Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyl Dichloroethene (DDE) in Human Milk: Effects on Growth, Morbidity, and Duration of Lactation

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Abstract: We followed 858 children from birth to one year of age to determine whether the presence of polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in breast milk affected their growth or health. Neither chemical showed an adverse effect on weight or frequency of physician visits for various illnesses, although differences were seen between breast-fed and bottle-fed children, with bottle-fed children being heavier and having more frequent gastroenteritis and otitis media. Children of mothers with higher levels of DDE were breast-fed for markedly shorter times, but adjustments for possible confounders and biases did not change the findings. In absence of any apparent effect on the health of the children, we speculate that DDE may be interfering with the mother's ability to lactate, possibly because of its estrogenic properties. (*Am J Public Health* 1987; 77:1294–1297.)

Introduction

Laug, *et al,* reported the presence of the pesticide dichlorodiphenyl trichloroethane (DDT) in human milk in 1951.[1] Surveys over three decades in many parts of the world have shown that DDT or the stable metabolite dichlorodiphenyl dichloroethene (DDE) is detectable in almost all samples of human adipose tissue or the fat of human breast milk.[2] Polychlorinated biphenyls (PCBs), which are electrical insulating compounds, have been reported as contaminants of human milk since 1966.[3] Surveys of breast milk show widespread prevalence of PCB contamination in industrialized countries.[2,4,5] Quantitatively, PCBs and DDT/DDE are the most important of the several organochlorine compounds that have been detected in human milk. Infant formula and commercial milk (in the United States) are essentially free of PCBs and DDT/DDE.

We began a project in 1978 in which we measured PCBs and DDE in breast milk and followed children to determine any effects on their health, growth, and development, including duration of lactation. We report here findings for the first year of life.

Methods

The North Carolina Breast Milk and Formula Project is a prospective birth cohort study that enrolled about 900 families between 1978 and 1982. Study design, chemical analysis methods, characteristics of the cohort, and findings on neonatal examination are given elsewhere.[5–7] Briefly, any mother who planned to deliver at one of three cooperating institutions and who would be available for at least six months of follow-up was allowed to enroll. The women who volunteered were predominantly White (92 per cent) and well educated. The children were seen at birth, six weeks, 3, 6, 12, and 18 months, and then yearly until age five. Breast milk, formula, or whatever the child was fed was collected at each visit until six months; after that, only breast milk was collected until the mother ceased lactation. Maternal serum, cord blood, and placenta were also collected. The children were examined and a medical history was taken at each visit; the mother was also asked about weaning. Medical records were abstracted. Of the 930 children whose mothers volunteered for the study, 858 participated beyond birth. Of the 858, 802 (93 per cent) were still participating at one year of age.

All biological samples and a 10 per cent sample of formula specimens were analyzed for PCBs and p,p'-DDE (all formula samples were essentially negative). PCB/DDE concentrations in milk at birth were estimated by combining all samples as described elsewhere.[5] Concentrations decline over the course of lactation; for example, concentrations of PCBs at six weeks averaged 93 per cent of concentrations at birth. To estimate a woman's concentration at any specific time point, the average decline was applied; values between visits were obtained by linear interpolation.

Duration of breast-feeding was reported as both the time during which the mother reported that the child was "mostly" breast-fed and the time until total cessation of breast-feeding. Reasons for weaning came from the answer chosen to a question that gave the mother several options (for example, "thought it was the usual time," "doctor advised it") or allowed her to provide her own answer if none (of the multiple choice responses) were suitable.

To examine the relation between PCBs and DDE and morbidity, we needed to assign a dose to each child. Dose is determined by three conditions: the concentrations of PCB/DDE in the fat of breast milk, the amount of fat in the milk, and the amount of milk consumed by the infant. We do not have enough data to deal with sustained differences in amount of milk fat among mothers, and thus use an average. PCB/DDE concentration and duration information were combined to provide estimated amounts of PCBs and DDE consumed. Milk was assumed to average 2.5 per cent fat over the entire lactation. We assumed that children consumed 700 g of milk daily as long as they were mostly breast-fed, and half that amount afterward until breast-feeding stopped. For this calculation, the time mostly breast-fed was taken to be at most nine months. This calculation is similar to that of Wickizer and Brilliant.[8] Note that although we have attempted to estimate absolute dose, only the relative dose is important for determining the trend with increasing dose.

