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Prenatal and postnatal exposure to polychlorinated biphenyls and child size at 24 months of age

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Abstract

Research suggests that exposure to polychlorinated biphenyls (PCBs) may result in decreased child growth, though the critical window(s) are unclear. We investigated the association between PCBs and child size at age 24 months (n=44). PCBs were measured in 1st trimester serum, breast milk, and child serum at age 24 months, and dichotomized at the median. Age- and gender-specific z-scores were calculated for anthropometric measures. Using linear regression, we observed no significant changes in z-scores with prenatal or postnatal serum PCB concentrations. PCB-77 in breast milk was associated with a significant decrease in z-score for length. To our knowledge, this study is the first to examine child size in relation to PCBs measured early in pregnancy, as well as quantifying a far greater number of congeners. Further research is needed to clarify critical windows, congener-specific effects, and effect modification by sex in relation to PCBs and child anthropometric measures.

Descriptive keywords

polychlorinated biphenyls; environmental exposure; growth and development; pregnancy; breast feeding

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Introduction

Polychlorinated biphenyls (PCBs) are ubiquitous in the environment due to past manufacturing releases, accidental spills and leaks, and improper storage and dumping. These compounds bioaccumulate and biomagnify within the food chain and are measurable in human biospecimens [1]. PCBs have been shown to cross the placenta [2,3] and are excreted in breast milk [4], serving as prenatal and postnatal routes of exposure for the fetus and nursing infant, respectively. A 1975 study of women from a representative sample of U.S. hospitals found at least trace amounts of PCBs in 99% of the 1,038 breast milk samples that were analyzed [5]. Given the high lipid content of breast milk, PCBs concentrations in this matrix tend to be higher than maternal or child serum concentrations, as well as cord blood concentrations [6,7].

Research suggests that exposures at environmentally relevant concentrations may result in decreased fetal growth and/or alterations in development, though the underlying mechanisms have not been fully delineated. One hypothesis suggests that PCBs alter thyroid function which in turn may impair fetal or child growth [8,9]. However, epidemiologic studies exploring the association between prenatal/breast milk PCB exposure and thyroid function have been inconsistent to date [10]; and recent animal studies investigating PCBs, thyroid function and growth have not observed an effect on offspring growth, despite some alteration in thyroid function [11,12].

Four studies have examined anthropometric measures among children in relation to maternal serum PCB concentrations directly quantified during pregnancy. Within the Child Health and Development Study, maternal serum PCBs concentrations measured during the second or third trimester of pregnancy were associated with a significant increase in height at age five years, but only among girls [13]. In contrast, Lamb and colleagues observed a significant decrease in weight at 4 and 7 years of age among girls in relation to third trimester maternal serum PCB concentrations, but again no effect among boys [14]. Patandin and colleagues measured PCBs in maternal serum collected during the last month of pregnancy, and observed a significantly reduced rate of growth (weight, length and head circumference) from 0–3 months of age, after which no association was observed [15]. Ribas-Fito and colleagues found no association between maternal serum PCB concentrations measured in the third trimester and child height at one, four or seven years of age within the Collaborative Perinatal Project [16]. Several studies have assessed PCB concentrations in cord blood [15,17,18], or breast milk [7] and have observed similar and significant decreases in anthropometric measures or growth rate at various ages, while others have found no association in these matrices [19,20]. Other studies investigating child anthropometric measures and growth have estimated PCB exposure based upon maternal serum samples collected before or after pregnancy [20–22], fish consumption [22], or accidental PCB poisoning [23–25]. The potential toxic effect associated with prenatal and lactational PCB exposure was noted among Japanese (Yusho cohort) and Taiwanese (Yu-Cheng cohort) populations exposed to high levels of PCBs through contaminated rice oil. Within the Yusho cohort, children born to women who were exposed during pregnancy were reported to have growth impairments [26]. Within the Yu-Cheng cohort, significant deficits in height and weight were observed among children exposed *in utero* or through lactation as compared to unexposed children [23,24].

To further examine this association, we prospectively investigated the relation between PCBs and child length, weight, weight-for-length and head circumference at age 24 months using maternal serum (first trimester of pregnancy), breast milk (approximately 4 weeks postpartum), and child serum (age 24 months) PCB concentrations. To our knowledge, this is the first study to examine child anthropometric measures in relation to maternal serum PCB concentrations measured early in pregnancy, as well as quantifying a far greater number of PCB congeners

than previous studies: 86 PCB congeners in maternal serum and all 209 congeners in breast milk and child serum.

Methods

Study design

This study utilized data from the Prospective Pregnancy Study and Child Development Study of the New York State Angler Cohort Study [27,28]. Data were collected longitudinally, following couples from preconception through childbirth and following children through 24 months of age. Women were consented prior to conception for the Prospective Pregnancy Study, and again postpartum for the Child Development Study.

Study population

From 1996 to 1999, one hundred and two women from 16 New York State counties surrounding Lakes Erie and Ontario, were successfully enrolled in the Prospective Pregnancy Study prior to attempting pregnancy, and followed for up to 12 menstrual cycles with intercourse during the estimated fertile window. Fifty-five (54%) women had a live birth of which 52 (95%) participated in the Child Development Study. Follow-up of the children at ages 12 and 24 months enabled the collection of prospective information on child anthropometric measures, development, and health status using standardized methodologies by a multidisciplinary, clinical and epidemiological research team.

