Breast-Feeding Among Women Exposed to Polybrominated Biphenyls in Michigan

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In the early 1970s, the largest industrial accident in the United States resulted in widespread contamination of the food supply in Michigan with polybrominated biphenyls (PBBs). The chemical similarity of PBBs to compounds implicated as endocrine disruptors has raised the question of whether PBBs could affect the reproductive system. In the present analysis we examine the relation between serum measurements of PBBs and the frequency and duration of lactation. Persons who lived on or received food from farms exposed to PBBs were enrolled in a registry by the Michigan Department of Public Health. Female members of the cohort were invited to participate in a telephone survey of reproductive outcomes. The three outcomes of interest in the present analysis were a) the decision to breast-feed (yes/no); b) the duration, in months, of breast-feeding as the main source of nutrition; and c) the total duration, in months, of breast-feeding. None of the three outcomes was significantly associated with serum PBB levels, even after controlling for maternal age, previous history of breast-feeding, body mass index, maternal education, household income, history of smoking in the year before pregnancy, consumption of alcohol during the first trimester of pregnancy, history of thyroid disorder, gestational age of the infant in weeks, time to pregnancy, and year of birth. Key words: human milk, infants, lactation, pregnancy, polychlorinated biphenyls, polybrominated biphenyls. Environ Health Perspect 109:1133–1137 (2001). [Online 23 October 2001] http://ehpnet1.niehs.nih.gov/docs/2001/109p1133-1137thomas/abstract.html

Since the 1800s, maternal milk has been known to contain chemical contaminants that could adversely affect nursing infants, and potentially hazardous persistent environmental chemicals were first detected in the 1950s (1). One class of these chemicals, chlorinated hydrocarbons [includes dichlorodiphenyl-dichloroethene (DDE), dichlorodiphenyl-trichloroethane (DDT), and polychlorinated biphenyls (PCBs)] has estrogenic and antiestrogenic activity and has attracted much attention as possible disruptors of the human reproductive system (2,3). In cohorts of women in North Carolina and in northern Mexico, higher levels of DDE were associated with shorter duration of lactation (4,5).

In 1973, the largest industrial accident in the United States resulted in widespread contamination of the food supply in Michigan with polybrominated biphenyl (PBB), a halogenated hydrocarbon chemically similar to PCB (6,7). In 1976–1977, the Michigan Department of Public Health organized nearly 4,000 persons who lived on or received food from farms quarantined by the Michigan Department of Agriculture into a registry and obtained baseline health information and serum, which was subsequently analyzed for PBB and PCB levels (8). Initial studies of exposed persons demonstrated no acute human health effects (9–13), but recent studies have suggested an increased risk for cancers of the digestive tract and lymphoma (14), and their chemical similarity to compounds implicated as endocrine disruptors has raised the question of whether PBBs could affect the reproductive system. As part of a larger study evaluating the association of PBBs with endocrine disruption, telephone interviews were conducted with women exposed to PBBs in the early 1970s. The purpose of the present analysis was to examine the relation between serum measurements of PBBs and frequency and duration of lactation in women in the Michigan PBB registry.

Methods

Population. The original cohort consisted of persons who lived on farms or who received food from farms quarantined by the Michigan Department of Agriculture. A total of 3,569 (94%) of the 3,797 people eligible for inclusion were enrolled into the cohort in 1976–1977 by the Michigan Department of Public Health [since renamed the Michigan Department of Community Health (MDCH)]. A blood sample was collected from 85% of the participants at this time. Two additional enrollments were conducted: in 1978, 2 procedures to enroll children born to women participants was established and, in 1982, an expanded enrollment to recruit farm family members who were not enrolled initially. The participants from the initial, infant, and expanded enrollments are now tracked in the PBB registry by the MDCH. All female members of the cohort who were active participants in the registry and who were at least 18 years of age by 1 August 1997 were invited to participate in a telephone survey of female health outcomes. Of the 1,530 women determined to be eligible by the MDCH, 88 (5.2%) could not be located, nine (0.6%) were deceased, and eight (0.5%) were too ill to participate. Of the remaining 1,425 women, 1,185 (83%) agreed to participate in the current study. We excluded an additional 10 women who were born after 1 January 1973 because we were not interested in in utero exposures for this particular outcome. The study was approved by the institutional review boards at the Centers for Disease Control and Prevention, Emory University, and the Michigan Department of Community Health. All subjects gave informed consent at study entry.

