exposure in the workplace separately from other sources.

A third limitation of this study was the small number of occupational exposed case mothers. This made it particularly challenging to fully assess a possible dose-response pattern and to adequately control for a full range of potential confounders. It also increased the likelihood that our results, though statistically significant, may have arisen by chance and thus require replication in future studies.

With an interview participation rate of 66.2%, this study was susceptible to selection bias. In general, NBDPS control participants differed from their base populations in maternal education, entry into prenatal care, birth weight, gestational age and plurality,³³ all of which may be related to SGA births and may impact generalisability to other populations. On the other hand, the participants did not differ in maternal age, smoking or diabetes. Selection

bias may also be partly responsible for the difference in prevalence of occupational PAH exposure in this study (4.2%) versus the Dutch study (1.3% with an interview response rate of 76.9%), even though both sought a representative sample of births in their respective populations.

While defining SGA using a birth weight below the 10th centile for a given gestational age is currently the most common threshold used in research and clinical practice for which adverse perinatal outcomes are substantially increased,^{34,35} there is no general agreement as to the most appropriate threshold value to use.^{36–38} Two analyses, for example, have examined SGA using birth weights < 5th³⁹ and <3rd⁴⁰ centiles for gestational age, and further note that using an alternative cut point may be more appropriate for understanding pathological growth restriction. Given the small number of subjects meeting the criteria for a <5th centile cut point in our sample, however, we were unable to assess the impact of a more restrictive threshold as an outcome in our analysis.

One of the major strengths of this study was its use of thorough interview data available from the NBDPS. It yielded data on potentially important confounding factors. The occupational exposure assessment improved accuracy compared with the use of only job title or self-reported exposure, and the cumulative exposure estimation allowed examination of exposure-response relationships.