Data collection

Maternal data on reproductive and medical history, as well as, lifestyle factors were collected during in-person interviews with mothers upon enrollment into the Prospective Pregnancy Study. In addition, women maintained daily diaries while attempting pregnancy recording vitamin, cigarette and alcohol use amongst other factors.

A prenatal blood sample was obtained from the woman during a home visit shortly after she reported a positive home pregnancy test. Breast milk was collected from nursing women at the first postpartum visit by the study nurse at approximately four weeks postpartum. Mothers were asked to collect breast milk using a standardized protocol. Specifically, women received by express mail, a small, contaminant-free glass bottle and freezer packs for the collection of breast milk. All samples (~4 ounces) were collected from nursing women after the second morning nursing (usually between 9 am and 11 am). Women were asked to refrigerate samples or to freeze samples if collection was more than 2 days prior to the nurse's visit.

At 12 and 24 months of age, home visits were completed by a multidisciplinary team. The three- to four-hour standardized visit included an assessment of anthropometric and neurodevelopmental status by a developmental pediatrician, a psychosocial assessment of the child by a clinical pediatric psychologist, and a home environment assessment conducted by a registered nurse. If the parent consented, a blood sample was obtained from the child at 24 months of age for the quantification of PCBs. Due to a brief interruption in funding, not all children completed a 12 month visit; therefore this analysis is limited to those children completing the 24 month visit.

Exposure assessment

For the purposes of this analysis, we used PCB concentrations measured in maternal serum at the prenatal visit (n=44), in breast milk at approximately four weeks post-partum among breastfed children (n=32), and in the child's serum at 24 months of age (n=17). For the prenatal sample, quantification of 62 single eluting, and 12 sets of coeluting PCB congeners (International Union for Pure and Applied Chemistry numbers 4_10, 5_8, 6, 7_9, 15_17, 16_32,

18, 19, 22, 24_27, 25, 28, 31, 33, 40, 42, 44, 45, 47, 48, 52, 55, 59, 60, 64, 66_95, 70, 74, 77_110, 81_87, 82, 94, 97, 99, 101, 105, 114, 118, 126, 128, 129, 132, 134, 135, 136, 138, 141, 147, 149, 153, 156_171, 157_200, 163, 167, 169, 170, 172, 174, 176, 177, 179, 180, 181, 183, 185, 187, 188, 189, 190, 194, 195, 196_203, 205, 206) was conducted at the Toxicology Research Center at the University at Buffalo by gas chromatography with electron capture detection as previously described [29,30].

Breast milk and child serum samples were analyzed for all 209 PCB congeners by high resolution gas chromatography/high resolution mass spectrometry using EPA Method 1668A, by a laboratory meeting World Health Organization criteria for the analysis of human milk and serum (AXYS Analytical Services Ltd.) [31–33]. The samples were run in batches including three quality control samples (one procedural blank, one spiked reference matrix, and one duplicate participant sample). Both serum and breast milk laboratory values were corrected only for recovery to minimize measurement error and to avoid potential biases associated with substitution of values below the limit of detection or automatic adjustment for lipids [34–36].

Serum and breast milk concentrations are presented in ng/g serum (ppb) or when lipid adjusted as ng/g lipid. Total lipids in serum and breast milk were measured by gravimetric methods and are presented as percent lipids. Due to limited sample, lipids were not quantified for three prenatal serum samples, three breast milk samples, and one child serum sample, in which case we imputed lipids as the median lipid value for the study population.

Outcome assessment

During the in-home assessment, the developmental pediatrician obtained anthropometric measurements on all children including weight, height, and head circumference. Children were weighed on the SECA Digital Baby Scale in the supine position with minimal clothing. The SECA scale has been shown to be accurate to 0.01 kg. Child length was measured by a developmental pediatrician using the SECA Baby and Adult Measuring Board. This measuring board has a fixed head board and moveable foot plate and channel lock for accuracy. It was used only in the recumbent position. A SECA Insertape was used for head circumferences [37] by placing the tape over the supraorbital ridge and around the occiput so that a maximum circumference was obtained. This tape has graduations of 0.1 cm. To limit measurement error, height and head circumference were measured three times each, and the average used for analyses.

Sex-specific standardized (z) scores were calculated for weight-for-age, length-for-age, and weight-for-length-for-age using the Epi Info Software Package and 1987 growth standard [38,39]. Head circumference z-scores were obtained from NCHS statistics developed by Johnson et al [40]. Parental height and weight were self-reported at the time of the home visit. In the absence of the father, the mother reported the father’s height and weight.

Statistical analysis

PCB congeners were summed for a measure representing total PCB exposure. PCB congeners 1, 2, and 3 were not included in the summation of breast milk PCBs due to missing values for two women; overall these congeners represented less than 0.02% of total PCBs. Total PCBs were not distributed normally in any of the matrices, and no one transformation method normalized the distribution consistently across matrices or congeners; therefore, we dichotomized all PCB variables at the median for analyses, after assessing them in their continuous form. Demographic, reproductive and anthropometric measures were compared across serum PCB groups using the chi-square test (categorical data), Student’s t-test (continuous, normally-distributed data) or Kruskal-Wallis test (continuous, non-normally-distributed data).