Data collection. Using the PBB registry database, MDCH staff sent a letter to all eligible female members of the cohort describing the proposed investigation and notifying them that interviewers would be calling them for a telephone interview. The telephone interview was conducted by trained interviewers using a structured questionnaire lasting approximately 30 min. The portion of the questionnaire addressing breast-feeding asked whether women breast-fed for each of their pregnancies, whether they supplemented breast milk with formula and why, how many months until they stopped breast-feeding completely, and what factors led them to stop breast-feeding completely. Additionally, women were asked about their level of education and household income at the time of interview, whether they had...
smoked cigarettes in the year before their pregnancy, whether they had consumed alcohol during the first trimester of their pregnancy, the sex of the infant, and the gestational age of the infant at birth. Maternal age at the time of pregnancy was calculated by subtracting the mother’s date of birth from the infant’s date of birth. We also looked for a possible cohort effect on rates of breast-feeding and duration of breast-feeding by dividing the cohort into 5-year intervals by year of birth of the index pregnancy (1973–1978, 1978–1983, 1983–1988, 1988–1993, 1993–1998).

**Exposure assessments.** PCBs and PBBs were measured in serum samples obtained from women at enrollment in the cohort and at times during follow-up using gas chromatography with electron-capture detection (15,16). Quantitation of PBB was based on the main congener, 2,2′,4,4′,5,5′-hexabromobiphenyl. PCB was measured as Aroclor 1254. The methods of PBB detection used have coefficients of variation of 7.1–14.0% and recovery ranges of 80–90% (16). The methods of PCB detection used have coefficients of variation slightly higher than that of PBB, ranging from 12 to 30%, and an average recovery of 82% (17).

**Measures.** The three outcomes of interest were a) the decision to breast-feed (yes/no); b) the duration, in months, of breast-feeding as the main source of infant nutrition among women who breast-fed; and c) the total duration, in months, of breast-feeding among women who breast-fed. Because breast-feeding behavior (including the decision to breast-feed and the duration of breast-feeding) during one pregnancy was likely to influence breast-feeding behavior for subsequent pregnancies, we chose to study only one pregnancy per woman to avoid problems with non-independence. For each woman, the first singleton live birth after the initial PBB serum measurement was the pregnancy used in the analysis. We estimated serum PBB levels at delivery of the infant using a decay rate model previously described (18). Exposure was evaluated both for initial serum PBB levels and for estimated PBB levels at birth. We treated exposure as a categorical variable, dividing women into three groups: a) the reference or low exposure group, consisting of women whose PBB levels were at or below the detection limit (1 ppb; n = 260); b) the moderate exposure group, made up of women whose levels were above the detection limit and below the 90th percentile of women in our study cohort (n = 141); and c) the high exposure group, composed of women whose levels were above the 90th percentile (n = 45). For initial levels, the 90th percentile corresponded to 13 ppb and, for estimated levels at delivery, 7 ppb. Additionally, we evaluated exposure to PCBs. PCB measurements were performed on the majority of the cohort (1976–1988) to determine whether PCBs, a widespread environmental contaminant, might be as important as PBB exposure for the cohort’s long-term health status (19). Women in the current study had a maximum of six PCB measurements taken between 1976 and 1988, with a correlation of 0.61 between values. Because PCB exposure is continual, due to consumption of fish and other dietary sources (20), initial serum PCB level was used as the estimated serum PCB level at delivery regardless of the time since the index breast-feeding event. For serum PCB, we divided the cohort into four groups, consisting of each tertile of serum PCB exposure and a fourth category for women who did not have serum PCB levels performed. The lowest tertile consisted of women whose PCB levels were ≤ 5 ppb (n = 244), the middle tertile included women whose levels were between 5 and 7 ppb (n = 49), the upper tertile contained women whose levels were > 7 (n = 114), and 39 women did not have serum PCB levels drawn.

