# INTELLECTUAL IMPAIRMENT IN CHILDREN EXPOSED TO POLYCHLORINATED BIPHENYLS IN UTERO

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## ABSTRACT

*Background* In utero exposure to polychlorinated biphenyls, a ubiquitous environmental contaminant, has been linked to adverse effects on neurologic and intellectual function in infants and young children. We assessed whether these effects persist through school age and examined their importance in the acquisition of reading and arithmetic skills.

*Methods* We tested 212 children, recruited as newborns to overrepresent infants born to women who had eaten Lake Michigan fish contaminated with polychlorinated biphenyls. A battery of IQ and achievement tests was administered when the children were 11 years of age. Concentrations of polychlorinated biphenyls in maternal serum and milk at delivery were slightly higher than in the general population. A composite measure of prenatal exposure was derived from concentrations in umbilical-cord serum and maternal serum and milk.

*Results* Prenatal exposure to polychlorinated biphenyls was associated with lower full-scale and verbal IQ scores after control for potential confounding variables such as socioeconomic status (P=0.02). The strongest effects related to memory and attention. The most highly exposed children were three times as likely to have low average IQ scores (P<0.001) and twice as likely to be at least two years behind in reading comprehension (P=0.03). Although larger quantities of polychlorinated biphenyls are transferred by breast-feeding than in utero, there were deficits only in association with transplacental exposure, suggesting that the developing fetal brain is particularly sensitive to these compounds.

*Conclusions* In utero exposure to polychlorinated biphenyls in concentrations slightly higher than those in the general population can have a long-term impact on intellectual function. (N Engl J Med 1996; 335:783-9.)

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POLYCHLORINATED biphenyls — synthetic hydrocarbon compounds once used as insulating materials in electrical transformers and capacitors — are among the most ubiquitous and persistent environmental contaminants.[1,2] Although these lipophilic compounds have been banned in the United States and most Western nations since the 1970s, their residues persist and can be detected in the tissues of most residents of industrialized countries.[3] Consumption of fatty sports fish from contaminated waters is a major source of human exposure.

Two prospective studies — one in Michigan,[4] the other in North Carolina[5] — have linked in utero exposure to polychlorinated biphenyls to adverse effects on neural development in children. The North Carolina sample was drawn from the general population; our Michigan sample overrepresented children whose mothers had eaten Lake Michigan fish contaminated with polychlorinated biphenyls. In North Carolina, the infants had neurologic anomalies at birth[6] and developmental delays in gross motor function during infancy.[7] In Michigan, we found deficits in fetal and postnatal growth[8,9] and poorer short-term memory in infancy[10] and at four years of age.[4] These findings have been corroborated in laboratory animals[11,12] and in prospective studies of more highly exposed Taiwanese children born to women who consumed rice oil contaminated with polychlorinated biphenyls and dibenzofurans.[13,14]

We conducted the present study to determine whether the deficits in infancy and early childhood associated with environmental exposure to polychlorinated biphenyls persist through school age and to examine their importance in the acquisition of reading and arithmetic skills.

## METHODS

### Subjects

We examined 212 children, 68 percent of the 313 newborns studied in 1980–1981, when 8482 women giving birth to infants in four hospitals in western Michigan were surveyed regarding their consumption of Lake Michigan fish.[4] Each species of fish was weighted according to degree of contamination with polychlorinated biphenyls on the basis of data provided by the Environmental Protection Agency. At that time, the 339 women who had eaten the equivalent of at least 11.8 kg of Lake Michigan salmon or lake trout during the preceding six-year period were invited to participate in the neonatal assessment phase of the study, as were 113 women who had not eaten Lake Michigan fish; 313 agreed. The characteristics and exposure levels of the 212 children who participated in the 11-year assessment are shown in Table 1. One hundred sixty-seven of these children were delivered of mothers who had eaten Lake Michigan fish. The participants were similar to those lost to follow-up with respect to maternal consumption of Lake Michigan fish, duration of breast-feeding, and postnatal exposure to polychlorinated biphenyls but were somewhat higher in prenatal exposure, socioeconomic status, and maternal age and education.