The association between total PCBs and child weight, length, weight-for-length, and head circumference at age 24 months was assessed using unadjusted and adjusted linear regression models with PCBs as a dichotomous variable (above or below the median concentration) and entering relevant covariates. Maternal prenatal serum, breast milk, and infant PCB concentrations (ng/g serum or milk) were modeled independently and adjusted for gravimetric lipids in the model. When different matrices were modeled together in the same model, standardized PCB concentrations (ng/g lipid) were employed. Child serum and breast milk PCB concentrations were not modeled together primarily due to the limited sample size, but also due to the strong correlation between breast milk and child serum concentrations. Factors assessed as potential confounders included maternal body mass index (BMI) defined as kilograms/meters^2 (continuous), height in meters (continuous), preconception weight in kilograms (continuous), parity (no prior live births versus 1 or more prior live births), gravidity (no prior pregnancies versus 1 or more prior pregnancies), and education (less than college degree versus college degree or higher); maternal preconception vitamin (yes/no), cigarette (yes/no), and alcohol (yes/no) use; paternal height in meters (continuous); and percent gravimetric lipids (continuous). Gestational age at delivery and birth weight were not considered as confounders, as they may be in the causal pathway [41]. Given evidence of potential effect modification by infant sex in other studies [13,14], we stratified prenatal serum and breast milk PCB models by child sex, though limited by sample size. Analyses of congener-specific data were carried out for PCB 153 (given its high relative weight to overall PCBs), and mono-ortho PCB congener 114 and non-ortho coplanar PCB congeners 77, 126, and 169 (given their dioxin-like effects and known toxicity [42,43]). Further sub-analyses were carried out limiting total PCBs to only those congeners assessed in all three matrices (prenatal serum, breast milk and child serum).

Results

Among the 52 children participating in the Child Development Study, 47 (90%) completed the 24 month home visit. The following analysis will focus on 44 children who completed the 24 month home visit and for whom prenatal PCB concentrations were available, and subsets of 32 children with breast milk samples, and 17 children with serum samples at 24 months of age. Mothers of included children (n=44) were significantly more likely to drink alcohol before conception than mothers of excluded children (n=8) (89% versus 50%, respectively; p=0.01); and included children tended to be taller at 24 months (z-score=0.5; standard deviation (SD): 0.9 versus −0.2 (SD: 0.1); p<0.001) as compared to excluded children. Included children were also more likely to be breastfed (75.0% vs. 38%; p=0.04) as compared to excluded children. Among the 44 eligible children, none were below the 5th percentile for weight, length, or weight-for-length at 24 months of age; two children were below the 5th percentile for head circumference.

Prenatal serum PCB concentrations

Among the 44 children included in analyses, the median prenatal total PCB concentration was 4.18 ng/g serum (IQR: 3.68, 5.38) (Table 1). There were no significant differences between prenatal serum total PCB groups above and below the median in relation to demographic, reproductive, lifestyle, or anthropometric factors, with the exception of child sex (Table 2). Mothers with serum PCB concentrations above the median were more likely to give birth to a girl than mothers with serum PCBs below the median (68% vs. 36%; p=0.04); an association that was not observed in relation to total PCBs in the full cohort [44]. Mean birth weight and gestational age did not differ by prenatal serum total PCB concentrations above and below the median.

No significant associations were observed between serum prenatal total PCBs and child anthropometric measures at age 24 months, in unadjusted analyses or after adjusting for gravimetric lipids and maternal anthropometric measures (Table 3). Summed coplanar PCBs (77_110, 126, and 169) and PCB congeners 114 and 153 were not associated with a significant change in z-scores. In sex-stratified models for prenatal total PCBs, we did not observe a significant change in z-scores in either stratum of child sex.

Breast milk PCB concentrations

Seventy-five percent (n=33) of children were breastfed for an average of 31.5 weeks (SD: 22.4) (Table 2) with a median total PCB concentration in breast milk (n=32 with samples) of 4.75 ng/g milk (IQR: 3.97, 7.19). Children who were breastfed were more likely to have mothers who graduated college (79% versus 27%; p=0.002), mothers with a higher preconception weight (67.2 kg versus 57.9 kg; p=0.08), a shorter gestation (39.1 weeks (SD: 2.2) versus 40.1 weeks (SD: 1.1), p=0.07), and a greater z-score for head circumference at 24 months (z-score: z-score = 1.1 (SD: 1.1) versus z-score = −0.3 (SD: 1.3); p=0.07) compared to children who were bottle fed. Breastfeeding was not associated with prenatal serum total PCB concentrations (breastfed: median=4.22 ng/g serum (IQR: 3.69, 5.37); bottle fed: median=4.11 ng/g serum (IQR: 3.46, 5.42; p=0.82)).

Among the subset of children who were breastfed and had breast milk concentrations (n=32; 97%), no significant associations were observed between breast milk total PCB concentrations and child anthropometric measures in unadjusted analyses or after adjusting for gravimetric lipids and maternal anthropometric measures (Table 3). PCB congener 77 was associated with a significant decrease in length z-score (β=−0.62; 95% CI: −1.17, −0.07). Among the subset of children for whom we had both prenatal serum and breast milk PCB concentrations (n=32), we modeled the lipid standardized PCB concentrations (ng/g lipid) together in the same model and found no significant effects in relation to total PCB concentrations. In sex-stratified models for breast milk total PCBs, we did not observe evidence for effect modification by child sex.