**Statistical analysis.** All analyses were conducted using SAS software (version 6.12; SAS Institute, Cary, NC). For the decision to breast-feed, associations between outcome, exposure to PBB, and other potential covariates were tested with chi-square analyses. A stratified analysis was conducted using the Breslow-Day test for homogeneity to assess possible interaction. A possible association between serum PBB measurement and the decision to breast-feed was evaluated using a logistic regression model. Initially, a full model containing all of the covariates found to be significant predictors of the decision to breast-feed or that could be potential confounders were entered into the model and assessed for collinearity using condition indices and variance decomposition proportions. Using a backward stepwise elimination strategy, we removed variables from the model if they were not associated with the outcome (p > 0.05) and if their removal did not alter parameter estimates for PBB exposure by more than 10%. We used the Hosmer and Lemeshow goodness of fit test to assess how effectively the model described the outcome.

For the remaining two outcomes (duration of breast-feeding as the main source of nutrition and total duration of breast-feeding), we initially examined associations between each outcome and exposure to PBB and other potential covariates using the PHREG procedure of SAS to calculate crude hazard ratios. A separate Cox proportional hazard model was then used to evaluate the relation between PBB exposure levels and each of the duration outcomes. Initially, we assessed a full model containing potentially confounding covariates for collinearity, then took a backward elimination approach. We retained variables in the model if the association with the outcome had α < 0.05 and if their removal altered parameter estimates for PBB exposure by more than 10%.

Finally, we examined the relation between duration of breast-feeding (for both duration of breast-feeding as the main source of nutrition and total duration of breast-feeding) and estimated serum PCB level after excluding women who reported extrinsic reasons for supplementing breast-feeding and for stopping completely. Women were classified as having an extrinsic reason for deciding to supplement if they agreed with one of the following responses: it became uncomfortable to only breast-feed; you were medically advised to supplement; you felt it was the right time to give formula or cow’s milk along with breast milk; it became inconvenient to only breast-feed; or other reason. Similarly, women who responded, “there was not enough breast milk,” to the question of why they stopped breast-feeding entirely were classified as having an intrinsic reason for ceasing to breast-feed and were retained in the analysis. For this subset of women, we calculated crude hazard ratios for the association between each outcome and PBB exposure. After excluding women with extrinsic reasons, we identified 49 women with an intrinsic reason for deciding to supplement breast milk and 56 women who gave an intrinsic reason for deciding to stop breast-feeding altogether. The small numbers of women in these subsets precluded construction of a multivariate model.

**Results**

Initial serum PBB levels were available for 1,020 (86.1%) of the 1,185 women who participated in the study. We did not find any differences in age at delivery, PBB level, or PCB level among responders compared to nonresponders. Among the 1,020 participants, 446 (43.7%) had a live-born infant after their initial serum PBB level. Characteristics of the cohort are shown in Tables 1 and 2. Table 1 depicts continuous variables, and Table 2 shows categorical variables. The mean initial

**Table 1. Characteristics of women in the Michigan PBB registry with one live-born infant after their initial serum PBB level (n = 446; continuous variables).**

| Characteristic               | Mean ± SD |
|-----------------------------|-----------|
| Maternal age (years)        | 25.6 ± 5.0|
| Mean initial serum PBB level (ppb) | 17.5 ± 99.7|
| Estimated serum PBB level at delivery (ppb) | 9.4 ± 61.9|
| Estimated serum PCB at delivery (ppb) | 5.5 ± 5.2|
| Duration of breast-feeding as main source of nutrition (months) | 2.6 ± 3.3|
| Total duration of breast-feeding (months) | 4.1 ± 5.3|
serum PBB level was 17.5 ppb (range 0.5–1,490), compared with a mean of 9.4 ppb using the estimated serum PBB level at the time of pregnancy (range 0–1,310). Results for the bivariate analyses and multivariate models were not different when using the initial levels and the estimated serum levels; only the analyses using the estimated serum levels at the time of the index pregnancy are presented here. Breast milk was the main source of nutrition for a mean of 2.6 months for this cohort of infants, and the mean total duration of breast-feeding was 4.1 months. Two-hundred ninety-three women (65.7%) breast-fed their first infant after the initial serum PBB level; only 49 women (11.0%) had previously breast-fed.