TABLE 1. CHARACTERISTICS OF THE CHILDREN IN THE STUDY.

| CHARACTERISTIC | VALUE* | NO. OF CHILDREN ASSESSED | CHARACTERISTIC | VALUE* | NO. OF CHILDREN ASSESSED |
|---|---|---|---|---|---|
| Demographic background | | | Exposure to polychlorinated biphenyls | | |
| Socioeconomic status — no. (%)†‡ | | 212 | Cord serum — ng/ml | 3±2 | 139 |
| Executive or professional | 31 (15) | | Maternal serum — ng/ml | 6±4 | 142 |
| Middle management or semiprofessional | 88 (42) | | Maternal milk — ng/g of fat | 841±386 | 113 |
| Skilled workers, clerical, or sales | 59 (28) | | Serum at 4 years — ng/ml | 2±3 | 179 |
| Semiskilled workers | 32 (15) | | Serum at 11 years — ng/ml | 1±1 | 156 |
| Unskilled workers | 2 (1) | | Exposure to other substances | | |
| Maternal age at child's birth — yr† | 27±5 | 212 | Maternal drinking before pregnancy†§§ | 0±0 | 212 |
| Marital status — no. with married parents (%)† | 181 (85) | 212 | Maternal drinking during pregnancy†§§ | 0±0 | 212 |
| Sex — no. (%)† | | 212 | Maternal smoking before pregnancy†¶¶ | 0±1 | 212 |
| Male | 111 (52) | | Maternal smoking during pregnancy†¶¶ | 0±1 | 212 |
| Female | 101 (48) | | Polybrominated biphenyls | | |
| Parity of mother†§ | 2±1 | 212 | Cord serum — ng/ml | 0±1 | 195 |
| No. of children currently in household† | 3±1 | 212 | Maternal serum — ng/ml | 3±4 | 132 |
| Maternal education — yr† | 14±2 | 212 | Maternal milk — ng/g of fat | 218±325 | 113 |
| Maternal Peabody Vocabulary Test score† | 100±15 | 212 | Serum at 4 years — ng/ml | 0±1 | 179 |
| HOME Inventory†¶ | 48±4 | 212 | Serum at 11 years — ng/ml | 0±0 | 155 |
| Familial stress‖ | | | DDT | | |
| Past year† | 4±2 | 212 | Serum at 4 years — ng/ml | 3±4 | 176 |
| Past five years† | 4±2 | 212 | Serum at 11 years — ng/ml | 1±1 | 155 |
| School-district quality** | | | Lead‖‖ | | |
| Reading | 39±12 | 171 | Blood at 4 years — μg/dl | 6±3 | 168 |
| Mathematics | 65±6 | 171 | Blood at 11 years — μg/dl | 2±1 | 155 |
| Age at testing — yr† | 11±0 | 212 | Mercury in hair at 11 years — μg/g†§*** | 1±1 | 212 |
| Grade in school† | 6±1 | 212 | | | |
| Prenatal influences | | | | | |
| Gravidity of mother | 2±3 | 212 | | | |
| Maternal consumption of contaminated fish — kg†† | 5±5 | 212 | | | |
| Delivery complications — no. (%)†‡‡ | 48 (23) | 212 | | | |
| Duration of breast-feeding — wk | 23±29 | 212 | | | |

*Plus–minus values are means ±SD.

†This characteristic was assessed for possible inclusion as a control variable in each multivariate analysis.

‡Socioeconomic status was assigned according to the system described by A.B. Hollingshead in his 1975 unpublished paper "Four-Factor Index of Social Status" (available from the authors). This characteristic was entered as a continuous variable in the multivariate analyses.

