Effects of Polychlorinated Biphenyl/Dioxin Exposure and Feeding Type on Infants' Mental and Psychomotor Development

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ABSTRACT. **Objective.** To evaluate the effects of in utero and lactational exposure to polychlorinated biphenyls (PCBs) and dioxins on the mental and psychomotor development of infants.

**Design.** Prenatal PCB exposure was estimated from the levels in maternal plasma during the last month of pregnancy. Postnatal PCB and dioxin exposure of breastfed infants was calculated from levels in human milk samples and the duration of breastfeeding. Infants were examined at 3, 7, and 18 months of age with the Bayley Scales of Infant Development.

**Setting.** General community.

**Participants.** Voluntary sample of 207 mother-infant pairs. One hundred five infants were breastfed and 102 were bottle-fed.

**Interventions.** None.

**Results.** Higher in utero exposure to PCBs was associated with lower psychomotor scores at 3 months of age: a doubling of the PCB load resulted in a decrease of 3 points. Breastfed infants scored significantly higher on the psychomotor score at 7 months of age, compared with formula-fed infants. However, when corrected for confounders, the psychomotor score of the 66% highest-exposed breastfed infants (>756 pg total PCB-dioxin toxic equivalent) was negatively influenced by this postnatal exposure to PCBs and dioxins, and was comparable to the psychomotor score of the formula-fed infants. Breastfed infants also scored higher on the mental scale at 7 months of age in a dose-dependent way. There was no significant influence of the perinatal PCB and dioxin exposure on the mental outcome at 3 and 7 months of age. At 18 months of age neither the mental nor the psychomotor score was related to perinatal PCB or dioxin exposure, nor to the duration of breastfeeding.

**Conclusions.** Prenatal PCB exposure has a small negative effect on the psychomotor score at 3 months of age. PCB and dioxin exposure through breastfeeding has an adverse effect on the psychomotor outcome at 7 months of age. The mental outcome at 7 months of age is positively influenced by breastfeeding per se; the perinatal exposure to PCBs and dioxins does not influence this outcome. At 18 months of age the development is affected neither by PCB and dioxin exposure nor by feeding type. Pediatrics 1996;97:700–706; PCBs, dioxins, infants, mental and psychomotor development.

ABBREVIATIONS. PCBs, polychlorinated biphenyls; PCDDs, polychlorinated dibenzo-p-dioxins; PCDFs, polychlorinated dibenzofurans; PDI, psychomotor developmental index of the Bayley Scales of Infant Development; MDI, mental developmental index of the Bayley Scales of Infant Development; LCPUFAs, long-chain polyunsaturated fatty acids; TEQ, toxic equivalent; HOME, Home Observation for Measurement of the Environment; TEF, toxic equivalent factor.

Polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs), are both widespread, highly-resistant pollutants in the environment with possible adverse health effects on humans.\(^1\) PCBs are industrial chemicals that have been used for diverse commercial applications such as dielectric fluids for capacitors and transformers. The production and use of these compounds were mainly banned in the late 1970s. Dioxins are formed as by-products during the process of combustion and manufacturing of organochlorine chemicals. Both toxins are lipophilic and accumulate in the food chain. Adults are mainly exposed through the consumption of dairy products, meat, and fish.\(^3\) Both compounds can pass through the placental barrier and are present in relatively high amounts in human milk.\(^4\) The embryo, fetus, and breastfed infant are exposed to PCBs and dioxins during the critical period of organ growth and differentiation. In formula, milk lipids are replaced by lipids of vegetable origin with a negligible content of PCBs and dioxins. As a consequence, the postnatal exposure to these toxins of formula-fed infants is of no concern. A subpopulation of Taiwanese and Japanese women who were accidentally exposed to high levels of PCBs and PCDFs, through contaminated rice oil, gave birth to infants who were small for gestational age and who showed mainly dermal lesions as chloracne and hyperpigmentation. In follow-up studies a delay in mental and psychomotor development has been described up until 7 years of age, in these prenatally high-exposed children.\(^5\) However, at 8 years of age the cognitive development of the exposed Taiwanese children had a tendency to catch up, and did not differ significantly any more from their controls.\(^10\)