Table 3 shows the crude associations between each breast-feeding outcome and the potential risk factors (for the decision to breast-feed, odds ratios are shown; for the other two outcomes, hazard ratios are given). Women who reportedly smoked during the year before the index pregnancy were more likely not to breast-feed, and women with more than a high school education were more likely to choose to breast-feed. Women whose index pregnancy occurred in the first 5 years of the study were less likely to breast-feed compared to the reference group of women who gave birth in the last 5 years of the study. We did not find an association between duration of breast-feeding as a main source of nutrition and any of the other covariates, nor did any of the potential risk factors influence total duration of breast-feeding.

Table 2. Characteristics of women in the Michigan PBB registry with one live-born infant born after their initial serum PBB level (n = 446; categorical variables).

| Characteristic          | Frequency | Percentage |
|-------------------------|-----------|------------|
| Education               |           |            |
| Some high school        | 6         | 1.3        |
| High school graduate    | 168       | 37.7       |
| Some college            | 152       | 34.1       |
| College graduate        | 120       | 26.9       |
| Income                  |           |            |
| < $20,000               | 44        | 9.9        |
| $20,000 to < $35,000    | 103       | 23.1       |
| $35,000 to < $50,000    | 131       | 29.4       |
| ≥ $50,000               | 146       | 32.7       |
| Missing                 | 22        | 4.9        |
| Consumed alcohol during first trimester of index pregnancy | 70 | 15.7 |
| Smoked during year before index pregnancy | 107 | 24.0 |
| Sex of infant, male     | 242       | 54.3       |
| Gestational age < 37 weeks | 25 | 5.6       |
| Previous breast-feeding | 49        | 11.0       |
| Breast-feed, index infant | 293      | 65.7       |

Table 3. Crude measures of association and 95% confidence intervals for each breast-feeding outcome and potential risk factors during index pregnancy of women in the Michigan PBB registry.

| Risk factor               | Did not breast-feed (n = 446) | As main source of nutrition, months (n = 291) | Total, months (n = 293) |
|---------------------------|-------------------------------|-----------------------------------------------|-------------------------|
|                          | OR 95% CI                      | HR 95% CI                                     | HR 95% CI               |
| Maternal education > 12 years | 0.51 (0.34–0.76)               | 0.98 (0.77–1.25)                              | 0.87 (0.68–1.11)        |
| Household income > $35,000 | 0.69 (0.46–1.05)               | 1.06 (0.82–1.36)                              | 1.15 (0.89–1.49)        |
| Consumed alcohol in first trimester of index pregnancy | 1.34 (0.79–2.26) | 1.14 (0.82–1.59) | 1.04 (0.75–1.45) |
| Smoked during year before index pregnancy | 1.81 (1.16–2.83) | 1.11 (0.83–1.49) | 1.16 (0.87–1.56) |
| Sex of infant, male       | 1.32 (0.80–1.96)               | 1.00 (0.79–1.26)                              | 1.00 (0.79–1.26)        |
| Previou history of breast-feeding | 0.52 (0.26–1.05) | 0.75 (0.53–1.06) | 0.69 (0.49–0.97) |
| Gestational age < 37 weeks | 1.08 (0.47–2.51)               | 1.07 (0.64–1.77)                              | 1.19 (0.72–1.98)        |
| Maternal age > 25 years   | 0.73 (0.50–0.93)               | 0.83 (0.66–1.05)                              | 0.79 (0.63–1.00)        |
| Year of birth             |                                |                                               |                         |
| 7/1/73–6/30/78            | 4.72 (1.87–11.96)              | 1.04 (0.62–1.74)                              | 0.85 (0.50–1.42)        |
| 7/1/78–6/30/83            | 2.22 (0.95–5.18)               | 1.04 (0.69–1.57)                              | 0.84 (0.58–1.27)        |
| 7/1/83–6/30/88            | 1.88 (0.79–4.48)               | 1.13 (0.73–1.74)                              | 0.92 (0.60–1.42)        |
| 7/1/88–6/30/93            | 2.23 (0.93–5.36)               |                                               |                         |
| 7/1/93–6/30/98 (reference group) | 1.00 (–) | 1.00 (–) | – |

Abbreviations: OR, odds ratio; CI, confidence interval; HR, hazard ratio.
significantly influenced the decision to breast-feed.