In summary, this study indicated a positive association between maternal occupational exposure to PAHs and SGA offspring. This was generally consistent with previous findings, and the study adds data to the sparse literature on maternal occupational PAH exposure studies. The large number of women in food service occupations and their slightly higher ORs may have implications for prevention strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profile for Polycyclic Aromatic Hydrocarbons (PAHs) (Update). (Monograph). US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry; 1995.
2. Brandt HC, Watson WP. Monitoring human occupational and environmental exposures to polycyclic aromatic compounds. *Ann Occup Hyg.* 2003; 47:349–78. [PubMed: 12855487]
3. Hansen AM, Mathiesen L, Pedersen M, et al. Urinary 1-hydroxypyrene (1-HP) in environmental and occupational studies—a review. *Int J Hyg Environ Health.* 2008; 211:471–503. [PubMed: 18222724]
4. Sjaastad AK, Svendsen K. Exposure to polycyclic aromatic hydrocarbons (PAHs), mutagenic aldehydes, and particulate matter in Norwegian a la carte restaurants. *Ann Occup Hyg.* 2009; 53:723–9. [PubMed: 19759173]
5. Madhavan ND, Naidu KA. Polycyclic aromatic hydrocarbons in placenta, maternal blood, umbilical cord blood and milk of Indian women. *Hum Exp Toxicol.* 1995; 14:503–6. [PubMed: 8519527]
6. Arnoud JP, Verhoest P, Bach V, et al. Detection of benzo[a]pyrene-DNA adducts in human placenta and umbilical cord blood. *Hum Exp Toxicol.* 1997; 16:716–21. [PubMed: 9429085]
7. Gladen BC, Zadorozhnaja TD, Chislovska N, et al. Polycyclic aromatic hydrocarbons in placenta. *Hum Exp Toxicol.* 2000; 19:597–603. [PubMed: 11211237]
8. Ravindra K, Mittal AK, Van Grieken R. Health risk assessment of urban suspended particulate matter with special reference to polycyclic aromatic hydrocarbons: a review. *Rev Environ Health.* 2001; 16:169–89. [PubMed: 11765907]
9. Myers SR, Zamora R, Ali Y, et al. Analysis of polycyclic aromatic hydrocarbons in amniotic fluid samples from smokers and nonsmokers. *Polycycl Aromat Compd.* 2008; 28:39–66.
10. Castano-Vinyals G, D'Errico A, Malats N, et al. Biomarkers of exposure to polycyclic aromatic hydrocarbons from environmental air pollution. *Occup Environ Med.* 2004; 61:e12. [PubMed: 15031403]
11. Choi H, Rauh V, Garfinkel R, et al. Prenatal exposure to airborne polycyclic aromatic hydrocarbons and risk of intrauterine growth restriction. *Environ Health Perspect.* 2008; 116:658–65. [PubMed: 18470316]
12. Bruckner JV. Differences in sensitivity of children and adults to chemical toxicity: the NAS panel report. *Regul Toxicol Pharmacol.* 2000; 31:280–5. [PubMed: 10915586]
13. Rennie MY, Detmar J, Whiteley KJ, et al. Vessel tortuosity and reduced vascularization in the fetoplacental arterial tree after maternal exposure to polycyclic aromatic hydrocarbons. *Am J Physiol Heart Circ Physiol.* 2011; 300:H675–84. [PubMed: 21148768]
14. Detmar J, Rennie MY, Whiteley KJ, et al. Fetal growth restriction triggered by polycyclic aromatic hydrocarbons is associated with altered placental vasculature and AhR-dependent changes in cell death. *Am J Physiol Endocrinol Metab.* 2008; 295:E519–530. [PubMed: 18559983]
15. Snijder CA, Roeleveld N, te Velde E, et al. Occupational exposure to chemicals and fetal growth: the Generation R study. *Hum Reprod.* 2012; 27:910–20. [PubMed: 22215632]
16. Dejmeek J, Solansky I, Benes I, et al. The impact of polycyclic aromatic hydrocarbons and fine particles on pregnancy outcome. *Environ Health Perspect.* 2000; 108:1159–64. [PubMed: 11133396]
17. Perera FP, Rauh V, Tsai WY, et al. Effects of transplacental exposure to environmental pollutants on birth outcomes in a multiethnic population. *Environ Health Perspect.* 2003; 111:201–5. [PubMed: 12573906]
18. Choi H, Jedrychowski W, Spengler J, et al. International studies of prenatal exposure to polycyclic aromatic hydrocarbons and fetal growth. *Environ Health Perspect.* 2006; 114:1744–50. [PubMed: 17107862]
19. Perera FP, Whyatt RM, Jedrychowski W, et al. A study of the effects of environmental polycyclic aromatic hydrocarbons on birth outcomes in Poland. *Am J Epidemiol.* 1998; 147:209–314. [PubMed: 9482493]
20. Tang D, Li TY, Liu JJ, et al. PAH-DNA adducts in cord blood and fetal and child development in a Chinese cohort. *Environ Health Perspect.* 2006; 114:1297–300. [PubMed: 16882543]