Negative effects on both mental and psychomotor development have also been measured after prenatal exposure to PCB background levels in the United
States. Jacobson et al\textsuperscript{11} described a significant dose-dependent relationship between a higher cord serum PCB level and a poorer performance on the Verbal and Memory Scale of the McCarthy Scales of Children's Abilities, in children at 4 years of age, whose mothers consumed Lake Michigan sport fish, which was contaminated with PCBs. Gladen et al\textsuperscript{12} and Rogan et al\textsuperscript{13} described an association between the prenatal PCB exposure in North Carolina, and poorer performance on the psychomotor developmental index (PDI) of the Bayley Scales of Infant Development at 6, 12, 18, and 24 months of age. They could not find a negative influence of the prenatal PCB exposure on the mental developmental index (MDI) at these ages, nor on any of the McCarthy Scales examined at 3, 4, and 5 years of age.\textsuperscript{14} Few adverse effects on the infants' development attributable to lactational exposure have been described: Jacobson et al\textsuperscript{15} reported a relationship between postnatal PCB exposure and a decrease in activity level at 4 years of age.

A beneficial effect of breastfeeding, particularly on the cognitive development of children, has been described in several studies. It was postulated that hormones, trophic factors, or long-chain polyunsaturated fatty acids (LCPUFAs), which are absent in formula-feeding, may account for these differences in development.\textsuperscript{16–18}

In this article we wish to examine the effects of prenatal and postnatal exposure not only to PCBs, but also to dioxins, the levels of which are relatively high in human milk samples from the Netherlands, and the effects of breastfeeding versus formula-feeding, on the mental and psychomotor development of infants at 3, 7, and 18 months of age. This study is part of the Dutch PCB/Dioxin study, a larger prospective longitudinal study on possible adverse health effects of these pollutants on humans.

**METHODS**

**Subjects**

During the last trimester of pregnancy women in the Rotterdam area were asked to volunteer for the study by their obstetrician or midwife, between June 1990 and February 1992. They were given written information about the study design and purposes. When they agreed to take part in the study, they were visited at their homes for further explanation of the study protocol by the examiner (C.K.E.). There is no information on the women who refused to take part in the study. To establish a homogeneous study population, only first- or second-born term infants (37 to 42 weeks' gestation) without congenital anomalies or diseases were included. Pregnancy and delivery had to be passed without overt signs of serious illness, or complications like a cesarean section, forces, or vacuum extraction. All infants were white. To study the effects of postnatal exposure to PCBs and dioxins, women were enrolled who intended to breastfeed human milk, which contains relatively high levels of both toxins, for at least 6 weeks, as well as women who volunteered to formula-feeding from one batch as a reference (Almiron M2, Nutricia NV, the Netherlands) during 7 months.

The study protocol had been approved by the medical ethical committee of the University Hospital Rotterdam/Sophia Children's Hospital. Informed consent had been given by the parents.

**Measures of Exposure**

A blood sample was taken from the mothers in the last month of their pregnancy (36th to 40th week) and from the umbilical cord for the measurement of the PCB congener levels 118, 138, 153, and 180 by gas chromatography with electron capture detection.\textsuperscript{19} These congeners are known to have concentrations in human blood that are high enough to be measured with a high degree of accuracy. The four congener levels were added and summarized as the PCB-plasma-sum. One maternal and 30 cord blood samples were missing for this analysis due to failures in organization. Dioxin levels could not be measured in the maternal or cord plasma samples because larger amounts of blood would have been necessary to measure accurately the low dioxin levels in relatively lean blood. In the second week after delivery the mothers who breastfed their infants collected a 24-hour representative human milk sample with a vacuum pump (Babyluxus 2, KAWECO, Stuttgart, Germany). Seventeen individuals of woman, congener and 24 PCB congener levels were measured by gas chromatography-high-resolution mass spectrometry\textsuperscript{20,21} and by gas chromatography with electron capture detection, respectively.