The Cox proportional hazard model for number of months that breast milk was the main source of nutrition (Table 6) did not reveal a relation between estimated serum PBB and duration of lactation, even after adjusting for other factors (previous history of breast-feeding, maternal age, maternal education, gestational age of the infant, PCB level, and history of alcohol consumption in the first trimester) that could potentially have confounded the relation between estimated serum PBB and the number of months breast milk was the main source of nutrition. Similarly, results of the Cox proportional hazards model for the total number of months of breast-feeding (Table 6) did not show an association with estimated serum PBB level.

**Discussion**

Our analysis had two major strengths. Participation was high (83%), minimizing the possibility of selection bias in recruiting women into the study. In terms of exposure to PBB, our study subjects were similar to women who did not participate: the mean initial serum PBB level of nonparticipants was 15.4 ppb (median = 2.0 ppb), compared with a mean initial level of 17.5 (median = 2.0 ppb) in the 446 women in our study cohort. We also had sufficient power to detect important differences in the decision not to breast-feed and in duration of lactation. Given that 31.2% of women in the reference group did not breast-feed (Table 3), we had 80% power to detect a risk ratio of 1.8 when comparing women in the high exposure group with the reference group. Similarly, in comparing women who breast-fed longer than the median total duration of breast-feeding with women who breast-fed for fewer months than the median, we had 80% power to detect a risk ratio of 1.6 when comparing women in the high exposure group with the reference group.

One of the weaknesses of our study was the retrospective study design, which carries a potential for recall bias. Because the mean interval between initial serum measurement and date of birth was more than 8 years, many of our study subjects were attempting to recall details of pregnancies that had occurred in the early 1980s, leading to potentially inaccurate estimates of duration of lactation because the interviews were conducted in 1997. Women were informed of their serum PBB levels, so our results could be biased if women with higher levels of PBB were more likely to remember difficulties with breast-feeding than women with lower levels of PBB. However, because we did not observe an association between PBB exposure and breast-feeding, this type of bias is unlikely.

In addition, it is unlikely that women were aware of the hypothesis that PBB might be associated with difficulties in breast-feeding, reducing the probability of differential recall bias. An expert panel of physicians and toxicologists convened in 1976 concluded that the benefits of breast-feeding outweighed the risks from PBB, and an advisory letter was sent to physicians in Michigan stating that women should not be advised against breast-feeding (22). Additionally, we examined the responses of all the women who answered "other reason" in response to the questions of why they decided to supplement in addition to giving breast milk and why they decided to stop breast-feeding altogether. None of the response categories was predominant (21).

**Table 4. Crude associations between estimated serum PBB level at time of pregnancy and breast-feeding outcomes among women in the Michigan PBB registry.**

| Estimated serum PBB at time of delivery | Did not breast-feed | Breast-fed | OR 95% CI |
|----------------------------------------|---------------------|------------|-----------|
| Low (< 1 ppb)                          | 81 (31.2)           | 179 (68.9) | —         |
| Moderate (> 1 ppb to ≤ 7 ppb)          | 56 (39.7)           | 85 (60.3)  | 1.46      | 0.95–2.32 |
| High (> 7 ppb)                         | 16 (35.6)           | 29 (64.4)  | 1.22      | 0.63–2.37 |
| Total                                  | 153 (34.3)          | 293 (65.7) | —         | —         |

**Table 5. Associations between PBB levels and duration of breast-feeding as main source of nutrition.**

| Estimated serum PBB at time of delivery | Median duration of breast-feeding (months) | HR 95% CI |
|----------------------------------------|--------------------------------------------|-----------|
| Breast-feeding as main source of nutrition | Entire cohort | Low (< 1 ppb) | 3 | — | — |
|                                         | Low (< 1 ppb) | Moderate (> 1 ppb to ≤ 7 ppb) | 3 | 1.01 | 0.78–1.30 |
|                                         | Low (< 1 ppb) | High (> 7 ppb) | 4 | 0.88 | 0.59–1.30 |
|                                         | Low (< 1 ppb) | Intrinsic reasons | 1 | — | — |
|                                         | Moderate (> 1 ppb to ≤ 7 ppb) | 1 | 0.82 | 0.24–2.80 |
|                                         | High (> 7 ppb) | 2.5 | 0.51 | 0.15–1.73 |
| Total duration of breast-feeding | Entire cohort | Low (< 1 ppb) | 4 | — | — |
|                                         | Low (< 1 ppb) | Moderate (> 1 ppb to ≤ 7 ppb) | 5 | 0.88 | 0.68–1.14 |
|                                         | Low (< 1 ppb) | High (> 7 ppb) | 7 | 0.84 | 0.57–1.25 |
|                                         | Low (< 1 ppb) | Intrinsic reasons | 3 | — | — |
|                                         | Moderate (> 1 ppb to ≤ 7 ppb) | 2 | 1.30 | 0.44–3.91 |
|                                         | High (> 7 ppb) | 2.5 | 1.02 | 0.36–2.88 |

