Relationship between child birth weight and concentration of polychlorinated biphenyls (PCBs) of the mother in Japan.
–Tohoku Study of Child Development (TSCD)–

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Introduction

Birth weight is considered to be a predictor of a variety of adverse developments in childhood and beyond, including obesity, high blood pressure, cardiovascular disease and depression. There is widespread concern about potentially adverse health effects of environmental chemicals on children. Infants exposed *in utero* and during the early neonatal period are particularly vulnerable because of cell differentiation, the immaturity of metabolic pathways, and development of vital organ systems[1]. Exposure to persistent organochlorine compounds, including pesticides and industrial chemicals, is associated with detrimental effects on childhood neurobehavioral development. Studies in rhesus monkeys and rats showed that prenatal exposure to polychlorinated biphenyls (PCBs) was associated with reduced birth weight. In addition, certain unusual exposures such as those resulting from accidental poisoning by PCBs in Japan and Taiwan, have definitely been associated with low birth weight. Some studies also observed reduced birth weight and shorter gestation in infants with elevated PCB levels whose mothers consumed contaminated fish[2,3]. Thus, there is reason to believe that exposure to PCBs *in utero* may adversely affect the developing infant. The present study examines the association between exposure to PCBs *in utero* and infant birth weight.

Materials and Methods

We have been conducting a prospective cohort study, the Tohoku Study of Child Development (TSCD), to examine the effects of perinatal exposure to PCBs and methylmercury on neurobehavioral development in Japanese children. From January 2001 through September 2003 we recruited healthy pregnant women with their informed consent at obstetrics wards of two urban hospitals in the Tohoku region of Japan. Our cohort study is being conducted in a large city with a population of more than one million in order to assess the effect of the average exposure in pregnant Japanese women. The details of the study protocol were reported previously[4]. The TSCD was approved by the Medical Ethics Committee of the Tohoku University Graduate School of Medicine, and all mothers provided signed informed consent. In this analysis, the subjects were mother-infant pairs whose variables including the PCB concentration in cord blood, birth weight and other covariates were available. The infants were all singletons from full-term (37-42 weeks) gestation without congenital anomalies or diseases.

Birth weight in all infants was 2500g or more since low birth weight was used as an exclusion criterion. Information was obtained about pregnancy, delivery and infant characteristics from medical records. We obtained information about smoking status (nonsmoker/ex-smoker and current smoker) and alcohol drinking (yes/no) during pregnancy from a questionnaire. Umbilical cord blood was collected into a clean bottle immediately after birth. The samples were frozen at -80°C until analysis. All 209 PCB congeners were analyzed using HR-GC/HR-MS. The analytical procedure was described previously[5]. The total PCB concentration represented the sum of all the measured congeners, expressed as ng/g-fat. The total mercury concentration in cord blood was measured by cold vapor atomic absorption. In the statistical analysis, total PCBs and mercury concentrations, birth weight and maternal body mass index (BMI) before pregnancy were logarithmically transformed because of skewed distribution. Parametric methods were applied throughout. Multiple regression analyses were performed for adjustment of covariates. The potential confounders were considered and identified on the basis of previous studies[2,3,6-10]. They were the maternal age at delivery, maternal BMI before pregnancy, mercury concentration in cord blood, maternal alcohol drinking and smoking during pregnancy, parity, gestational age, and the sex and birth weight of the infant. The significance level was set at 5%.