Illnesses were counted as recorded in the child's medical records, and represent data from visits to a physician or other health care provider. No attempt was made to verify diagnoses.

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TABLE 1—Duration of Lactation and Percentage of Women with Lactation Failure by Chemical Levels*

Chemical Levels	No. of Women	Median Weeks	% with Lactation Failure
DDE			
0.31– 0.99	54	26	5
1.00– 1.99	205	26	6
2.00– 2.99	217	23	6
3.00– 3.99	135	24	8
4.00– 4.99	48	18	15
5.00– 5.99	27	9	24
6.00–23.80	48	10	10
PCBs			
0.49– 0.99	43	26	5
1.00– 1.49	192	25	8
1.50– 1.99	232	24	9
2.00– 2.49	134	23	7
2.50– 2.99	60	18	10
3.00– 3.49	31	26	10
3.50– 3.99	18	26	0
4.00–15.80	24	13	13

*Amounts of DDE and PCBs are estimated concentrations in mother's milk fat at birth in parts per million. Weeks represent number of weeks child was mostly breast-fed. See text for definition of lactation failure used here.

Study personnel usually did not provide care. Illness reports were reviewed centrally, any necessary clarification was sought from field personnel, and the individual illnesses were grouped into similar categories. Weights were obtained from the physical examination at each study visit; when a visit was missed, weights were taken from medical records if possible.

In general, neither mothers nor study personnel were aware of the results of the chemical analyses until the child was at least two years old. Observations concerning chemical exposures are therefore double blind. Women who had two children in the study knew the results from their first set of analyses during their second lactation.

Results

About 88 per cent of the children in the study were breast-fed. This figure does not apply to all women who gave birth at these institutions, and probably reflects the heightened interest participating families had in infant nutrition. Women with higher levels of DDE and perhaps PCBs had shorter lactations (Table 1). We did a multiple linear regression analysis in which duration of breast-feeding (i.e., weeks mostly on the breast) was the dependent variable, and mother's age, race, education, occupation, smoking, drinking, and estimated PCB and DDE concentrations in milk at birth were the independent variables (there was also a marker term for the three data collection sites). Table 2 shows the regression coefficients. In this model, the coefficients for DDE and for PCBs are negative, i.e., higher levels are associated with shorter lactation. There is a decline in duration of lactation of about one week for each additional ppm of chemical. There are also differences by occupation, with women who identify themselves as students or housewives breast-feeding longer. Better educated and older mothers breast-feed longer than younger ones, and non-smokers longer than smokers.[9–11] The correlation between PCBs and DDE is only .23, so the effects of the chemicals are not confounded.

We have shown elsewhere that levels of PCBs and DDE decline over the course of lactation, and that levels seen in a first lactation are higher than those seen in subsequent ones.[5] That finding produces a problem in this analysis if one posits the existence of a group of women who have breast-fed a

TABLE 2—Results of Regression of Duration of Lactation on Chemical Levels and Other Factors in All Lactations and First Lactations

	All Lactations		First Lactations Only	
	Coefficient	95% Confidence Interval	Coefficient	95% Confidence Interval
Maternal age (years)	0.9	(0.5, 1.2)	0.8	(0.3, 1.3)
Maternal race				
White	0	—	0	—
Black	−2.3	(−9.3, 4.8)	−5.6	(−14.4, 3.1)
Other	3.1	(−20.5, 26.7)	1.7	(−21.8, 25.2)
Maternal education (years)	1.1	(0.3, 1.9)	1.0	(0.1, 2.0)
Maternal occupation				
White collar	−12.2	(−19.5, −5.0)	−15.3	(−23.4, −7.2)
Professional	−10.0	(−17.0, −3.1)	−10.7	(−18.4, −3.1)
Laborer/farmer	−9.6	(−19.3, 0.1)	−8.9	(−19.6, 1.8)
Paraprofessional	−5.3	(−13.3, 2.7)	−9.8	(−18.7, −0.9)
Housewife	−1.6	(−9.0, 5.9)	−5.2	(−14.1, 3.7)
Student	0	—	0	—
Maternal smoking				
No	4.8	(1.4, 8.3)	3.9	(−0.3, 7.9)
Yes	0	—	0	—
Maternal alcohol				
< one drink per week	0.9	(−1.7, 3.5)	1.2	(−2.0, 4.4)
> = one drink per week	0	—	0	—
Study area				
Pitt	−3.5	(−6.6, −0.5)	−2.4	(−6.0, 1.3)
Durham	−2.3	(−5.2, 0.6)	−1.3	(−4.9, 2.3)
Wake	0	—	0	—
PCBs (ppm in milk fat)	−1.1	(−2.2, 0.1)	−0.7	(−1.9, 0.6)
DDE (ppm in milk fat)	−1.1	(−1.7, −0.5)	−0.9	(−1.7, −0.1)