§We transformed the data for this variable by recoding the single value more than 3 SD above the mean to one point greater than the highest observed value, as recommended by Winer.[16]

¶HOME denotes Home Observation for Measurement of the Environment; it was administered at four years of age. This score was estimated by multiple regression analysis for nine children on the basis of the fathers' education, maternal vocabulary scores, number of children in the households, and mothers' ages.

‖Values are the highest levels of stress reported on a six-point scale in any of four domains: financial, health, marital, or other.

**School-district quality was assessed for all children attending public school through the Michigan Educational Assessment Program Tests administered at the end of the fourth grade. The reading score reflects the percentage of children in each child's school district receiving a satisfactory score on all of the reading selections tested. The mathematics score reflects the median for each child's school district.

††Values are the average annual consumption of Lake Michigan fish during or before pregnancy, whichever was greater, in which each fish species was weighted to reflect its degree of contamination with polychlorinated biphenyls.

‡‡This variable was defined as the occurrence of any of the following delivery complications associated with potential damage to the central nervous system: emergency cesarean section, labor longer than 20 hours, placenta previa or abruptio placentae, toxemia, cyanosis, fetal distress, meconium staining, infected cord, or knot in cord.

§§Values are the numbers of ounces of absolute alcohol per day estimated by the method of Kuzma and Kissinger.[16] Only three mothers drank heavily (≥1.0 oz) before pregnancy; during pregnancy none drank heavily, and only five drank even at moderate levels (≥0.5 oz). To convert values for alcohol to milliliters, multiply by 30.

¶¶Values are the numbers of packs per day; 36.8 percent of the mothers smoked before pregnancy, and 27.8 percent during pregnancy.

‖To convert values for lead to micromoles per liter, multiply by 0.048.

***Mercury concentrations were estimated for nine children on the basis of the average value for this sample. To convert values for mercury to micromoles per gram, multiply by 0.005.

## Measures of Exposure

We obtained umbilical-cord and maternal blood samples shortly after delivery, maternal milk samples within 0.2 to 4.5 months post partum (median, 1 month), and blood samples from the children at 4 and 11 years of age. Serum and milk samples were analyzed soon after collection for polychlorinated biphenyls by packed-column gas chromatography; the Webb–McCall method[17] was adapted to a computer data system with Aroclors 1016 and 1260 as reference standards.[18] All samples were also analyzed for polybrominated biphenyls, and those obtained when the children were 4 and 11 years of age were analyzed for seven organochlorine pesticides — dichlorodiphenyl trichloroethane (DDT), hexachlorobenzene, beta-hexachlorobenzene, oxychlordane, heptachlor epoxide, trans-nonachlor, and Mirex, among which only DDT was detected. Blood lead was measured at 4 and 11 years of age by atomic absorption spectrophotometry with the use of the Delves cup method. These analyses and measurements were performed by the Center for Environmental Health Sciences of the Michigan Department of Public Health. Quality control was maintained by interlaboratory comparison with the use of protocols established by the Centers for Disease Control and Prevention and the Environmental Protection Agency. In addition, when the children were 11 years of age, hair samples were analyzed for mercury by cold-vapor atomic absorption spectrometry by the University of Rochester Environmental Health Services Center, Rochester, New York. The detection limit for polychlorinated biphenyls was 3.0 ng per milliliter; DDT, 2.0 ng per milliliter; polybrominated biphenyls and the other pesticides, 1.0 ng per milliliter; lead, 2.0 μg per deciliter (0.1 μmol per liter); and mercury, $5 \times 10^{-4}$ μg per gram ($2.5 \times 10^{-6}$ μmol per gram).