Child serum PCB concentrations

Children with available serum PCB concentrations (n=17) were more likely to have a mother who smoked cigarettes prior to conception (52.9% versus 18.5%, p=0.02), and a higher z-score for length at age 24 months (z-score=0.88 (SD: 0.82) versus z-score=0.26 (SD: 0.85); p=0.02) as compared to children without serum PCB concentrations (n=27); no other significant differences were observed. The median total PCB concentration was 0.88 ng/g serum (IQR: 0.56, 1.75), with breastfed children having significantly higher serum total PCB concentrations (median=1.36 ng/g serum; IQR: 0.72, 3.26) compared to bottle fed children (median=0.56 ng/g serum; IQR: 0.51, 0.74; p=0.04). Child serum total PCB concentrations were significantly correlated with length of breastfeeding (R^2=0.54; p=0.02; n=17). We observed no significant associations between child serum PCB concentrations (total or congener-specific) and anthropometric measures. Adjusting the models for breastfeeding or prenatal serum concentrations (ng/g lipid), did not change the results.

Given that only 86 PCB congeners were measured in maternal serum compared to 209 congeners in breast milk and infant serum, we reran all analyses, limiting total PCBs to only those congeners that were measured in all three matrices, and observed no major changes in the point estimates. Within this subgroup of congeners, maternal prenatal serum total PCB concentrations (ng/g lipid) were not significantly correlated with either child serum total PCBs at 24 months (R^2=0.24; p=0.35; n=17) or breast milk total PCBs (R^2 =0.15; p=0.42; n=32), nor was breast milk total PCBs significantly correlated with child serum total PCBs (R^2 =0.38; p=0.25; n=11). Congener-specific data on the median, inter-quartile range, minimum and

maximum values, percent relative weight and percent above the limit of detection are provided in the Appendix for each matrix.

Discussion

Overall, we observed no significant associations between prenatal serum, breast milk, or child serum total PCB concentrations and child anthropometric measures at 24 months of age. While we did observe small, non-significant changes in z-scores for some congener specific analyses, it is unclear if these findings reflect a true association, or are simply due to residual confounding or chance.

This is the first study to examine the association between maternal serum PCB concentrations measured early in pregnancy and child anthropometric measures at age 24 months. While no association was observed in relation to total prenatal PCB concentrations, we did observe small increases in z-scores for weight, weight-for-length, and head circumference in relation to prenatal summed coplanar PCB concentrations. Verhulst and colleagues observed a significant increase in BMI standard deviation scores (SDS) (adjusted β=0.003, SE: 0.001, p=0.03) between age 1 and 3 years in relation to cord blood total PCB concentrations [18]. Hertz-Picciotto and colleagues observed a non-significant increase in weight z-score at age five in relation to prenatal PCB concentrations measured during the second or third trimester (adjusted β=3.8; 95% CI: −0.52, 8.10), and a significant increase in height z-score for girls (adjusted β=4.5 z-score; 95% CI: 0.05, 9.00), but not for boys when comparing PCB exposure in the 90^{th} percentile to 10^{th} percentile [13]. These results are in contrast with some studies that measured maternal PCB concentrations later in pregnancy or in cord blood and found an association with decreased infant or child weight and/or height [7,14,15,17,18,21–24]. Maternal serum PCB concentrations may decrease during the first trimester due to increasing blood volume or other homeostatic changes as previously suggested [30] and then gradually increase over pregnancy to the neonatal period [2,30,45]; therefore, the timing for measuring exposures needs to be considered in relation to peak velocities of fetal growth. Specifically, the velocity for fetal head circumference velocity peaks around 24 weeks gestation, abdominal circumference at 27 weeks, and femur length at 21 weeks [46]. Furthermore, fetal growth trajectories may differ by sex [47].

While breast milk total PCBs were not significantly associated with anthropometric measures, we did observe small decrements in some z-scores at age 24 months in relation to concentrations of summed coplanar PCBs and congeners 77, 114 and 153. Regardless of PCB exposure, breastfed children tended to be heavier, have a greater weight-for-length z-score, and greater head circumference at 24 months of age compared to non-breastfed children though not statistically significant; however, breastfed children tended to be shorter than non-breastfed children. Within a cohort of children from the Faroe Islands, Grandjean and colleagues observed a decrease in weight (β= −0.43 kg; 95% CI: −0.79, −0.06), as well as height (β= −0.88 cm; 95% CI: −1.52,−0.24) at 18 months of age in relation to breast milk PCB concentrations after adjusting for birth weight, sex, maternal height, smoking, and age [7]. The association with breast milk PCBs may be due to the higher concentrations of PCBs transferred to the child as compared to transplacental transfer given the high lipid content of breast milk.

Given the different congeners measured, different quantification methods, and different means for handling limits of detection and lipid adjustment that have been used, it is difficult to compare PCB concentrations across studies. We observed lower concentrations of PCB congener 153 in prenatal serum (median 62.2 ng/g lipid; 5^{th} and 95^{th} percentile: 33.3, 108.0) as compared to Hertz-Picciotto and colleagues (median 133 ng/g lipid; 5^{th} and 95^{th} percentile: 72, 273) which may be due to varying sources of exposure and temporal differences with the later cohort representing serum PCBs in either the second or third trimester, as well as thirty

years earlier than the Prospective Pregnancy Study and prior to the manufacturing phase-out of PCBs in the 1970s. While serum PCB concentrations have decreased over the decades particularly among anglers as shown by Tee and colleagues [48], our PCB 153 concentrations were also lower than an Inuit cohort in 1995 which measured maternal serum at delivery (geometric mean (gm) 105.1 ng/g lipid; 95% CI: 92.5, 119.5), maternal milk approximately one month postpartum (gm 129.9 ng/g lipid; 95% CI: 112.9, 149.5), and infant serum at six months (gm 75.1 ng/g lipid, 95% CI: 58.1, 97.1) [6]. This Inuit population consumes high quantities of fish as well as marine mammals, which may explain the higher PCB concentrations.