Dependent variable in regression is number of weeks mostly breast-fed. Independent variables are the factors listed. For categorical factors, the reference category is shown with a coefficient of zero and no confidence interval.

TABLE 3—Per Cent of Children Ever Having Upper Respiratory Infection (URI), Otitis Media (Ear), or Gastroenteritis (GI) in Various Age Intervals by Feeding Method and Contaminant Amounts

	0–3 Months					3–6 Months					6–12 Months				
			% Ever Having					% Ever Having					% Ever Having		
	mg	No. of Children	URI	Ear	GI	mg	No. of Children	URI	Ear	GI	mg	No. of Children	URI	Ear	GI
Bottle-feeders		80	16	18	24		80	28	33	13		80	48	58	25
Ex-breast-feeders		—	—	—	—		172	35	39	14		321	54	63	29
Breast-feeders		689	21	11	11		503	24	22	6		353	49	52	17
PCBs															
	0–1	74	36	22	27	0–1	71	37	25	10	0–1	54	33	50	17
	1–2	194	20	14	11	1–2	180	24	29	5	1–2	84	62	65	21
	2–3	238	22	9	8	2–3	164	23	14	6	2–3	95	48	48	15
	3–5	145	13	8	6	3–4	51	12	14	4	3–4	69	54	47	16
	5+	38	11	5	16	4+	37	16	22	3	4+	51	41	47	18
DDE															
	0–2	201	25	18	15	0–1	72	33	25	7	0–1	54	35	50	13
	2–3	153	25	12	9	1–2	113	23	23	4	1–2	64	55	55	9
	3–5	214	14	7	7	2–3	119	25	29	6	2–3	67	54	54	18
	5–8	89	18	6	11	3–5	143	21	15	7	3–5	96	51	52	20
	8+	32	19	6	17	5+	56	16	16	4	5+	72	49	51	24

For each time period, children are divided into bottle-feeders, ex-breast-feeders, and current breast-feeders. Current breast-feeders are further divided by the estimated amount (mg) of PCBs and DDE consumed during the time period. Entries are the per cent of children ever having the disease during the time period. Diseases are upper respiratory infections (URI), otitis media (ear), and gastroenteritis (GI).

previous child and who breast-feed a long time for reasons that we did not measure and thus cannot adjust for. Such women will have reduced their body burden by their longer lactations, and thus will start out their study lactation at a lower level. They will then proceed to breast-feed for a long time, thus producing an artifactual relationship between lower levels and duration. The simplest way to address this problem is to confine the analysis to women who have not previously breast-fed. This restriction reduces the number available for the analysis by 36 per cent (Table 2). The effects of DDE, education, occupation, smoking, and age are similar to those estimated in the previous analysis; the wider intervals are due to the smaller sample size. Some of the PCB effect appears artifactual since its estimate nearly is halved.

The association between DDE and duration of lactation could have occurred because employed women had to go back to work earlier and also had higher levels. We thus separated the reasons given for weaning into those relating to the child's progress (insufficient milk, poor weight gain, baby allergic to milk, baby had difficulty breast-feeding, baby became ill) and social, occupational or other reasons (inconvenient, back to work, breast infection, mother became ill). We defined lactational failure operationally as short duration of lactation (at most one month mostly breast-fed and two months until final weaning) caused by a reason from the former group. Table 1 shows that higher levels of DDE (but not PCBs) are associated with higher rates of lactational failure. If we restrict to women who have not previously breast-fed, the patterns are unchanged.