Because of limitations in the Webb–McCall method available during the early 1980s, polychlorinated biphenyls were not detectable in 70 percent of the cord-serum samples and 22 percent of the maternal serum samples. Because placental transfer provides the sole route of fetal exposure to these compounds, which are in equilibrium in fat deposits throughout the body, maternal serum and milk concentrations provide alternatives to cord serum for evaluating prenatal exposure.[5] To improve reliability and sensitivity in the assessment of fetal exposure, the values for cord serum and maternal serum and milk were converted to z scores and averaged together; serum values were included only if they exceeded the detection limit.[19] For 11 children, no milk specimen was available and values for cord serum and maternal serum were both undetectable; these children were assigned a prenatal-exposure score at the 10th percentile of the distribution. The composite prenatal-exposure scores were divided into five groups for dose-response analysis based on the a priori cutoff points used in our four-year follow-up study for the polychlorinated biphenyl concentration per gram of fat in milk: <0.50 μg, 0.50 to 0.74 μg, 0.75 to 0.99 μg, 1.00 to 1.24 μg, and >1.25 μg.[4]

## Cognitive Assessments

Each child was tested individually at home at a mean (±SD) age of 11.0±0.2 years with the revised Wechsler Intelligence Scales for Children IQ test, the spelling and arithmetic subtests of the Wide Range Achievement Test — Revised, and the word- and passage-comprehension subtests of the Woodcock Reading Mastery Tests — Revised. Reading comprehension was computed as the average of the scores for word and passage comprehension. None of the eight examiners were aware of the children's exposure histories or any of the biochemical values. The interobserver reliability in recording the children's response times (r) ranged from 0.98 to 1.00.

Descriptive statistics for the cognitive outcomes are shown in Table 2. Although all test scores were normalized to a mean (±SD) value of 100±15, the population mean for the Wechsler IQ test had risen to 108 since its most recent standardization in 1974.[20] One highly exposed child with an IQ of 63, who had been given a diagnosis of mental retardation, was excluded from the statistical analysis to avert undue influence of extreme scores. Factor

| TEST | SCORE* | NO. OF CHILDREN TESTED† |
|---|---|---|
| Wechsler Intelligence Scales for Children — Revised | | |
| Full-scale IQ | 107±12 | 211 |
| Verbal IQ | 106±13 | 211 |
| Performance IQ | 107±13 | 211 |
| Verbal comprehension | 11±2 | 211 |
| Perceptual organization | 11±2 | 211 |
| Freedom from distractibility | 10±2 | 211 |
| Wide Range Achievement Test — Revised | | |
| Spelling | 99±14 | 209 |
| Arithmetic | 97±16 | 209 |
| Woodcock Reading Mastery Test — Revised | | |
| Word comprehension | 100±12 | 210 |
| Passage comprehension | 98±14 | 210 |
| Reading comprehension | 98±13 | 210 |

*Scores are given as means ±SD.

†Data for one child with a very low IQ score were excluded.

analysis of the 12 IQ subtests suggested three summary scales similar to those derived by Kaufman[21]: verbal comprehension — the average of the information, similarities, arithmetic, vocabulary, and comprehension subtests; perceptual organization — the average of the picture-completion, picture-arrangement, block-design, and object-assembly subtests; and freedom from distractibility — the average of the digit-span, coding, and mazes subtests.

## Control Variables

Twenty-four control variables were evaluated in this study: the 19 variables indicated by daggers in Table 1, the identity of the examiner, and four composite measures of exposure to other environmental contaminants. A composite prenatal score for exposure to polybrominated biphenyls was constructed by averaging z scores for the cord-serum and maternal serum and milk values. Composite postnatal scores for exposure to polybrominated biphenyls, DDT, and lead were constructed by averaging the z scores for the values at 4 and 11 years of age. Each child's grade level was used as a control variable in analyses of the achievement and reading scores but not in analyses of IQ-test performance because IQ is more likely to influence grade-level placement than the reverse. Log (x + 1) transformation was performed on the following highly skewed variables (skew, >3.0) to reduce the influence of outliers: serum polychlorinated biphenyl concentration when the children were 11 years of age; maternal consumption of alcohol before and during pregnancy; and the two composite scores for exposure to polybrominated biphenyls.