According to the toxic equivalent (TEQ) concept, the dioxin and dioxin-like PCBs (IUPAC no. 77, 126, 169, 105, 118, 156, 170, and 180) were added and summarized as the total PCB-dioxin TEQ level, as described in a previous article.\textsuperscript{4} The PCB congener levels 118, 138, 153, and 180 in human milk were also added and summarized as the PCB-milk-sum in comparison with the PCB-plasma-sum. The same measurements were performed in samples of the formula-feeding. Of the 105 human milk samples, 80 could be measured with sufficient accuracy for the total PCB-dioxin TEQ level, and 100 for the PCB-milk-sum. The other analytical measurements were inaccurate due to either interferences in the chromatograms, or to too small volumes of human milk samples; these measurements were not used in the statistical analyses.

**Test Material and Procedure**

The MDI and PDI of the infants was determined with the Dutch standardized version of the Bayley Scales of Infant Development,\textsuperscript{22} the BOS 2-30,\textsuperscript{23} at 3, 7, and 18 months of age. The Bayley scales were originally standardized for the Dutch population to a mean of 100 and a standard deviation of 15. All Bayley tests were performed at the infants' homes in the presence of the parent(s) by one examiner (C.K.E.), who was unaware of the infants' PCB and dioxin exposures. At the age of 3 months, MDI scores were missing for 7 infants and PDI scores were missing for 9 infants. At 18 months of age, the PDI score was missing for 1 child.

**Data Analysis**

Exposure. Data analysis was performed by using the Statistical Package for the Social Sciences (SPSS/PC, Cary, NC). In the analysis the relationship between mean Bayley scores and the pernatal PCB/dioxin exposure was studied.

As a measure of prenatal exposure, the PCB-plasma-sum in maternal and umbilical cord plasma was examined, both after log transformation. Dioxin levels in human milk are known to be highly correlated with the dioxin levels in maternal plasma and in adipose tissue and are therefore a good estimation of the prenatal dioxin exposure.\textsuperscript{24} Because dioxins and dioxin-like PCBs in this study could only be measured in human milk, the total PCB-dioxin TEQ level in human milk was separately studied as an estimation of the prenatal dioxin exposure of the breastfed infants. Because it is assumed that breastfeeding per se has positive effects on the development of children, the amount of breastfeeding received was studied separately. This variable called "duration of breastfeeding in weeks", was divided into three categories: zero (formula-fed), short, and long (Table 1). In the multiple regression analysis this categorical variable was entered as a continuous independent variable with the value 0, 1, or 2. We chose to use linearity because the difference between category 1 and 2 is half the difference between category 1 and 3.

The postnatal PCB exposure and the total PCB-dioxin TEQ

| TABLE 1. Categories of Duration of Breastfeeding |
|-----------------|-----------------|-----------------|-----------------|
|                 | 3 Months        | 7 and 18 Months |                 |
|                 | Weeks of Breastfeeding | Weeks of Breastfeeding |
| Category low    | 102             | 0               | 102             | 0               |
| Category medium | 26              | 6–10            | 54              | 6–16            |
| Category high   | 79              | 11–12           | 51              | >16             |
exposure were calculated separately as a multiplication of the PCB-milk-sum, respectively, the total PCB-dioxin TEQ level in human milk, and the duration of breastfeeding in weeks. Both variables were divided into three categories: low, medium, and high-exposed (Table 2).

Multiple regression analysis was used to study the effects of prenatal and postnatal exposure to PCBs and dioxins separately as well as combined.

**Confounders.** The socioeconomic, obstetric, and neonatal conditions were assessed by means of the obstetrical optimality scale. The following potential confounding variables were identified with univariate analyses: the level of education of the parents (high (1), at least secondary education completed, or low (0)) and profession (divided into three categories: student, unemployed, or unskilled worker; skilled worker or middle class employee; independent middle class or higher profession), maternal smoking and alcohol usage (yes or no), parity (first or second, reference category is "first"), duration of gestation, birth weight, Apgar score after 1 and 5 minutes, sex of the infant, and duration of breastfeeding (in weeks). Total triiodothyronine, total thyroxine, free thyroxine, and thyroid-stimulating hormone were measured in maternal plasma during the last month of pregnancy, in cord plasma, and in the infants' plasma in the second week, and in the third and eighteenth month after birth by chemiluminescence immunoassay, using Amerlite assay kits (Amersham, England). The Home Observation for Measurement of the Environment, the HOME Inventory, was examined at the age of 18 months.

