# Effects of Prenatal Exposure to Dioxins and Methyl Mercury on Birth Weight

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**Abstract**
Several studies have demonstrated that background-level exposure to environmental chemicals such as polychlorinated biphenyls (PCBs) and methyl mercury negatively influences births. However, the effects of background-level exposure to dioxins (PCDDs, PCDFs and coplanar-PCBs) in regard to birth outcomes have not been clarified in a human study. This article presents the effects of prenatal exposure to dioxins on birth weight, while also considering methyl mercury exposure effects.
We recruited 514 pregnant women who donated serum specimens and completed a self-administered questionnaire survey. We measured individual isomer levels of dioxins in 270 serum specimens and methyl mercury levels in 430 maternal hair samples.
Birth weights correlated negatively with total PCDF levels in the overall sample of infants ($r$= -0.141; $p$= 0.024) and particularly in the male subjects ($r$= -0.241; $p$= 0.009). Using multiple regression analysis of the association between the levels of dioxins and birth weight, a significant adverse effect was observed regarding total PCDF and total PCDF-TEQ levels. However, we did not find such adverse effects in relation to methyl mercury levels. Moreover, there is a noted difference between boys and girls regarding the effects on birth weight.

**Introduction**
Polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and polychlorinated biphenyls (PCBs) are ubiquitous and highly toxic compounds distributed throughout the environment. Furthermore, they may contribute to numerous adverse health effects including growth retardation of the fetus and infants, neuro-developmental dysfunction, thyroid deficiency, immune deficiency, reproductive effects, and cancer. [1,2] One of the most significant concerns regarding health effects is the potential harmful influence PCBs and PCDD/Fs may have on future generations, stemming from prenatal and/or postnatal exposure.
Dozens of studies concerning low-level (background-level) exposure to these contaminants have been performed since the latter half of the 1980s. However, the findings have not been consistently replicated across studies. As regards births, such as lower birth weight and preterm delivery, the findings have also not been consistent among groups from the general population exposed to background-levels of PCBs and PCDD/Fs. Several studies observed a negative association of PCBs with lower birth weight. In a population-based study from the Netherlands, both umbilical cord and maternal plasma PCB levels were negatively associated with birth weight. They were also significantly associated with lower growth rates from birth to 3 months. [3] On the other hand, the negative associations have not been demonstrated in other studies. A Faeroese study found no significant correlation between PCB exposure and birth weight. [4] A Finnish study reported significant correlation between PCBs and birth weight, but a weak negative correlation between breast milk concentrations of PCDD/Fs and birth weight. [5] In addition, specific differences between the sex of the subjects was demonstrated, with PCB exposure and reduced fetal growth correlations appearing much more conspicuously in boys. [5,6]
The influence of dioxin exposure at birth has not been reported as frequently as PCB exposure at birth. While previous epidemiologic studies have found a relationship between methyl mercury exposure and birth weight, a study concerning the influence of background levels of PCDD/Fs and coplanar-PCBs is much needed.
Taking such matters into account, the aim of the present study was to examine the influence of PCDD/Fs and coplanar-PCBs on the birth weight, while also considering methyl mercury exposure.

## Materials and Methods

We recruited a total of 514 pregnant women between July 2002 and September 2005 from Sapporo Toho Hospital in Hokkaido, Japan.

A 40-ml blood sample was taken from the maternal peripheral vein after the second trimester of their most recent pregnancy. The concentrations of dioxins in the maternal blood sample were measured using a high-resolution gas chromatography/high-resolution mass spectrometer (HRGC/HRMS) equipped with a solvent-cut large-volume injection system. The levels of dioxins were measured in twenty-nine isomers [seven polychlorinated dibenzo-p-dioxins (PCDDs), ten polychlorinated dibenzofurans (PCDFs), four non-ortho PCBs, eight mono-ortho PCBs]. We measured concentration of dioxins in 270 maternal blood samples.

Maternal hair samples were also collected within a week after delivery. The hair samples were analyzed by an oxygen combustion- gold amalgamation method using an atomic absorption detector in order to detect total mercury levels. We measured total mercury levels in 430 maternal hair samples.

A self-administered questionnaire survey provided us with potential confounding variables in relation to past medical histories of both the mothers and their partners. Prenatal medical information of the mothers and their children were collected from their medical records at the hospital. We obtained infant birth weights and gestational ages from the medical records.