## Statistical Analysis

Correlation analysis was used to determine which control variables to include in multivariate analyses to control for confounding. Since a control variable cannot cause an observed deficit unless it is related to both exposure and outcome,[22] association with either exposure or outcome can be used as the criterion for inclusion. In this study, we selected control variables in relation to outcome, which has the additional advantage of increasing precision by also including covariates unrelated to exposure.[23] Each cognitive outcome was evaluated in four hierarchical regression analyses: one for prenatal exposure to polychlorinated biphenyls and three for postnatal exposure. One analysis of postnatal expo-

| TEST | No. TESTED | r | $\beta^*$ | P VALUE |
|---|---|---|---|---|
| Wechsler Intelligence Scales for Children — Revised | | | | |
| Full-scale IQ | 178 | -0.16 | -0.17 | 0.02 |
| Verbal IQ† | 178 | -0.15 | -0.16 | 0.02 |
| Performance IQ‡ | 178 | -0.14 | -0.13 | 0.08 |
| Verbal comprehension† | 178 | -0.15 | -0.16 | 0.02 |
| Perceptual organization§ | 178 | -0.12 | -0.11 | 0.13 |
| Freedom from distractibility¶ | 178 | -0.17 | -0.17 | 0.02 |
| Wide Range Achievement Test — Revised | | | | |
| Spelling‖ | 176 | -0.06 | -0.07 | 0.26 |
| Arithmetic** | 176 | -0.01 | -0.04 | 0.56 |
| Woodcock Reading Mastery Tests — Revised | | | | |
| Word comprehension†† | 177 | -0.18 | -0.17 | 0.01 |
| Passage comprehension‡‡ | 177 | -0.11 | -0.09 | 0.20 |
| Reading comprehension‡‡ | 177 | -0.14 | -0.13 | 0.06 |

*$\beta$ is the standardized regression coefficient for prenatal exposure to polychlorinated biphenyls from a multiple regression analysis. All the regressions controlled for socioeconomic status, maternal education and vocabulary, and the Home Observation for Measurement of the Environment (HOME) Inventory. In addition, we controlled for the covariates listed in the following footnotes.

†The additional covariates were maternal marital status and smoking during pregnancy.

‡The additional covariates were number of children in the household, delivery complications, and prenatal exposure to polybrominated biphenyls.

§The additional covariate was number of children in the household.

¶The additional covariates were number of children in the household, child's sex, and exposure to mercury.

‖The additional covariates were child's sex and grade, drinking during pregnancy, smoking during pregnancy, and exposure to mercury.

**The additional covariates were maternal age, child's age and grade, drinking and smoking during pregnancy, and prenatal exposure to polybrominated biphenyls.

††The additional covariates were parity, child's sex and grade, and drinking and smoking during pregnancy.

‡‡The additional covariates were parity, stress within past year, child's sex and grade, drinking and smoking during pregnancy, and exposure to mercury.

sure was based on the polychlorinated biphenyl concentration in milk and the number of weeks of breast-feeding, one on the serum polychlorinated biphenyl concentration at 4 years of age, and one on the concentration at 11 years of age. All control variables even weakly related to the outcome in question (P<0.20) were entered at the first step of each regression, and the exposure measure or measures at the second step. A toxic effect was inferred only when the relation to exposure was significant (P<0.05) after adjustment for the effects of the potential confounding variables.

## RESULTS

### Exposure to Polychlorinated Biphenyls

Maternal body burdens of polychlorinated biphenyls (Table 1) were similar to or slightly above general population levels in the United States. The children who were breast-fed for extended periods accumulated substantial body burdens, and at four years of age many had serum concentrations similar

to those of their mothers.[24] By the age of 11, the serum concentrations had declined substantially (P<0.001), suggesting that there was little additional exposure after weaning.