**RESULTS**

Two hundred sixty-eight women were involved in the study. After birth 231 mother-infant pairs fulfilled the inclusion criteria of the study protocol. A vacuum extraction or cesarean section was the main reason for excluding 37 women from the study. Six weeks after delivery 24 pairs were excluded from the study mainly due to the cessation of breastfeeding before this time. Of these 61 excluded pairs no PCB or dioxin analysis were performed nor were the infants tested with the Bayley scales. Of the remaining 207 infants, 105 were breastfed and 102 were formula-fed. Eighty of 105 breast milk samples could be measured with sufficient accuracy for the total PCB-dioxin TEQ level: the characteristics of the mother-infant pairs whose milk samples were analyzable did not differ significantly from those whose samples were not.

In Table 3 the mean Bayley scores (± SD) are summarized for the whole group, as well as for the breast and formula-fed infants separately. Breastfed infants scored significantly higher on the MDI-7 (*P* = .03), the MDI-18 (*P* = .01), and on the PDI-7 (*P* = .05) compared with formula-fed infants. The PCB-cord-plasma-sum averaged 0.5 ± 0.3 ng/g; the PCB-maternal-plasma-sum 2.2 ± 1.0 ng/g; and the total-PCB-dioxin-sum in human milk 66.6 ± 24.2 pg TEQ/g fat. The two measurements of prenatal exposure (the PCB-plasma-sum in maternal and cord plasma) were highly correlated (r = 0.72, *P* < .001). Levels in formula-feeding were below the limits of determination. Table 4 gives an overview of the potential confounders (gestational age, parity, HOME-score, and maternal education), which were correlated at a level *P* < .10, with at least one of the dependent outcome variables, and which were entered into the multiple regression analysis as independent variables. Because there were high correlations between the socioeconomic variables, we chose maternal education as a potential confounding variable in the multivariate regression. The sex of the infants was equally divided in the breast and formula-fed group, and was not significantly related to any of the outcome variables. There was a weak positive relation between the PCB and dioxin exposure levels and the education of the mothers and the HOME-score of the infants. The other possible confounders were not significantly related to exposure levels.

In Table 5 the effects of the prenatal PCB exposure, measured in maternal plasma, on the PDI at 3 months of age, examined with multiple regression analysis are presented; there is a significantly negative relation between prenatal PCB exposure and the PDI score. A doubling of the PCB-plasma-sum (eg, 1 ng/g compared with 0.5 ng/g, or 2 ng/g compared with 1 ng/g) would result in a decrease by 3 points of the PDI-3 (*P* = −.48 × Ln2). When the PCB-sum in cord plasma was used, only 175 cases could be analyzed. No effect of prenatal PCB exposure could then be found. This cannot be attributable to selection, because in this group the maternal PCB-plasma-sum...
still had a significantly negative influence on the PDI-3. When the total PCB-dioxin TEQ level in human milk was entered into the regression analysis, instead of the PCB-plasma-sum, as an estimation of the prenatal dioxin and dioxin-like PCB exposure of the breastfed infants, there was also a negative influence of this transplacental exposure on the PDI-3 outcome (B = -7.4, SE = 4.0, \( P = .07 \)). The duration of breastfeeding is not significantly related to the PDI-3. Of the other potential confounders, only the gestational age was of a significantly positive influence (\( P = .0001 \)). Examination of the postnatal exposure revealed no significant effect of the total PCB-dioxin TEQ exposure on the PDI-3 outcome. When the prenatal PCB exposure and the postnatal total PCB-dioxin TEQ exposure were entered together in the multiple regression analysis the results remained almost the same: a decrease by 3 points of the PDI-3 when the prenatal PCB exposure would double, and no significant effect of the postnatal exposure.

