# CHILDHOOD HEALTH AND DEVELOPMENT IN RELATION TO PERSISTENT ORGANOCHLORINE COMPOUNDS

## FETAL AND EARLY CHILDHOOD GROWTH IN RELATION TO PRENATAL PCB AND ORGANOCHLORINE PESTICIDE EXPOSURES

Hertz-Picciotto I,[1] Keller J,[1] Willman E,[2,3] James R,[1] Teplin S,[4] Charles MJ.[2]

[1] University of North Carolina, Chapel Hill, CB#7400, Department of Epidemiology, Chapel Hill, NC 27599-7400
[2] University of California, Davis, Department of Environmental Toxicology, One Shields Ave., Davis, CA 95616
[3] Currently at Barnstead | Thermolyne Corp., Dubuque, IA.
[4] University of North Carolina, Chapel Hill, CB# 7255, Center for Development and Learning and Department of Pediatrics, Chapel Hill, NC 27599-7255

### Introduction

Several studies provide evidence that prenatal exposures to persistent organochlorine pollutants (POPs) may have adverse effects on fetal growth and development. In a cohort of Dutch children whose mothers consumed PCB-contaminated fish, Patandin et al (1) found that higher cord and maternal plasma PCB levels were associated with lower birthweight. In Finland, birthweights for boys were slightly decreased with increasing concentrations of several dioxins and furans, and with TCDD toxic equivalents (2). In a case-control study conducted in Sweden, infants born between 1973 and 1991 with low birthweight were compared with normal birthweight infants; concentrations of PCB #153 in plasma were measured and used to estimate the concentration at the time of the birth (3). Lower birth weight and head circumference were reported to be associated with higher serum PCB levels in infants of mothers who consumed PCB-contaminated fish from Lake Michigan (4).

Given several studies that indicate an adverse effect of PCB or other organochlorine exposure on intrauterine growth, this study investigated birthweight, head circumference, gestational age, and growth to age five years in relation to *in utero* POP exposure among children born 1964-1967 in Northern California.

### Materials and Methods

During the early 1960's, a large cohort of approximately 20,000 pregnant women were enrolled in the Child Health and Development Study (CHDS) through a health maintenance organization (Kaiser Foundation Health Plan Medical Centers). Women were interviewed regarding their reproductive histories, medication use, medical conditions, smoking, alcohol, demographic factors and occupation. An attempt was made to collect sera specimens in each trimester. These were stored at -20°. Subsets of the children from these pregnancies were enrolled in specialized developmental studies.

In this study, 414 children born between April 1964 and April 1967 who participated in a developmental examination at age five years were selected. The goal was to relate concentrations

of PCB congeners and organochlorine pesticides to measures of cognitive development, growth *in utero*, postnatal growth to age five, hearing, speech, vision, and morbidity to age five. We report here the results on intrauterine and postnatal growth.

Children were excluded if they did not complete all components of the developmental examination. Other exclusions were: sera specimen not available for second or third trimester; mother took thyroid medication within 60 days before serum was drawn; mother took iodine-containing drugs during six months before conception or during pregnancy; mother had rubella; mother was congenitally deaf; child was a twin; or child had severe anomalies.

One serum specimen collected in the second or third trimester for each pregnancy was shipped to the laboratory of Dr. M. Judith Charles at the University of California, Davis for analysis using GC/ECD. In each batch, one specimen was split and analyzed in duplicate. Individual PCB standards and organochlorine pesticide and herbicide standards were purchased from ChemService, Ultra Scientific, and Cambridge Isotopes. Calibration standards were prepared by serially diluting a stock solution which contained all of the organochlorine standards except PCB 204, the internal standard, and PCB 66 and PCB 165, the surrogate standards. Extraction was carried out with hexane and a florisil column. Analysis was performed by gas chromatography with electron capture detection (GC/ECD) (Hewlett-Packard 6890 Series) in parallel using an RTX-5MS and an RTX-1701 column to resolve co-elution problems. Based on the limits of quantitation with the volume of sera we had available, we focussed on analyses for PCBs #118, 138, 153, 170, 180, and 187; and for 2,4-DDE, 4,4-DDE, and 4,4-DDT. We also evaluated results for total PCBs, based on the above congeners. Lipids, namely cholesterol and triglycerides, were measured by the enzymatic method.