21. Sram RJ, Binkova B, Dejmek J, et al. Association of DNA adducts and genotypes with birth weight. *Mutat Res.* 2006; 608:121–8. [PubMed: 16837240]
22. Yoon PW, Rasmussen SA, Lynberg MC, et al. The National Birth Defects Prevention Study. *Public Health Reports.* 2001; 116(Suppl 1):32–40. [PubMed: 11889273]
23. Zhang J, Bowes WAW. Birth weight-for-gestational-age patterns by race, sex, and parity in the United States population. *Obstet Gynecol.* 1995; 86:200–8. [PubMed: 7617350]
24. Overpeck MD, Hediger ML, Zhang J, et al. Birth weight for gestational age of Mexican American infants born in the United States. *Obstet Gynecol.* 1999; 93:943–7. [PubMed: 10362159]
25. United States Department of Labor, Bureau of Labor Statistics. [accessed 29 Aug 2009] Standard Occupational Classification. http://www.bls.gov/soc/soc_majo.htm
26. United States Department of Labor, Bureau of Labor Statistics. [accessed 29 Aug 2009] North American Industry Classification System. <http://www.bls.gov/bls/naics.htm>
27. Jackson LW, Correa-Villasenor A, Lees PS, et al. Parental lead exposure and total anomalous pulmonary venous return. *Birth Defects Res A Clin Mol Teratol.* 2004; 70:185–93. [PubMed: 15108245]
28. Correa A, Min YI, Stewart PA, et al. Inter-rater agreement of assessed prenatal maternal occupational exposures to lead. *Birth Def Res A Clin Mol Teratol.* 2006; 76:811–24.
29. Verburg BO, Steegers EA, De Ridder M, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound Obstet Gynecol.* 2008; 31:388–96. [PubMed: 18348183]
30. Topinka J, Milcova A, Libalova H, et al. Biomarkers of exposure to tobacco smoke and environmental pollutants in mothers and their transplacental transfer to the foetus. Part I: bulky DNA adducts. *Mutat Res.* 2009; 669:13–9. [PubMed: 19433098]
31. Perera FP, Dickey C, Santella R, et al. Carcinogen-DNA adducts and gene mutation in foundry workers with low-level exposure to polycyclic aromatic hydrocarbons. *Carcinogenesis.* 1994; 15:2905–10. [PubMed: 8001254]
32. Olsson AC, Fevotte J, Fletcher T, et al. Occupational exposure to polycyclic aromatic hydrocarbons and lung cancer risk: a multicenter study in Europe. *Occup Environ Med.* 2010; 67:98–103. [PubMed: 19773276]
33. Cogswell ME, Bitsko RH, Anderka M, et al. Control selection and participation in an ongoing, population-based, case-control study of birth defects. *Am J Epidemiol.* 2009; 170:975–85. [PubMed: 19736223]
34. Alexander GR, Himes JH, Kaufman RB, et al. A United States national reference for fetal growth. *Obstet Gynecol.* 1996; 87:163–8. [PubMed: 8559516]
35. Zhang J, Merialdi M, Platt LD, et al. Defining normal and abnormal fetal growth: promises and challenges. *Am J Obstet Gynecol.* 2010; 202:522–8. [PubMed: 20074690]
36. Usher R, McLean F. Intrauterine growth of live-born Caucasian infants at sea level: standards obtained from measurements in 7 dimensions of infants born between 25 and 44 weeks gestation. *J Pediatr.* 1969; 74:901–10. [PubMed: 5781799]
37. Breart G, Rabarison Y, Plouin PF, et al. Risk of fetal growth retardation as a result of maternal hypertension: preparation to a trial on antihypertensive drugs. *Dev Pharmacol Ther.* 1982; (4 Suppl):116–23. [PubMed: 7128382]
38. Seeds JW, Peng T. Impaired growth and risk of fetal death: is the tenth percentile the appropriate standard? *Am J Obstet Gynecol.* 1998; 178:658–69. [PubMed: 9579427]
39. Zhang J, Mikolajczyk R, Grewal J, et al. Prenatal application of the individualized fetal growth reference. *Am J Epidemiol.* 2011; 173:539–43. [PubMed: 21252054]
40. McIntire D, Bloom S, Casey B, et al. Birth weight in relation to morbidity and mortality among newborn infants. *New Eng J Med.* 1999; 340:1234–8. [PubMed: 10210706]

What this study adds

- While some of the highest maternal exposures to polycyclic aromatic hydrocarbons (PAHs) occur in the workplace, there is only one previous study of occupational PAH exposure and adverse pregnancy outcomes. We sought to extend this literature using control data from a large multisite birth defects study.
- Almost half the jobs with occupational PAH exposure were related to food preparation and serving. There was a significant association of occupational exposure with small for gestational age offspring (OR=2.2, 95% CI 1.3 to 3.8). However, there was no clear exposure-response relationship.

Table 1
 Association of maternal and infant factors with small for gestational age (SGA) offspring among National Birth Defects Prevention Study controls, 1997–2002