Using the questionnaire which was completed at the time of collecting the hair samples, we were able to gather information on the amount and species of fish consumed. We estimated the daily consumption levels of fish by using information provided in the questionnaire. Pearson's correlated 2-taile's test and a multiple linear regression model were used to examine the association between birth weights and the levels of dioxins found in the maternal blood samples. A multiple linear regression model was adjusted for relevant covariates such as predictors of birth weight and other known potential confounders. Statistical analysis was performed using SPSS software version 13.0 J.

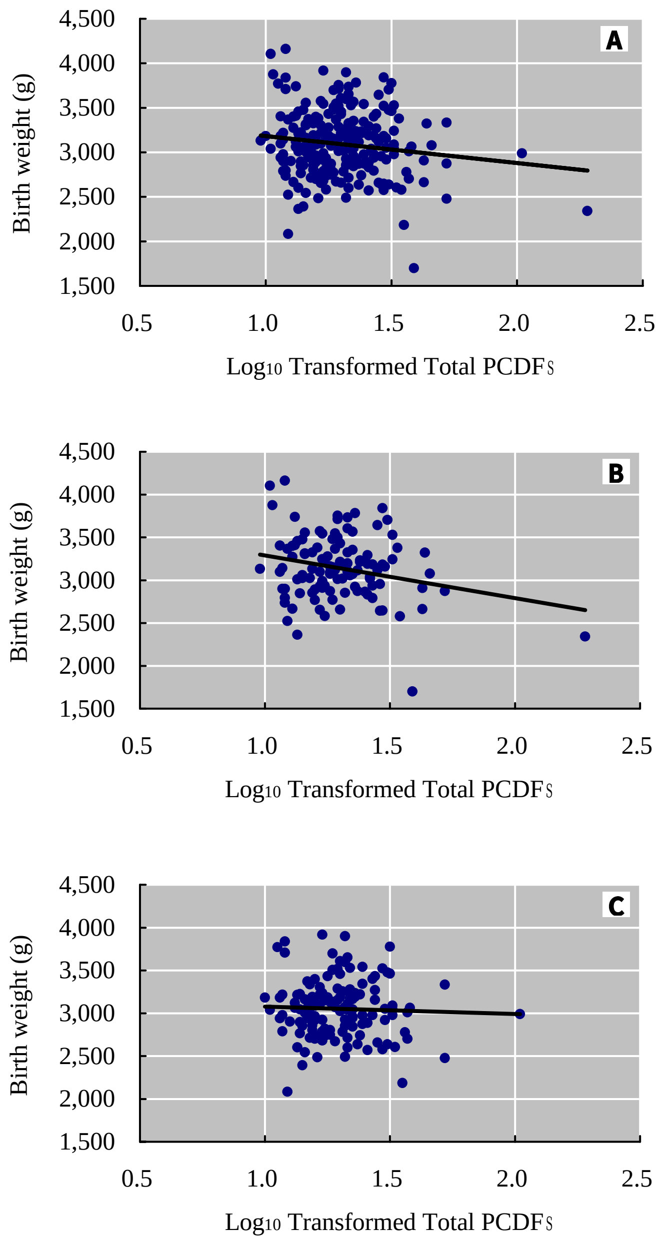


**Figure 1.** Correlation between newborn child's birth weight and Log10 Transformed Total PCDF levels in maternal blood samples. (A) Among all children (slope=-302). (B) Among all male children (slope=-499). (C) Among all female children (slope=-87).

**Results and Discussion**

Using Pearson's correlated 2-taile's test, we examined the relationships between birth weight and both total dioxin and total TEQ levels. We only found a negative correlation between birth weight and total PCDF levels. Birth weights correlated negatively with $\log_{10}$ transformed total PCDF levels of maternal blood among all children ($r$= -0.141; $p$= 0.024; n= 256; Fig. 1A) and among the male infants ($r$= -0.241; $p$= 0.009; n= 117; Fig. 1B), but not among the female infants ($r$= -0.039; $p$= 0.645; n= 139; Fig. 1C).