Results and discussion

The number of mother-infant pairs was 438. The characteristics of the mothers and infants are shown in Table 1. The mean maternal age at delivery was 31.3 (SD 4.4, range 20-42) years. BMI before pregnancy ranged between 16.0 and 45.0 kg/m^2, with only 27 (6.1%) being over 25 kg/m^2, which is defined as overweight. The mean weight of all infants was 3100.5 (SD 319.7) g, the median was 3097.0 g, with a range between 2506 and 4176 g. The infants consisted of 225 boys and 213 girls. The mean total PCB concentration in cord blood was 54.0 ng/g-fat (SD 33.1) (median 47.2), and total maternal fish intake was 23.5 kg/year (SD 16.7) (median 20.5). Table 2 shows the results of multiple regression analyses. The BMI before pregnancy and gestational age were positively associated with birth weight. There was no significant difference statistically in birth weight between nonsmokers and smokers (including ex-smokers) during pregnancy. The total PCB and mercury concentration in cord blood were negatively associated with birth weight, whereas the total fish intake was positively associated with birth weight. Thus, the results suggested that prenatal PCB exposure adversely affected fetal growth.

Our study found a significant decrease in birth weight associated with the total PCB concentration in cord blood at delivery. Several studies have investigated the potential association between PCB exposure and birth weight[2,3,6,8-11]. However, one strength of our study is that we used the cord blood PCB concentrations as the indicator of intrauterine exposure, not approximations such as a food frequency questionnaire. Although we have found that PCBs and mercury may be associated with reduced birth weight, the underlying mechanisms remain unknown. In addition, levels of toxicants such as PCB and mercury, as well as nutritive factors, including n-3 PUFA, vary among different fish types. The Japanese diet relies heavily on rice, fish and vegetables. Indeed, the Japanese eat great amounts of many kinds of fish. Regarding fish consumption, there is a report that some polyunsaturated fatty acids ingested from fish, in particular docosapentaenoic acid (DPA), increase birth weight[7].

Another report showed that fish consumption was a major source of mercury exposure for pregnant women, and a relationship between elevated mercury levels and increased risk of very preterm delivery[12]. Although we have found that fish consumption is associated with an increase in birth weight, we have not yet considered the polyunsaturated fatty acids that may be confounders in this analysis. Polyunsaturated fatty acids are provided by seafood and may be beneficial for pregnancy and offspring. Since both polyunsaturated fatty acids and PCBs have the same origin and thus are likely to be correlated, fish and seafood consumption may confound the association between PCBs and birth weight. Further studies will require consideration of the potential risks of fish intake in the context of potential benefits. Since the TSCD study is a prospective cohort study, we will readdress these health issues when the children become older.

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Table 1. Characteristics of the study population in this analysis

Variables	Mean±SD	Range
Birth weight（g）	3100.5±319.7	2506-4176
Mother's age at delivery (years)	31.3±4.4	20-42
Fish consumption (g/year)	23460±16716	0-147278
Body mass index before pregnancy（kg/m^2）	21.0±2.85	16.0-45.0
Gestational age（weeks）	39.7±1.13	37.0-41.9
Total PCB concentration（ng/g-fat）	54.0±33.12	6.37-274.21
Total mercury concentration (ng/g)	11.4±6.24	1.77-43.90

Variables	Number of participants by categories	
Infant gender	Boys: n=225	Girls: n=213
Parity	First: n=233	Second or more: n=205
Smoking status during pregnancy	Nonsmoker: n=396	Smoker/ex-smoker: n=42
Alcohol drinking during pregnancy	No: n=349	Yes: n=88

Table 2. Multiple linear regression results for independent predictors of birth weight in this analysis

Variables	β	Standardized β	p value
Mother's age at delivery	0.001	0.062	0.207
Fish consumption (g/year)	0.011	0.110	0.016
Body mass index before pregnancy (kg/m^2)	0.170	0.199	<0.001
Gestational age (weeks)	0.030	0.330	<0.001
Total PCB concentration（ng/g-fat）	-0.024	-0.126	0.009
Total mercury concentration (ng/g)	-0.017	-0.089	0.051
Infant gender (Boys)	0.014	0.139	0.001
Parity (2nd or more)	0.012	0.058	0.244
Smoking status (nonsmoker)	0.006	0.033	0.461
Alcohol drinking (No)	-0.005	-0.036	0.411