At 7 months of age there was no significant effect of prenatal exposure on the PDI outcome. Table 6 shows the effects of postnatal total PCB-dioxin TEQ exposure on the PDI-7 outcome in the multiple regression. There was a significantly positive relationship with the duration of breastfeeding: infants being breastfed between 6 and 16 weeks would score 7 points higher and infants being breastfed between 17 and 30 weeks would score 14 points higher on the PDI-7 compared with formula-fed infants. This was a positive influence of breastfeeding itself. However, there is a negative influence of the postnatal PCB and dioxin exposure by breastfeeding on the PDI-7: infants who received a medium or high total PCB-dioxin TEQ exposure through breastfeeding had significantly lower PDI-7 scores (-10 points and -8 points, respectively), compared with formula-fed infants and breastfed infants who received a low total PCB-dioxin TEQ exposure through breastfeeding had significantly lower PDI-7 scores (-10 points and -8 points, respectively), compared with formula-fed infants and breastfed infants who received a low total PCB-dioxin TEQ exposure through breastfeeding. The Figure shows that infants being breastfed between 6 and 16 weeks (short), with a low total PCB-dioxin TEQ exposure, would score 7 points higher on the PDI-7, and infants being breastfed between 17 and 30 weeks (long), with a low total PCB-dioxin TEQ exposure would score 14 points higher on the PDI-7.

**Figure.** Psychomotor development at 7 months of age related to breastfeeding.
compared with formula-fed infants. Infants being breast-fed for a short period with a medium or high total PCB-dioxin TEQ exposure would score 3 points (1 point lower, respectively) and infants being breast-fed for a long period with a medium or high total PCB-dioxin TEQ exposure would score 4 points (6 points higher, respectively) compared with formula-fed infants, which is of no significant difference. Furthermore, the PDI-7 is significantly negatively related to the number of older siblings \( (P < .0001) \). When the prenatal PCB exposure and the postnatal total PCB-dioxin TEQ exposure were entered together in the multiple regression analysis the results showed the same trends: no effect of the prenatal exposure, and a negative influence of the postnatal exposure on the PDI-7 outcome, although of no significance (overall \( P = .09 \)).

The PDI outcome at 18 months of age was neither significantly influenced by the prenatal or postnatal PCB and dioxin exposure, nor by the duration of breastfeeding, nor by the other confounders. The MDI score at 3 months of age was neither significantly related to the perinatal PCB or dioxin exposure, nor to the duration of breastfeeding. Gestational age was the only confounder with a significant relationship to the MDI-3 \( (P < .0001) \).

Table 7 shows the results of the multiple regression analysis with the MDI at 7 months of age as the dependent variable. The duration of breastfeeding is significantly positively related to the MDI-7. Infants who were breastfed for a short or long period would have an advantage of 2 and 4 points, respectively, compared with formula-fed infants. Neither the prenatal nor the postnatal PCB or total PCB-dioxin TEQ exposure have significant influences on the MDI-7 outcome. The MDI-18 was neither significantly influenced by the duration of breastfeeding, nor by PCB/dioxin exposure. However, there is a strong positive relationship between the HOME score and the MDI-18 outcome \( (P < .0001) \). Secondly a higher level of education of the mother gives an increase by 7 points on the MDI-18 score \( (P = .01) \).

Instead of the postnatal total PCB-dioxin TEQ exposure, all analyses were repeated with the PCB-milk-sum multiplied by the duration of breastfeeding as an estimation of the postnatal exposure. The effect of this postnatal PCB exposure on the Bayley scores was not significant. There was no significant relationship between the thyroid hormone levels and the mental or psychomotor outcome at any age.