Table 1 shows the results of multiple regression analysis regarding associations between the level of dioxins and birth weight with adjustments made for gestational age, maternal age, maternal weight at and before pregnancy, parity, smoking during pregnancy, and the sex of the child. Because models were run with dioxins on the $\log_{10}$ scale, a unit of increase would mean a 10-fold increase in the dioxins. Total PCDF (β= -0.153 g; $p<0.01$) and total PCDF TEQ (β= -0.145 g; $p<0.05$) levels were significantly negatively associated with birth weight among all children, with a similar association (Total PCDFs; β= -0.197 g; $p<0.05$) found among boys, but no significant association found among girls. We did not find a negative association between maternal hair mercury levels and birth weight.

In this study, we found a negative correlation between birth weight and Total PCDF levels in the maternal blood samples. Even with multiple linear regression analysis adjusted for relevant covariates, the total PCDF and total PCDF TEQ levels were significantly negatively associated with birth weight among all children and in the boys. The Finnish study reported that no correlation was found between birth weight and breast milk concentrations of ΣPCBs, PCB-TEQs, or individual PCB congeners, but a weak negative correlation was found between birth weight and breast milk concentrations of PCDD/Fs. Moreover, the Finnish study found a negative relation, especially among boys.[5] In the Dutch study, umbilical cord and maternal plasma PCB levels were both negatively associated with birth weight.[3] Except for the differences in the exposure measurement materials, these results were highly consistent with our findings.

In conclusion, our findings support the hypothesis that *in utero* exposure to dioxins affects fetal growth and birth weight. Harmful influences on the fetus should be avoided by reducing maternal exposure to dioxins.

Table 1. Multiple linear regressions for birth weight in relation to dioxins and mercury level

| $log_{10}$ scale | | Overall [a] β | Overall [a] P values | | Boys [b] β | Boys [b] P values | | Girls [b] β | Girls [b] P values |
|---|---|---|---|---|---|---|---|---|---|
| <Total> | (pg/g lipid) | | | | | | | | |
| Total PCDDs | | -0.073 | 0.205 | | -0.075 | 0.376 | | -0.078 | 0.341 |
| Total PCDFs | | -0.153 | 0.009 | ** | -0.197 | 0.023 | * | -0.124 | 0.138 |
| Total PCDDs/PCDFs | | -0.078 | 0.175 | | -0.083 | 0.330 | | -0.081 | 0.324 |
| Total Non-*ortho* PCBs | | -0.047 | 0.443 | | 0.032 | 0.733 | | -0.130 | 0.125 |
| Total Mono-*ortho* PCBs | | -0.036 | 0.571 | | -0.028 | 0.772 | | -0.061 | 0.487 |
| Total Coplanar PCBs | | -0.037 | 0.566 | | -0.028 | 0.774 | | -0.062 | 0.479 |
| Total Dioxins | | -0.041 | 0.515 | | -0.034 | 0.724 | | -0.066 | 0.455 |
| <WHO-98> | (TEQs pg/g lipid) | | | | | | | | |
| Total PCDDs TEQ | | -0.072 | 0.260 | | -0.066 | 0.495 | | -0.084 | 0.348 |
| Total PCDFs TEQ | | -0.145 | 0.018 | * | -0.160 | 0.077 | | -0.146 | 0.095 |
| Total PCDDs/PCDFs TEQ | | -0.105 | 0.100 | | -0.109 | 0.253 | | -0.110 | 0.218 |
| Total Non-*ortho* PCBs TEQ | | -0.041 | 0.503 | | 0.024 | 0.800 | | -0.119 | 0.167 |
| Total Mono-*ortho* PCBs TEQ | | -0.034 | 0.610 | | -0.038 | 0.706 | | -0.044 | 0.632 |
| Total Coplanar PCBs TEQ | | -0.051 | 0.422 | | -0.005 | 0.962 | | -0.109 | 0.215 |
| Total TEQ | | -0.092 | 0.158 | | -0.081 | 0.404 | | -0.114 | 0.207 |
| Maternal hair mercury | (ppm) | 0.045 | 0.284 | | 0.065 | 0.310 | | 0.027 | 0.641 |

Abbreviations:TEQ,toxicity equivalency quantity; WHO,World Health Organization.

[a] Results are calculated as multiple linear regression models adjusted for gestational age, maternal age, maternal weight before pregnancy, parity, smoking during pregnancy, and sex of child.

[b] Results are calculated as multiple linear regression models adjusted for gestational age, maternal age, maternal weight before pregnancy, parity, and smoking during pregnancy.

*p<0.05; **p<0.01.

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