Characteristic	SGA		Not SGA		p Value*
	n	%	n	%	
Total	221		2582		
Age (years)					
<20	10	4.5	216	8.4	0.35
20–24	64	29.0	551	21.3	
25–29	58	26.2	706	27.3	
30–34	45	20.4	747	28.9	
35+	44	19.9	362	14.0	
Missing	0		0		
Race/ethnicity					
White non-Hispanic	141	63.8	1690	65.5	0.14
Black non-Hispanic	19	8.6	334	12.9	
Hispanic	47	21.3	442	17.1	
Other	14	6.3	116	4.5	
Missing	0		0		
Education (years)					
<12	31	14.0	246	9.5	0.04
12	56	25.3	637	24.7	
>12	134	60.6	1697	65.8	
Missing	0		2		
Parity/number of previous live births					
0	82	37.1	1148	44.5	0.15
1	92	41.6	895	34.6	
2+	47	21.3	539	20.9	
Missing	0		0		
Infant sex					
Male	121	54.8	1280	49.6	0.14

Characteristic	SGA		Not SGA		p Value*
	n	%	n	%	
Female	100	45.2	1302	50.4	
Missing	0		0		
Cigarette smoking [†]					
Yes	58	26.2	522	20.2	0.03
No	163	73.8	2060	79.8	
Missing	0		0		
Secondhand smoking at home [†]					
Yes	53	24.0	463	17.9	0.03
No	168	76.0	2119	82.1	
Missing	0		0		
Secondhand smoking at work [†]					
Yes	52	23.5	512	19.8	0.19
No	169	76.5	2070	80.2	
Missing	0		0		
Alcohol drinking [†]					
Yes	108	48.9	1209	46.8	0.56
No	113	51.1	1373	53.2	
Missing	0		0		
Pregnancy body mass index					
Underweight	17	8.0	126	5.0	0.01
Normal weight	136	63.8	1437	56.7	
Overweight	36	16.9	588	23.2	
Obese	24	11.3	385	15.2	
Missing	8		46		
Folate antagonist medication [†]					
Yes	1	0.5	2	0.1	0.22 [‡]
No	220	99.5	2580	99.9	
Missing	0		0		
Folic acid supplements [†]					

Characteristic	SGA		Not SGA		p Value*
	n	%	n	%	
Yes	204	92.3	2437	94.4	0.20
No	17	7.7	145	5.6	
Missing	0		0		
Household income (\$)					
<20 000	62	32.3	573	25.3	0.47
20 000–49 999	66	34.4	805	35.6	
50 000+	64	33.3	886	39.1	
Missing	29		318		
Study centre					
Arkansas	32	14.5	323	12.5	0.79
California	23	10.4	306	11.9	
Iowa	28	12.7	364	14.1	
Massachusetts	32	14.5	370	14.3	
New Jersey	34	15.4	347	13.4	
New York	22	9.9	297	11.5	
Texas	29	13.1	267	10.3	
CDC/Atlanta	21	9.5	308	11.9	
Missing	0		0		

* Probability calculated with χ^2 test based on non-missing values.

† Maternal exposure during the period from 1 month before conception through delivery.

‡ Fisher's exact test.

Table 2

Association between maternal occupational exposure to polycyclic aromatic hydrocarbons (PAHs) and small for gestational age (SGA) offspring, National Birth Defects Prevention Study, 1997–2002

	Crude analysis			Adjusted analysis*		
	SGA n	Not SGA n	OR 95% CI	SGA n	Not SGA n	OR 95% CI
Dichotomous Exposure						
No PAH exposure	204	2480	1.0 (Reference)	204	2480	1.0 (Reference)
Any PAH exposure	17	102	2.0 (1.2 to 3.5)	17	102	2.2 (1.3 to 3.8)
Cumulative Exposure ^{†‡}						
No PAH exposure (0)	204	2480	1.0 (Reference)	204	2480	1.0 (Reference)
Low PAH exposure (8–205)	9	50	2.2 (1.1 to 4.5)	9	50	2.5 (1.2 to 5.3)
High PAH exposure (206–3086)	8	52	1.9 (0.9 to 4.0)	8	52	1.9 (0.9 to 4.2)

* Adjusted for maternal age.

[†] Cumulative exposure (unit-hours) was estimated by: (weighted intensity in $\mu\text{g}/\text{m}^3/\text{h}$) \times ((exposure frequency in hrs/week)/(40 h/week)) \times ((hours worked per week)/(7 days per week)) \times (number of days worked from 1 month before conception to delivery).

[‡] Cumulative exposure measured in $\mu\text{g}/\text{m}^3\text{-h}$.