Though limited by sample size, this study has several strengths over previous studies. The study cohort was followed prospectively from pre-conception through 24 months of age with PCB concentrations measured during multiple sensitive windows, as well as, in different matrices (prenatal serum in the first trimester, breast milk approximately 4 weeks postpartum, and child serum at age 2 years) providing estimates of prenatal and postnatal exposures. This is the first study to measure maternal serum PCB concentrations early in pregnancy. Multiple PCB congeners were measured including 86 in prenatal serum and all 209 in breast milk and child serum compared to other studies that have quantified only a few select congeners. This allowed for the full quantification of PCB congeners in both breast milk and child serum. Statistical analyses were carried out on PCB congeners selected *a priori* based upon their relative weight and potential toxicity. Furthermore, we have provided congener-specific statistics for all three matrices in the Appendix which will allow for comparison across studies. In regards to the outcome, height, weight, and head circumference were measured on all children using a standardized protocol and instrumentation by the same research team reducing the potential for measurement error.

Given the skewed distribution of PCBs and small sample size, we chose to dichotomize PCB concentrations at the median after assessing them in their continuous form, which may have reduced our power to detect an association, particularly if there is a threshold effect above the median. In addition, we lacked information on exposures during pregnancy such as smoking and alcohol consumption and maternal weight gain that have been associated with altered anthropometric measures in children. Preconception vitamin, alcohol and cigarette use were not significant predictors of child anthropometric measures at 24 months in this cohort, however, preconception use may not accurately reflect pregnancy exposures. Overall, 32% of women reported smoking prior to pregnancy with women who smoked being more likely to have prenatal total PCBs concentrations below the median as compared to those who did not smoke. Almost all women drank alcohol prior to conception (89%), and 82% reported taking vitamins. These and other unmeasured confounders, as well as the limited power to add all measured potential confounders to our final models, may have led to residual confounding in our results. All models were adjusted for gravimetric lipids; in addition, weight and head circumference z-score models were adjusted for maternal preconception weight, length z-score models adjusted for maternal height, and weight-for-length z-score models adjusted for maternal preconception BMI. Our small study population was a homogenous population of anglers from upper New York State representing a relatively healthy population. No children were below the 5^{th} percentile for weight, length or weight-for-length. This homogeneity may have limited our ability to detect differences should they exist. Finally, several studies have observed differences by sex which we were unable to assess effectively in this cohort given the limited sample size.

In this first study to examine maternal serum PCB concentrations early in pregnancy and child weight, height, weight-for-length, and head circumference at age 24 months, we did not observe a significant difference in anthropometric parameters by total PCB concentrations. A small and non-significant change in z-scores was observed in analyses of some congener-specific

data. These associations may be due to chance or residual confounding, or alternatively reflect a true association. Potential effects of specific congeners as observed here may be obscured when summing all PCB congeners given the different properties of specific congeners or groups of congeners [12]. Though inconsistent, some studies have found an association between PCB concentrations and altered thyroid function [10]; however, it is unclear if these alterations are great enough to induce alterations in growth [11,12]. Given inconsistencies across studies, further research is needed to further clarify critical windows of exposure, congener-specific effects, and effect modification by sex in relation to PCB concentrations and child anthropometric measures, should an effect actually exist.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Centers for Disease Control and Prevention. Third National Report on Human Exposure to Environmental Chemicals. Atlanta (GA): CDC; 2005.
2. Kodama H, Ota H. Transfer of polychlorinated biphenyls to infants from their mothers. Arch Environ Health 1980;35:95–100. [PubMed: 6768342]
3. Masuda Y, et al. Transfer of polychlorinated biphenyls to the foetuses and offspring of mice. Food Cosmet Toxicol 1978;16:33–7. [PubMed: 415949]
4. Schwartz PM, et al. Lake Michigan fish consumption as a source of polychlorinated biphenyls in human cord serum, maternal serum, and milk. Am J Public Health 1983;73:293–6. [PubMed: 6401943]
5. Lucas, R.; Iannacchione, V.; Melroy, D. Polychlorinated biphenyls in human adipose tissue and mother's milk. Research Triangle Institute; 1982. RTI/1864/50-03F
6. Ayotte P, et al. Assessment of pre- and postnatal exposure to polychlorinated biphenyls: lessons from the Inuit Cohort Study. Environ Health Perspect 2003;111:1253–8. [PubMed: 12842782]
7. Grandjean P, et al. Attenuated growth of breast-fed children exposed to increased concentrations of methylmercury and polychlorinated biphenyls. FASEB J 2003;17:699–701. [PubMed: 12586743]
8. Karmaus W, et al. Childhood growth and exposure to dichlorodiphenyl dichloroethene and polychlorinated biphenyls. J Pediatr 2002;140:33–9. [PubMed: 11815761]
9. Osius N, et al. Exposure to polychlorinated biphenyls and levels of thyroid hormones in children. Environ Health Perspect 1999;107:843–9. [PubMed: 10504153]
10. Hagmar L. Polychlorinated biphenyls and thyroid status in humans: a review. Thyroid 2003;13:1021–8. [PubMed: 14651786]
11. Kobayashi K, et al. Effects of in utero exposure to 2,2′,4,4′,5,5′-hexachlorobiphenyl (PCB 153) on somatic growth and endocrine status in rat offspring. Congenit Anom(Kyoto) 2008;48:151–7. [PubMed: 18983581]
12. Kobayashi K, et al. Effects of in utero exposure to 2,2′,4,4′,5,5′-hexachlorobiphenyl on postnatal development and thyroid function in rat offspring. Ind Health 2009;47:189–97. [PubMed: 19367049]
13. Hertz-Picciotto I, et al. In utero polychlorinated biphenyl exposures in relation to fetal and early childhood growth. Epidemiology 2005;16:648–56. [PubMed: 16135941]
14. Lamb MR, et al. Prenatal exposure to polychlorinated biphenyls and postnatal growth: a structural analysis. Environ Health Perspect 2006;114:779–85. [PubMed: 16675437]