**TABLE 7. Results of the Multiple Regression Analysis of the Mental Developmental Index at 7 Months of Age**

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Standard Error</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constant</strong></td>
<td>88.1</td>
<td>27.1</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>.12</td>
<td>.59</td>
</tr>
<tr>
<td>Parity (no siblings, one or more siblings)</td>
<td>-1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>HOME-score</td>
<td>.46</td>
<td>.28</td>
</tr>
<tr>
<td>Education of mother (low, high)</td>
<td>-1.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Ln PCB-plasma-sum (ng/g)</td>
<td>2.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Duration of breastfeeding (0, 6-16, or 17-30 weeks)</td>
<td>2.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In this study we examined whether the early mental and psychomotor development of full-term, healthy infants was influenced by perinatal exposure to PCBs and dioxins or by breastfeeding versus formula-feeding. We found a significantly negative relationship between prenatal PCB exposure and the PDI-3 outcome; there was no influence of this exposure at 7 and 18 months of age. In contrast to our study, Rogan et al\(^{18}\) and Gladen et al\(^{13}\) described a negative relationship between prenatal PCB exposure and PDI scores at the ages of 6, 12, 18, and 24 months examined with the Bayley scales, although the negative influence found at 18 months was of no significance. It remains difficult to compare the exposure levels of our study to the levels reported by Rogan et al and Gladen et al because of differences in analytical methods. They measured a total PCB level in human milk as an estimation of the prenatal PCB exposure. Instead of that, we measured four specific PCB congener levels in maternal plasma, which is a more accurate method. The PCB exposure we measured is assumed to be as high as the levels in the United States. In addition to the negative effect of prenatal PCB exposure on the PDI-3, we found a significantly positive effect of the gestational age on the PDI-3 outcome. Although all infants were born at term, a range in gestational age of 5 weeks (37-42 weeks) is of significant influence on the PDI outcome at this age. The longer the infants were in utero, the higher the points were of the psychomotor outcome (increase by 2 points per week). In general, developmental test outcomes of term infants are not corrected for gestational age.

At 7 months of age we found a significant, dose-dependent positive effect of breastfeeding per se on the PDI, the effect of which was decreased when the infants received a postnatal medium or high total PCB-dioxin TEQ exposure via breastfeeding. Rogan et al and Gladen et al studied influences of breastfeeding on the psychomotor scales of the Bayley test as well. They measured a significantly higher PDI score at 24 months of age in the infants who received breastfeeding for at least 20 weeks.\(^{18}\) Although they reported negative effects of the prenatal PCB exposure on psychomotor development, they never found a negative influence of postnatal PCB exposure by breastfeeding on the infants' development. They did not measure dioxin levels in human milk. Because the dioxin levels in human milk samples of industrialized countries in Western Europe are relatively high compared with the dioxin levels in the United States,\(^{22}\) it might be possible that the dioxin exposure is responsible for the negative effect that we measured on psychomotor development. At 18 months of age, we no longer detected a negative effect of postnatal exposure on the PDI outcome. Because most infants were no longer breastfed after 1 year of age, and because PCB and dioxin levels in children's tissues decline considerably due to growth, the actual exposure is much lower at this age.
We could not find an adverse effect of transplacentral or breastfeeding exposure to PCBs and dioxins on the mental development of the infants. Neither Rogan et al.\textsuperscript{12} nor Gladen et al.\textsuperscript{13} found an effect of perinatal PCB exposure on mental development. However, adverse effects have been reported on children’s cognitive development after accidentally high prenatal exposure to PCBs, up until 7 years of age.\textsuperscript{3-9} Jacobson et al.\textsuperscript{11} also described a significant dose-dependent relationship between higher prenatal PCB exposure and a poorer performance on the Verbal and Memory scale of the McCarthy Scales of Children’s Abilities in children at 4 years of age, whose mothers consumed Lake Michigan sport fish, which was contaminated with PCBs.