Birthweight, birth length, gestational age, and head circumference were recorded at the time of delivery. At age five years, standing and sitting height and head circumference were measured to the $16^{th}$ of an inch; other measurements of growth were measured with the Harpenden digital anthropometer, and recorded in millimeters, including: standing height, sitting height, bi-iliac distance, bi-acromial distance, head circumference, and chest depth. Sex- and age-specific growth curves were used to obtain standardized height measures.

Multiple linear regression was used to examine the associations between POPs and these early growth parameters. Potential confounding variables included in all models were: maternal age, smoking, alcohol, maternal and paternal height, pre-pregnancy maternal body mass index, race, parity and sex of the child. In models predicting birthweight, gestational age at delivery was included. All models were adjusted for total lipids and for batch. Bivariate models stratified by sex indicated that males appeared to be more sensitive to POPs than females. Therefore, an interaction of each organochlorine by sex was included in all models.

## Results

Table 1 shows characteristics of this study sample. Approximately half the sample was non-white, 30% were nulliparous and 31% smoked. Only 46% of the children were male.

Table 1: Characteristics of the 414 mother/child pairs in this study.

| | Mean or percent | $10^{th}$ – $90^{th}$ percentile |
|---|---|---|
| Maternal age at delivery (years) | 27.4 | 20-36 |
| Birthweight (grams) | 3300 | 2722-3827 |
| Head circumference at birth (cm) | 34.0 | 31.8-35.6 |
| Height at 5 years (cms) | 110 | 104-117 |
| Race (% nonwhite) | 50.7% | |
| Parity (% nulliparous) | 30.0% | |
| Smoking (% current) | 31.0% | |
| Alcohol | | |
| % who drank 1-4 times/week | 40.8% | |
| % who drank 5+ times/week | 10.6% | |
| Sex of child (% male) | 46.4% | |

Table 2 presents medians, and $10^{th}$ and $90^{th}$ percentiles for selected POPs. The concentrations are in ng/kg wet weight. Pesticide concentrations are far higher than those reported in current Western populations, whereas PCB concentrations are similar to or slightly higher than those currently being reported in most Western populations.

Table 2: Univariate statistics for selected PCB congeners

| PCB | median | $10^{th}$ – $90^{th}$ percentile |
|---|---|---|
| #118 | .61 | .36-1.07 |
| #138 | .85 | .52-1.55 |
| #153 | 1.06 | .65-1.85 |
| #170 | .23 | .13-.44 |
| #180 | .53 | .31-.90 |
| #187 | .23 | .12-.45 |

Table 3 displays regression coefficients, standard errors, and p-values for selected POP's in relation to selected growth parameters, after adjustment for factors such as maternal smoking, alcohol consumption, maternal and paternal height, maternal pre-pregnancy BMI, race, maternal age, and parity. (In models for birthweight, gestational age was also included.) There is an inverse association between total PCB's and both birthweight and birth length in males, but not in females. A similar association was seen for head circumference at birth. For a few organochlorines, associations were observed with deficits in growth at age five, e.g., 2,4-DDT and chest depth; again, these associations are seen for boys only. Shorter gestational age at delivery for male births is also associated with increased PCB concentrations. These results confirm previous reports suggesting that prenatal exposure to POPs is associated with reduced fetal growth, particularly in males. They also provide the most detailed data to date on growth to age five in a population with background environmental levels common 30 years ago in the U.S.

Table 3: Results of multiple linear regression models

| Outcome: | Organochlorine(s) | β | SE(β) | p-value |
|---|---|---|---|---|
| Birthweight | Total PCBs | -36.5 | 19.3 | .06 |
| | PCB #180 | -237.3 | 135.2 | .08 |
| | 2,4-DDT | -60.5 | 31.2 | .05 |
| Birth length | Total PCBs | -.36 | .12 | .002 |
| | PCB #153 | -.70 | .43 | .10 |
| | PCB #180 | -1.9 | .84 | .03 |
| Head circumference (birth) | Total PCBs | -.13 | .07 | .07 |
| | #138 | -.57 | .31 | .06 |
| | #180 | -1.0 | .50 | .05 |
| Gestational age | Total PCBs | -1.2 | .65 | .06 |
| | PCB #153 | -4.1 | 2.3 | .08 |
| Chest depth, age 5 | Total PCBs | -.89 | .52 | .09 |
| | 2,4-DDT | -1.9 | .87 | .03 |
| Bi-iliac distance, age 5 | PCB #118 | -5.9 | 3.0 | .05 |
| Head circumference, age 5 | PCB #138 | -.72 | .31 | .02 |

**References**

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