15. Patandin S, et al. Effects of environmental exposure to polychlorinated biphenyls and dioxins on birth size and growth in Dutch children. Pediatr Res 1998;44:538–45. [PubMed: 9773843]
16. Ribas-Fito N, et al. Prenatal exposure to 1,1-dichloro-2,2-bis (p-chlorophenyl)ethylene (p, p′-DDE) in relation to child growth. Int J Epidemiol 2006;35:853–8. [PubMed: 16606643]
17. Jacobson JL, Jacobson SW, Humphrey HE. Effects of exposure to PCBs and related compounds on growth and activity in children. Neurotoxicol Teratol 1990;12:319–26. [PubMed: 2118230]
18. Verhulst SL, et al. Intrauterine exposure to environmental pollutants and body mass index during the first 3 years of life. Environ Health Perspect 2009;117:122–6. [PubMed: 19165398]
19. Rogan WJ, et al. Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human milk: effects on growth, morbidity, and duration of lactation. Am J Public Health 1987;77:1294–7. [PubMed: 3115123]
20. Gladen BC, Ragan NB, Rogan WJ. Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. J Pediatr 2000;136:490–6. [PubMed: 10753247]
21. Blanck HM, et al. Growth in girls exposed in utero and postnatally to polybrominated biphenyls and polychlorinated biphenyls. Epidemiology 2002;13:205–10. [PubMed: 11880762]
22. Rylander L, Stromberg U, Hagmar L. Weight and height at 4 and 7 years of age in children born to mothers with a high intake of fish contaminated with persistent organochlorine pollutants. Chemosphere 2007;67:498–504. [PubMed: 17123573]
23. Guo YL, et al. Musculoskeletal changes in children prenatally exposed to polychlorinated biphenyls and related compounds (Yu-Cheng children). J Toxicol Environ Health 1994;41:83–93. [PubMed: 8277528]
24. Guo YL, Lambert GH, Hsu CC. Growth abnormalities in the population exposed in utero and early postnatally to polychlorinated biphenyls and dibenzofurans. Environ Health Perspect 1995;103 (Suppl 6):117–22. [PubMed: 8549457]
25. Yoshimura T, Ikeda M. Growth of school children with polychlorinated biphenyl poisoning or yusho. Environ Res 1978;17:416–25. [PubMed: 122586]
26. Harada M. Intrauterine poisoning: clinical and epidemiological studies and significance of the problem. Bull Inst Constit Med 1976;25 (suppl):1–69.
27. Buck Louis, GM., et al. Human Reproduction. 2008. Polychlorinated bipheyl serum concentrations, lifestyle and time to pregnancy. In press
28. Senn KM, et al. Longitudinal study of babies born to mothers enrolled in a preconception prospective pregnancy study: study design and methodology, New York State Angler cohort study. Environ Res 2005;97:163–9. [PubMed: 15533332]
29. Greizerstein HB, et al. Standardization of a method for the routine analysis of polychlorinated biphenyl congeners and selected pesticides in human serum and milk. J Anal Toxicol 1997;21:558–66. [PubMed: 9399126]
30. Bloom MS, et al. Maternal serum polychlorinated biphenyl concentrations across critical windows of human development. Environ Health Perspect 2007;115:1320–4. [PubMed: 17805422]
31. AXYS Analytical Services LTD. AXYS method document MLA-010. Analytical method for the determination of 209 PCB congeners by EPA method 1668A. 2003
32. United States Environmental Protection Agency. Method 1668, Revision A: chlorinated biphenyl congeners in water, soil, sediment, and tissue by HRGC/HRMS. Washington, DC: United States Environmental Protection Agency; 1999. [EPA-821-R-00-002]
33. WHO. Interlaboratory quality assessment of levels of PCBs, PCDDs and PCDFs in human milk and blood plasma. Bilthoven: WHO European Center for Environment and Health; 2000.
34. Richardson DB, Ciampi A. Effects of exposure measurement error when an exposure variable is constrained by a lower limit. Am J Epidemiol 2003;157:355–63. [PubMed: 12578806]
35. Schisterman EF, et al. The limitations due to exposure detection limits for regression models. Am J Epidemiol 2006;163:374–83. [PubMed: 16394206]
36. Schisterman EF, et al. Lipid adjustment in the analysis of environmental contaminants and human health risks. Environ Health Perspect 2005;113:853–7. [PubMed: 16002372]

37. Cameron, N. The methods of auxological anthropometry. In: Cameron, N., editor. The Measurement of Human Growth. New York: Premium Press; 1986. p. 3-46.