**Table 6. Multivariate estimates of association between estimated serum PBB level at time of pregnancy and decision not to breast-feed, number of months of breast-feeding as main source of nutrition, and total duration of breast-feeding.**

| Outcome, PBB exposure | Measure of association | 95% CI |
|-----------------------|------------------------|-------|
| Decision not to breast-feed | Low | 1.29 | 0.81–2.07 |
|                        | Moderate | 1.5 | 0.93–2.56 |
| Duration of breast-feeding as main source of nutrition | Low | 1.03 | 0.79–1.35 |
|                        | Moderate | 0.92 | 0.61–1.37 |
| Total duration of breast-feeding (months) | Low | 0.90 | 0.69–1.22 |
|                        | Moderate | 0.84 | 0.56–1.25 |

*CI, confidence interval.

*Odds ratios from logistic regression model for decision not to breast-feed, adjusted for history of breast-feeding, maternal education, gestational age < 37 weeks, sex of infant, and serum PCB level.

*Hazard ratios for the Cox proportional hazards model for reduced duration of breast-feeding as a main source of nutrition, adjusted for history of breast-feeding, maternal education, gestational age < 37 weeks, maternal age > 25 years, reported consumption of alcohol in first trimester, and serum PCB level.

*Hazard ratios for the Cox proportional hazards model for reduced duration of breast-feeding, adjusted for history of breast-feeding, maternal education, gestational age < 37 weeks, maternal age > 25 years, reported consumption of alcohol in first trimester, and serum PCB level.
them cited concerns about their PBB level or advice from a physician to stop breast-feeding as a reason for supplementing or stopping breast-feeding.

Another type of bias that may have been introduced into our study may be exposure misclassification due to the lack of actual serum measurements of PBB and PCB at the time of pregnancy. We relied on a decay model to estimate serum PBB levels rather than actual serum PBB levels at the time of delivery, and we based our analysis on initial serum PCB levels rather than on estimated PCB levels at the time of pregnancy because of difficulties in estimating serum PCB half-life (22).

Another limitation of the study may have been lack of control of confounding for important determinants of breast-feeding. Although we collected information on several factors known to predict breast-feeding behavior (maternal age and education, income, previous history of breast-feeding, cigarette smoking, and alcohol use), breast-feeding is a complex process and is influenced by other factors such as the availability of support systems and attitudes toward breast-feeding that we did not inquire about in our questionnaire (23–25).

We also may have misclassified study participants on the basis of maternal education and income, since we asked about these characteristics at the time of the interview, not at the time of delivery. However, although these factors may be important determinants of breast-feeding, none of them was associated with exposure in our study and thus would not be an important source of confounding.

The studies that documented an association between DDE and shortened duration of lactation (4,5) excluded women who terminated breast-feeding for extrinsic reasons that intruded on the breast-feeding process (i.e., illness of the mother, separation of mother and child) to focus on women with solely physiologic reasons for terminating breast-feeding. We attempted to duplicate this approach by analyzing the relation between serum PBB and duration of lactation, excluding women with extrinsic reasons for supplementing breast-feeding and women with extrinsic reasons for completely stopping breast-feeding. We failed to find an association between serum PBB and shortened duration of lactation even in this group of women with presumably physiologic reasons for ceasing to breast-feed, although the number of women in the highest exposure group in this analysis was small (n = 3).

In summary, despite having an adequate sample size and minimal potential for selection or recall bias, this analysis did not demonstrate a link between serum PBB level and the decision to breast-feed or to two measures of duration of lactation. Future studies of the role of potential endocrine disruptors in lactation should control for factors related to psychosocial and cultural determinants of breast-feeding, and data should be collected either prospectively or as close to the pregnancy as possible.

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