The three most common reasons for doctor visits were upper respiratory illness (including cold, flu, sore throat, and similar symptoms), otitis media, and gastroenteritis (including diarrhea, vomiting, etc.). Table 3 shows the per cent of children with these illnesses during three time periods: 0–3 months, 3–6 months, and 6–12 months. By looking within relatively short intervals, we hoped to alleviate some of the potential confounding arising since illness can terminate breast-feeding.[12] Within the intervals, the children are divided into those who never breast-fed, those who previously breast-fed but are now weaned, and those who breast-fed at some time during the period. Those who breast-fed during the period are further subdivided into groups by estimated amount of PCBs and DDE consumed during the period.

None of these diseases showed any evidence of harmful effects of PCBs or DDE; in fact, the trends usually were in the other direction. The only strong upward trend with dose was for gastroenteritis and DDE in the 6–12 month period; as there is no discernible trend in the other time periods, this may be a chance finding. Note also that the gastroenteritis rate seen at the highest DDE levels is comparable to that seen among bottle-feeders. The apparent beneficial effects of these chemicals are presumably artifactual, and arise because lower cumulative doses are partially produced by weaning early in the time period, sometimes because the child is ill. We also did analyses (data not shown) confined to children who continued to breast-feed, thus eliminating the weaning problem. The results are essentially similar.

We examined eczema, asthma, other allergy, and lower respiratory infections. These are all relatively rare at this age. There are no differences between breast-fed and bottle-fed children. There is a negative association between PCBs and lower respiratory illness and between DDE levels and allergy. Analysis of weight gain showed the familiar lighter weight among breast-fed children, but no effect of PCBs or DDE. Tabular data for all these analyses are available from the authors.

Discussion

The levels of PCBs and DDE seen in this study are as high as have been observed in the US outside of specific high-exposure situations.[5] Close comparisons among studies are not justified, since analytic methods differ, but PCB levels in these data are as high or higher than those seen in Michigan among women who regularly ate contaminated Lake Michigan fish. Thus the lack of morbidity seen here is reassuring.

More rapid weight gain is known to occur among bottle-fed children,[13] and its interpretation is not clear. For our purposes, the issue of which weight is optimal is sec-

ondary to the point that the weights do not vary by chemical level.

We see little evidence for an effect of chemical levels on morbidity. The only trends seen are a decrease in upper respiratory infections with PCBs early in lactation and an increase in gastroenteritis with DDE late in lactation. A small increase in specific illnesses cannot be ruled out, of course.

We hypothesize that the shorter duration of breast-feeding we see is more likely due to an inhibitory effect on lactation by the chemicals than to production of illness in the child and subsequent weaning. This hypothesis is consistent with the lack of association between DDE or PCB levels and increased rates of illness. DDE is a reasonable candidate to produce such toxicity. The o,p′ form of DDE (and DDT) is a weak estrogen in various animal test systems[14]; although we measured p,p′-DDE, o,p′-DDE should be proportional. Estrogens at high doses are used clinically as lactation suppressants, and initiation of lactation is carried out in a relatively estrogen-free system, although women can and do lactate after the resumption of their cycles. Contraceptive estrogens are known to decrease the duration of lactation, and it has recently been shown that as little as 30 μg/day of ethinyl estradiol lowers milk volume in Indian women.[15] Some PCBs also have estrogenic properties.[16]

Although this is a large study in terms of the number of samples analyzed, larger cohorts would have to be studied to show small effects of chemical contaminants on specific illnesses. This study is not suitable for the investigation of rare, late-onset events, such as cancer. However, we do continue to keep the cohort under clinical surveillance until age five and we plan to keep a registry intact after that.

There has been one previous report of shortened duration of lactation in association with an environmental chemical in breast milk: Weil, *et al,* observed that women exposed to polybrominated biphenyls (PBBs) during a food contamination episode in rural Michigan had shorter lactations than a control group in Ann Arbor.[17] The women had their milk analyzed and the results available in time to affect their decision to continue to lactate. There was considerable concern in Michigan about the toxicity of PBBs, and so it is plausible that women curtailed lactation on being notified of their contaminated milk.

The observation of shortened lactation with DDE in the US leads to speculation on the role of DDT and other estrogenic pesticides in the lactation failure seen in other countries. Areas with higher population DDE levels than are seen in the US offer opportunities to investigate the issue further.

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