38. Dean, A., et al. Epi Info. Atlanta: US Department of Health and Human Services, Public Health Service, CDC; 1990.

39. Dibley MJ, et al. Development of normalized curves for the international growth reference: historical and technical considerations. Am J Clin Nutr 1987;46:736–48. [PubMed: 3314468]

40. Johnson CL, et al. Basic data on anthropometric measurements and angular measurements of the hip and knee joints for selected age groups 1–74 years of age. Vital Health Stat 1981;11:1–68.

41. Hertz-Picciotto I. Commentary: When brilliant insights lead astray. Int J Epidemiol 2001;30:1243–4. [PubMed: 11821315]

42. Safe S. Toxicology, structure-function relationship, and human and environmental health impacts of polychlorinated biphenyls: progress and problems. Environ Health Perspect 1993;100:259–68. [PubMed: 8354174]

43. Van den Berg M, et al. The 2005 World Health Organization reevaluation of human and Mammalian toxic equivalency factors for dioxins and dioxin-like compounds. Toxicol Sci 2006;93:223–41. [PubMed: 16829543]

44. Taylor KC, et al. Preconception maternal polychlorinated biphenyl concentrations and the secondary sex ratio. Environ Res 2007;103:99–105. [PubMed: 16780830]

45. Longnecker MP, et al. Serial levels of serum organochlorines during pregnancy and postpartum. Arch Environ Health 1999;54:110–4. [PubMed: 10094288]

46. Snijders RJ, Nicolaides KH. Fetal biometry at 14–40 weeks' gestation. Ultrasound Obstet Gynecol 1994;4:34–48. [PubMed: 12797224]

47. Lampl M, Jeanty P. Timing is everything: a reconsideration of fetal growth velocity patterns identifies the importance of individual and sex differences. Am J Hum Biol 2003;15:667–80. [PubMed: 12953179]

48. Tee PG, et al. A longitudinal examination of factors related to changes in serum polychlorinated biphenyl levels. Environ Health Perspect 2003;111:702–7. [PubMed: 12727597]

Table 1

Median and interquartile range for total polychlorinated biphenyl (PCB) and lipid concentrations by type and timing of specimen collection, New York State Angler Cohort Study (1996–2002)

	Median	25th percentile	75th percentile
Prenatal serum (n=44)			
Total PCBs (ng/g serum)	4.18	3.68	5.38
Total standardized PCBs (ng/g lipid)	1170.18	791.94	1411.40
Percent lipids	0.41	0.33	0.45
Postnatal breast milk (n=32)			
Total PCBs (ng/g milk)	4.75	3.97	7.19
Total standardized PCBs (ng/g lipid)	162.45	118.26	204.01
Percent lipids	3.28	2.34	4.08
Child serum at age 24 months (n=17)			
Total PCBs (ng/g serum)	0.88	0.56	1.75
Total standardized PCBs (ng/g lipid)	165.22	106.29	271.38
Percent lipids	0.54	0.49	0.58

Table 2

Maternal and child characteristics by maternal serum prenatal total polychlorinated biphenyl (PCB) concentrations, New York State Angler Cohort Study (1996–2002)

	Total prenatal PCB concentrations						
	Total (n=44)		<4.18 ng/g serum (n=22)		>4.18 ng/g serum (n=22)		p- value[1]
	N	%	N	%	N	%	
Maternal Characteristics							
Maternal education							
Less than college degree	15	34.1	9	40.9	6	27.3	0.34
College degree or higher	29	65.9	13	59.1	16	72.7	
Gravidity							
No pregnancies	7	15.9	4	18.2	3	13.6	0.68
1 or more pregnancies	37	84.1	18	81.8	19	86.4	
Parity							
No live births	8	18.2	5	22.7	3	13.6	0.43
1 or more live births	36	81.8	17	77.3	19	86.4	
Preconception smoking	14	31.8	9	40.9	5	22.7	0.20
Preconception alcohol consumption	39	88.6	19	86.4	20	90.9	0.64
Preconception vitamin use	36	81.8	19	86.4	17	77.3	0.43
Child Characteristics							
Preterm delivery (<37 weeks)	4	9.1	1	4.6	3	13.6	0.29
Low birth weight (<2500 g)	3	6.8	1	4.6	2	9.1	0.55
Size for gestational age							
Small	1	2.3	1	4.6	0	0.0	0.47
Appropriate	35	79.6	18	81.8	17	77.3	
Large	8	18.2	3	13.6	5	22.7	
Infant Sex							
Male	21	47.7	14	63.6	7	31.8	0.04
Female	23	52.3	8	36.4	15	68.2	
Breastfed	33	75.0	16	72.7	17	77.3	0.73