### Effects of Prenatal Exposure to Polychlorinated Biphenyls

Prenatal exposure to polychlorinated biphenyls was associated with significantly lower full-scale and verbal IQ scores (Table 3). An analysis of covariance (Fig. 1) indicated that the effect was primarily in the most highly exposed children — that is, those with prenatal exposures equivalent to at least 1.25 μg per gram in maternal milk, 4.7 ng per milliliter in cord serum, or 9.7 ng per milliliter in maternal serum. The IQ scores of the most highly exposed group averaged 6.2 points lower than those of the other four groups, after adjustment for potential confounding variables (P = 0.007). The pattern of group differences in verbal and performance IQ resembled that shown for full-scale IQ in Figure 1.

In terms of the IQ summary scales derived from the factor analysis, prenatal exposure to polychlorinated biphenyls was associated with poorer verbal comprehension and freedom from distractibility (Table 3). Within the verbal-comprehension scale, exposure had the greatest effect on scores for the vocabulary, information, and similarities subtests, which are considered the strongest indicators of general intellectual ability.[25] Vocabulary and information scores also reflect long-term memory, and similarities scores the formation of verbal concepts. Within the freedom-from-distractibility scale, prenatal exposure was associated with poorer scores on the coding and mazes subtests, both of which assess focused attention. In addition, the coding subtest assesses short-term memory,[26] and the mazes subtest assesses executive function, a component of attention involving the organization, planning, and execution of appropriate responses.[26]

On the academic achievement tests, prenatal exposure to polychlorinated biphenyls was associated with poorer word comprehension and overall reading comprehension (Table 3). Exposure was associated with poorer performance on all three word-comprehension subtests: antonyms (P = 0.005), synonyms (P = 0.05), and analogies (P = 0.03). These effects were largest in the children in the two groups with the highest exposures (Fig. 1) — that is, those born to mothers with milk concentrations of polychlorinated biphenyls of at least 1.00 μg per gram of fat. In terms of age-equivalent norms, the more highly exposed children lagged behind their peers in word comprehension by an average of 7.2 months. The mean (±SD) age-equivalent level of word comprehension of the two groups with the highest exposures was 11.1±1.7 years, after adjustment for confounding variables, as compared with 11.7±1.7 years for the others (P = 0.02).

**Prenatal Exposure to Polychlorinated Biphenyls (μg/g of fat)**

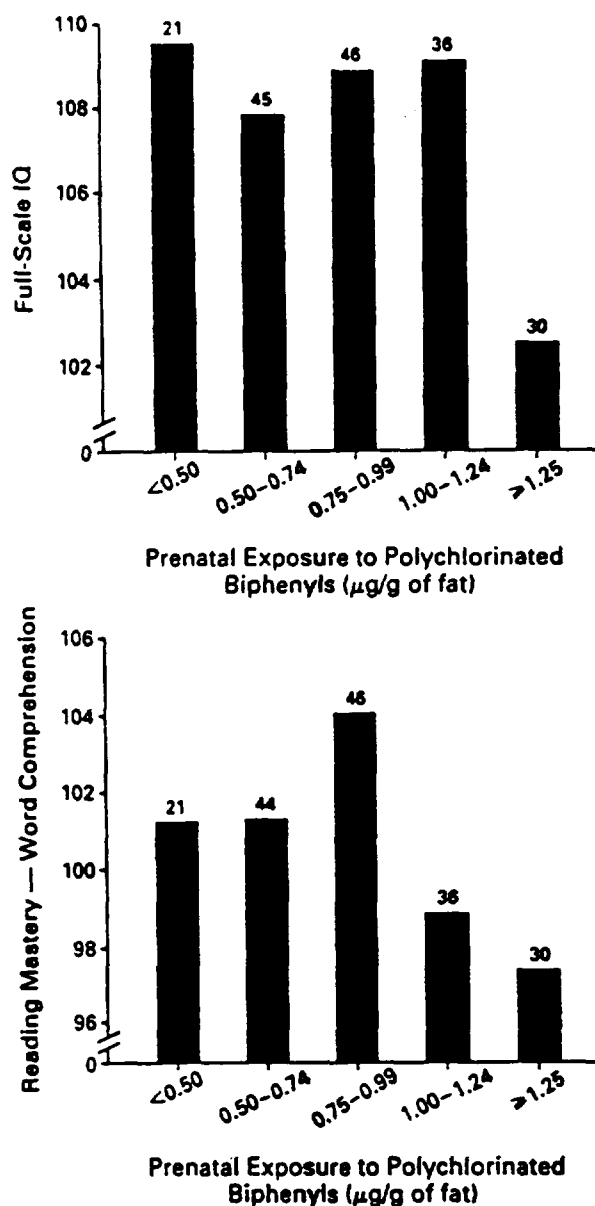**Prenatal Exposure to Polychlorinated Biphenyls (μg/g of fat)**