We measured a significant positive and dose-dependent relationship between the duration of breastfeeding and the MDI score at 7 months of age. At the age of 18 months breastfed children also scored significantly higher on the MDI outcome, compared with the formula-fed children. At this age, however, this higher score on the MDI outcome was not related to breastfeeding itself but to better environmental (HOME-score) and socioeconomic circumstances: in the breastfed group 53% of the mothers received higher education compared with 28% in the formula-fed group. Advantages of breastfeeding on mental development have been described in different studies of preterm as well as full-term children. Morrow-Tlucak\textsuperscript{9} described a dose-dependent positive effect of breastfeeding on the MDI score at 12 and 24 months of age with the Bayley scales. Gladen and Rogan\textsuperscript{10} also investigated influences of the duration of breastfeeding on the MDI scores at 6, 12, 18, and 24 months of age. Children who were breastfed for long periods (>20 weeks) scored significantly higher compared with children who were formula-fed and breastfed for short periods (0–4 weeks) at 24 months of age. At later ages these children had also higher scores on the cognitive skills of the McCarthy Scales. Lucas et al.\textsuperscript{19} described an advantage on the cognitive development of children born prematurely, who received breast milk by stomach tube compared with formula-fed premature infants, at the ages of 1, 5, and 8 years. Birch et al.\textsuperscript{17} described a dose-dependent positive influence of breastfeeding on the visual development of preterm as well as full-term infants. The visual development was positively related to the level of LCPUFAs in the red blood cells of the infants. These LCPUFAs, formed from essential fatty acids in breastfeeding, are crucial for retinal and other neural tissue growth and development. The formula-fed infants in our cohort received formula without these essential fatty acids. It is possible that LCPUFAs or other essential fatty acids, trophic factors, or hormones, which are present in breast milk and absent in formula, are responsible for the positive effects we measured on the infants’ development.

We described an influence of perinatal PCB and dioxin exposure on the infants’ thyroid hormone levels,\textsuperscript{20} which are essential for normal brain development.\textsuperscript{31} However, in this study there was no relationship between thyroid hormone levels and development.

The study group is not an at random chosen group, which might be a source of selection bias. It was ethically not possible to randomize the mothers for breastfeeding or formula-feeding their infants. Besides, the women were asked to give blood samples for themselves and their infants to collect human milk samples during a 24-hour period and to have examined their infants at different time points in their homes. It would not have been possible to collect all these data completely than in a group who volunteered for this study protocol. The educational level and profession of the parents in the breastfed group was higher compared with the parents in the formula-fed group. Overall, the characteristics of the mother-infant pairs in this study, measured with several possible confounding variables, conforms well to data of the general Dutch population.

We expressed the postnatal dioxin and dioxin-like PCB exposure by breastfeeding as the total PCB-dioxin TEQ, which is a summation of individual congener levels multiplied by their toxic equivalent factor (TEF),\textsuperscript{4} corresponding to the TEQ concept.\textsuperscript{28} This method is based on animal experiments in which effects mediated by the aryl-hydrocarbon receptor were the studied end points eg, aryl-hydrocarbon hydroxylase/ethoxy-resorufin-o-deethylase enzyme induction, LD50, hepatotoxic effects, body weight loss, and thymic atrophy, and not neurologic or developmental outcome. Individual PCB and dioxin congeners may have a different effect on these outcome parameters and might receive other TEF values for neurotoxicity. There are studies indicating other routes for neurotoxicity by PCBs and dioxins, like altering hormone and neurotransmitter levels.\textsuperscript{32,33} The TEQ concept neither accounts for additive nor inhibiting effects, although it is known that these effects exist after exposure to a mixture of congeners. When considering the individual congener levels in human milk, we did not find a clear relationship between certain congeners and developmental outcome. At this moment, the TEQ concept is the best available method for studying effects of a mixture of many different congeners such as human milk.

In conclusion, prenatal as well as postnatal exposure to Dutch levels of PCBs and dioxins has a small, adverse effect on early psychomotor development. Breastfeeding per se has an important positive influence on mental and psychomotor development at 7 months of age. Although the postnatal dioxin and dioxin-like PCB exposure through breastfeeding had a negative effect on the PDI outcome at 7 months of age, breastfed infants never scored significantly lower compared with formula-fed infants. Therefore, mothers can be supported, also in the western industrialized part of the world, to breastfeed their infants. However, it is not clear if the small, adverse effects we found on early development, which are caused in a critical period of organ growth and differentiation, might represent differences in neurobehaviour that become apparent later in life. Therefore, it remains necessary for governments worldwide to reduce the...
expulsion and dumping of these toxins as much as possible. Follow-up studies are being performed in school-age children at this moment.

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