	Total prenatal PCB concentrations						
	Total (n=44)		<4.18 ng/g serum (n=22)		>4.18 ng/g serum (n=22)		p- value[1]
	N	%	N	%	N	%	
	Mean	SD	Mean	SD	Mean	SD	
Parental Characteristics							
Maternal age at delivery (years)	31.8	2.1	31.4	2.3	32.3	1.9	0.16
Maternal preconception BMI (kg/m^2)	23.7	5.2	25.0	6.1	22.3	3.6	0.09
Maternal preconception weight (kg)	64.9	16.3	67.7	20.6	62.1	10.2	0.26
Maternal height (m)	1.7	0.1	1.6	0.1	1.7	0.1	0.15
Paternal height (m)	1.8	0.1	1.8	0.1	1.8	0.1	0.31
Child Characteristics							
Gestational age at delivery (weeks)	39.4	2.0	39.6	1.9	39.1	2.2	0.46
Birth weight (g)	3482.0	565.1	3502.0	567.0	3462.0	575.8	0.82
Weeks breastfed (n=33)[2]	31.5	22.4	30.8	25.9	32.2	19.2	0.55
Weight 24 months (kg)	12.7	1.5	12.7	1.4	12.7	1.6	0.88
Weight 24 months (z-score)	0.4	1.0	0.4	0.9	0.4	1.2	0.91
Length 24 months (cm)	87.5	3.0	87.5	3.5	87.5	2.5	0.99
Length 24 months (z-score)	0.5	0.9	0.4	1.0	0.6	0.7	0.68
Weight-for-length 24 months (z-score)	0.2	0.9	0.2	0.8	0.3	1.1	0.86
Head circumference 24 months (cm)	49.0	1.6	49.1	1.9	48.9	1.3	0.66
Head circumference 24 months (z-score)	0.3	1.1	0.2	1.3	0.4	1.0	0.66
Specimen Characteristics							
Days from LMP to serum collection[2]	62.8	19.2	62.2	13.0	63.4	24.1	0.58
Days from birth to breast milk collection[2]	24.4	8.6	23.6	7.3	25.3	9.9	0.70

LMP – last menstrual period

[1] P-value for chi-square test (categorical) or t-test (continuous) unless otherwise noted.

[2] P-value for Kruskal Wallis test.

Table 3

The association between polychlorinated biphenyl (PCB) concentrations at critical windows of exposure and child size at age two years, New York State Angler Cohort Study (1996–2002)[1]

Outcome	Prenatal Serum (ng/g serum)			Breast Milk (ng/g milk)			Child Serum (ng/g serum)		
	N	Beta	95% CI	N	Beta	95% CI	N	Beta	95% CI
Total PCBs unadjusted model									
Weight z-score	44	0.02	−0.29, 0.34	32	−0.34	−1.09, 0.41	17	0.18	−0.76, 1.12
Length z-score	44	0.11	−0.43, 0.65	32	−0.02	−0.67, 0.63	17	−0.16	−1.03, 0.72
Weight-for-length z-score	44	0.05	−0.53, 0.63	32	−0.46	−1.16, 0.24	17	0.12	−0.66, 0.90
Head circumference z-score	44	0.15	−0.55, 0.85	32	0.01	−0.78, 0.79	17	0.13	−1.06, 1.32
Total PCBs adjusted model[2]									
Weight z-score	44	0.02	−0.63, 0.66	32	−0.30	−1.12, 0.52	17	−0.23	−1.23, 0.77
Length z-score	44	−0.14	−0.68, 0.40	32	−0.31	−0.92, 0.30	17	−0.57	−1.45, 0.30
Weight-for-length z-score	44	0.07	−0.54, 0.68	32	−0.28	−1.07, 0.50	17	−0.23	−1.01, 0.55
Head circumference z-score	44	0.34	−0.29, 0.97	32	−0.04	−0.74, 0.66	17	−0.21	−1.39, 0.97
Summed coplanar PCBs adjusted model[2,3]									
Weight z-score	44	0.40	−0.24, 1.04	32	−0.51	−1.44, 0.42	17	−0.13	−1.05, 0.78
Length z-score	44	−0.18	−0.71, 0.35	32	−0.34	−1.04, 0.36	17	−0.19	−1.06, 0.69
Weight-for- length z-score	44	0.58	−0.01, 1.16	32	−0.42	−1.31, 0.47	17	−0.13	−0.86, 0.60
Head circumference z-score	44	0.51	−0.10, 1.13	32	−0.25	−1.05, 0.55	17	−0.59	−1.61, 0.43
PCB congener 114 adjusted model[2]									
Weight z-score	44	−0.16	−0.78, 0.46	32	−0.57	−1.35, 0.22	17	−0.66	−1.59, 0.28
Length z-score	44	−0.15	−0.67, 0.36	32	−0.34	−0.93, 0.25	17	−0.61	−1.34, 0.12
Weight-for- length z-score	44	−0.14	−0.72, 0.44	32	−0.40	−1.16, 0.37	17	−0.39	−1.16, 0.38
Head circumference z-score	44	0.45	−0.15, 4.04	32	−0.08	−0.76, 0.61	17	−0.61	−1.75, 0.52
PCB congener 153 adjusted model[2]									
Weight z-score	44	−0.20	−0.81, 0.41	32	−0.64	−1.46, 0.18	17	−0.57	−1.58, 0.43
Length z-score	44	−0.16	−0.67, 0.34	32	−0.53	−1.14, 0.08	17	−0.52	−1.36, 0.31
Weight-for- length z-score	44	−0.21	−0.79, 0.37	32	−0.53	−1.32, 0.27	17	−0.38	−1.19, 0.44
Head circumference z-score	44	−0.43	−1.02, 0.16	32	−0.39	−1.09, 0.32	17	0.36	−0.88, 1.59

[1] PCB concentrations dichotomized at the median.

[2] Models adjusted for gravimetric lipids and weight is adjusted for maternal preconception weight; length is adjusted for maternal height; weight-for-length is adjusted for maternal preconception BMI; and head circumference is adjusted for maternal preconception weight.

[3] Coplanar PCBs 77, 126, and 169. In prenatal serum, PCB congener 77 coeluted with congener 110.