**Figure 1.** Scores for Full-Scale IQ Tests and Word Comprehension in Reading According to Prenatal Exposure to Polychlorinated Biphenyls (Expressed in Terms of the Fat Concentration of Maternal Milk).

Scores were adjusted for the potential confounding variables listed in the footnotes to Table 3. The number of children in each group is given above the bars. One child was not tested for reading mastery.

Confounding by reading and mathematics scores for each school district and by the composite scores for postnatal exposure to polychlorinated biphenyls, DDT, and lead was evaluated in separate regression analyses of the subsamples for which these scores were available. Up to three additional regressions were run

for each developmental outcome: one for school-district scores (139 children); one for postnatal exposure to polychlorinated biphenyls and DDT (164 children); and one for lead exposure (162 children). All the cognitive outcomes that related significantly to prenatal exposure to polychlorinated biphenyls in Table 3 also related to it significantly in these additional regression analyses. Among the other environmental contaminants assessed, only lead and mercury related significantly to poorer outcome after we controlled for confounding variables. A higher lead concentration when the children were four years of age was associated with lower verbal IQ scores ($P = 0.04$) and verbal-comprehension scores ($P = 0.04$) and poorer word ($P = 0.04$), passage ($P = 0.05$), and reading ($P = 0.03$) comprehension; these effects were evident primarily in children with blood lead concentrations of at least 10 μg per deciliter (0.48 μmol per liter).[27] A higher mercury concentration at 11 years of age was associated with poorer spelling ($P = 0.006$).

### Effects of Postnatal Exposure to Polychlorinated Biphenyls

Exposure during breast-feeding, assessed in analyses based on polychlorinated biphenyl concentrations in milk and the number of weeks of nursing, was not associated with a poorer performance on any of the tests listed in Table 3. The serum concentration of polychlorinated biphenyls at four years of age was related to a lower freedom-from-distractibility score after control for confounding variables ($P = 0.02$), but this effect was apparently spurious, because when both prenatal exposure and four-year serum concentration were included in the analysis, only the prenatal effect remained significant ($P = 0.02$). The serum concentration of polychlorinated biphenyls at four years was also related to poorer performance on the arithmetic achievement test ($P = 0.05$), but that effect was not significant ($P = 0.41$) when prenatal exposure was included in the analysis. The serum concentration of polychlorinated biphenyls at 11 years of age was not related to any of the IQ or achievement measures.

### Functional Importance

The functional importance of the deficits was examined in terms of the incidence of poor performance, defined as a score more than 1 SD below the mean for IQ and at least two years behind age-based norms for reading mastery. On the basis of these criteria, the most highly exposed children were more than three times as likely to perform poorly in terms of the scores for full-scale IQ, verbal comprehension, and freedom from distractibility and more than twice as likely to be at least two years behind in word comprehension in reading (Table 4).

### DISCUSSION

Our results indicate that in utero exposure to polychlorinated biphenyls and related contaminants

| TEST | PRENATAL EXPOSURE† | | P VALUE‡ |
|---|---|---|---|
| | <1.25 µg/g OF FAT (N = 148)§ | ≥1.25 µg/g OF FAT (N = 30) | |
| | no. with poor performance (%) | | |
| Full-scale IQ | 17 (11) | 12 (40) | <0.001 |
| Verbal comprehension | 16 (11) | 12 (40) | <0.001 |
| Freedom from distractibility | 18 (12) | 11 (37) | <0.001 |
| Reading mastery — word comprehension | 14 (10) | 7 (23) | 0.03 |

*Values are the numbers of children at each exposure level meeting the criterion for poor performance after adjustment for potential confounding variables. Poor performance was defined as a value >1 SD below the sample mean for the IQ measures and at least two years behind same-age peers for word comprehension in reading.

†Prenatal exposure is expressed in terms of the equivalent concentration of polychlorinated biphenyls in maternal milk.

‡P values were derived from a two-by-two (performance by exposure) contingency-table analysis.

§Only 147 children were assessed for word comprehension in reading.

is associated with poorer intellectual function in school-age children. These findings confirm our earlier reports linking fetal exposure to poorer short-term memory during infancy[10] and early childhood[4] and are consistent with reports of reduced IQ scores in Taiwanese children whose mothers had ingested rice oil contaminated with polychlorinated biphenyls and dibenzofurans.[14] Our IQ results indicate deficits in general intellectual ability, short-term and long-term memory, and focused and sustained attention. The 6.2-point deficit in IQ in the most highly exposed children is similar to that reported for low-level exposure to lead (1 to 30 µg per deciliter [0.048 to 1.45 µmol per liter]).[27,28] There was no evidence of gross intellectual impairment among the children we studied. Only one child was mentally retarded, and none were in the mildly retarded range (IQ score of 70 to 80), after adjustment for confounding. Nevertheless, there was a substantial increase in the proportion of children at the lower end of the normal range (Table 4), who would be expected to function more poorly in school. This intellectual deficit seemed to interfere particularly with reading mastery. Eight of the 12 highly exposed children with low IQ scores were at least one year behind their peers in word or reading comprehension, and all but 1 were at least six months behind.

Although much larger quantities of polychlorinated biphenyls are transferred postnatally through lactation than in utero, intellectual impairment occurred only in relation to transplacental exposure, a pattern consistent with previous findings in both

Michigan[4,10] and North Carolina[7] and in studies of laboratory animals.[13] The mechanism responsible for this heightened intrauterine vulnerability is not known; however, migratory cells and cells undergoing mitosis are particularly sensitive to toxic insult.[29] In utero exposure to polychlorinated biphenyls has been linked to reduced serum concentrations of thyroid hormones,[30] which are needed to stimulate neuronal and glial proliferation and differentiation.[31] The fetus also lacks important capacities for drug detoxification that are found postnatally,[32] and incomplete development of the blood–brain barrier further increases fetal vulnerability to central nervous system insult.[33]

These deficits are not attributable to maternal drinking or smoking during pregnancy, the quality of intellectual stimulation by parents, postnatal exposure to lead, or numerous other control variables. However, environmental exposure to polychlorinated biphenyls typically also entails exposure to polychlorinated dibenzofurans and dibenzo-p-dioxins, highly toxic byproducts of the manufacture and combustion of polychlorinated biphenyls that accumulate with them in fish and human tissue but are present only in trace concentrations and could not be measured. Moreover, polychlorinated biphenyls are complex mixtures of various congeners, each with its own unique molecular structure and potentially different toxic effects, which could not be identified by the analytic methods available for this study.

The implications of these findings are not limited to the offspring of women who eat fish from Lake Michigan. Women who eat no fish may accumulate these compounds from other food sources, including dairy products, such as cheese and butter, and fatty meats, particularly beef and pork.[34] Unlike exposure to lead or illicit drugs, which occurs predominantly in economically disadvantaged families, prenatal exposure to polychlorinated biphenyls is unrelated to socioeconomic status. Although in the United States environmental concentrations of these contaminants have declined in recent years, the risk of exposure from toxic industrial waste continues because the amount in use in older electrical equipment and in landfills exceeds the total quantity that has escaped into the environment to date.[2]

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