Determinants of Polybrominated Biphenyl Serum Decay among Women in the Michigan PBB Cohort

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Accidental contamination of the food chain in Michigan in 1973 with polybrominated biphenyls (PBBs) led to the establishment of a registry of exposed individuals in 1976. Serum was collected and analyzed for PBB at the time of enrollment and for targeted studies in the following years. We used the archived PBB data to study the elimination of PBB and to identify factors associated with elimination. A total of 380 women ≥ 16 years of age who had an initial PBB level of 2 ppb and at least two serum samples drawn when they were not pregnant were included in the analysis. The mean initial PBB level was 20.9 ppb (median 4) and mean time between the first and last measurement was 4.2 years (range 0.5–11.1). PBB was assumed to reach equilibrium in the body before substantial amounts were eliminated and before the first serum measurements were taken; therefore, the entire body was modeled as a single compartment for PBB with exponential decay. Subject-specific decay rate estimates were regressed on predictor variables including initial age, body mass index (BMI), smoking history, breast-feeding duration, and parity. In women with an initial PBB level < 10 ppb, the median half-life was 12.9 years; in those with > 10 ppb, the median half-life was 28.7 years. Decay was significantly slower among women with an initial BMI at or above the median (BMI ≥ 23). The calculated half-life values are estimates of decay and can be used to estimate body burden of PBB at various points in time other than at the time of serum collection. *Key words*: body mass index, decay, elimination, half-life, pharmacokinetics, polybrominated biphenyl. *Environ Health Perspect* 108:147–152 (2000). [Online 7 January 2000] *http://ehpnet1.niehs.nih.gov/docs/2000/108p147-152blanck/abstract.html*

A mixture of polybrominated biphenyls (PBBs) was manufactured in the United States in the early 1970s under the trade name FireMaster (Michigan Chemical Co., St. Louis, MI). PBBs were used as fire retardants for molded plastic parts, such as the cases of televisions, typewriters, and business machines. In 1973, an industrial accident resulted in the inadvertent substitution of FireMaster for NutriMaster (feed-grade magnesium oxide), a nutritional supplement, into livestock feed. In the following months, many Michigan residents unknowingly ate animal and dairy products that had been contaminated with PBBs. Once the PBB contamination was discovered, public concern prompted assessment of possible adverse health consequences in exposed individuals. A pilot study was conducted in 1974 and a registry of exposed individuals was established in 1976. Details of the incident and the cohort have been described previously (*1–5*).

There is renewed interest in the possible human health effects of PBBs because of their potential role as endocrine disruptors. Endocrine-disrupting chemicals include a family of structurally similar halogenated organics that have the ability to mimic or block normal hormonal activity. They are widespread in occurrence, resistant to degradation, and accumulate in fatty tissue. These chemicals include DDT and its degradation product DDE; 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD); polychlorinated biphenyls (PCBs); and PBBs. The Michigan PBB cohort presents an opportunity to study the elimination of one member of this class of compounds from the body.

The Michigan contamination episode involved a mixture of PBBs; however, the main congener was 2,2′,4,4′,5,5′-hexabromobiphenyl (*6*), which is called PBB153 under the numbering system of Ballschmiter and Zell (*7*). Monitoring of rat feces has shown that > 90% of an oral dose of PBB153 (dose range 1–30 mg/kg) is absorbed (*8*). Results from numerous animal and *in vitro* studies have shown that congeners with at least four bromine atoms undergo little or no metabolism in animals or humans (*9*); therefore, the Michigan individuals were mainly exposed to virtually unchanged PBB153. In the absence of metabolism, elimination is a slow process. Some PBB is eliminated through feces and hair. In women, PBB can be eliminated through lactation. There is also evidence that some PBB is transferred to offspring during pregnancy (*4,10,11*). The highest PBB concentrations in the body are found in adipose tissue, but it can also be detected at lower concentrations in serum and other lipid-rich tissues, such as the skin and liver.

There are two previous reports of serum PBB half-life in women. Both of these studies were conducted using data from the Michigan PBB cohort (*12,13*). The Lambert et al. (*12*) study was based on two serum measurements from 15 women ≥ 20 years of age with an initial PBB level of at least 5 ppb and whose previous value was greater than the current value. This small study found a median half-life of 12.0 years [95% confidence interval (CI), 4–97]. The analysis by Rosen et al. (*13*) included 51 women ≥ 18 years of age with two to four PBB measurements and an initial PBB level of at least 20 ppb. This study found a mean half-life of 13.0 years (CI, 6.3–infinite) and a median of 18.5 years (CI, 9.5–40.1). In the Rosen et al. (*13*) study, the estimation of half-life differed in men (14.2 years) and women (infinite years) in the highest quartile of body mass index (BMI). Neither of these studies examined the effect of breast-feeding duration, pregnancy, or smoking history on PBB elimination.

The objective of the present analysis was to determine the decay of PBB in the serum of women with a broad range of PBB levels and to determine whether a number of covariates, such as age, BMI, smoking history, pregnancy, and breast-feeding duration, are associated with PBB elimination. This analysis may also aid in understanding the elimination of PCB153 (the analogous

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PCB congener), which is a major component of human milk samples (ranging from 12 to 43% of total PCBs) (*14,15*).

Methods

Study population. From 1976 through 1978, the Michigan Department of Public Health (Lansing, MI) enrolled into an exposure registry > 4,000 persons who primarily lived on or received food from farms that had animals with at least 1 ppm PBB in milk or tissue fat. During the initial enrollment, informed consent was given, a health questionnaire was completed, and a serum sample was drawn and later analyzed for PBB and other chemicals. Additional serum samples were drawn at other times from some members of the cohort for various reasons, including for use in follow-up studies performed from 1982 through 1987 and for additional tests at individuals' requests. Cohort members with higher initial PBB levels were more likely to have multiple measurements because they were oversampled in various follow-up studies (*12*). In 1997, a total of 2,262 women in the registry had at least one PBB measurement and 1,407 (62%) had two measurements. We used the measurements from these 1,407 women for the current study.

To be included in this study, a woman had to have at least two serum PBB measurements taken at least 6 months apart while the woman was not pregnant, she had to have been at least 16 years of age at the time of the initial measurement, and she had to have had an initial measurement of at least 2 ppb PBB (Table 1). We chose 2 ppb because it is twice the limit of detection (LOD) and allows generalization of the results to the majority of the cohort. The age and pregnancy criteria were imposed because both may affect measured PBB levels (*16,17*). The level of PBB in a child's serum decreases as the child grows because of dilution caused by increasing body weight. Pregnancy may cause the mobilization of chemicals from storage tissue to serum, resulting in inflated serum levels (*16*). Using these criteria, 380 women were eligible for this study. Samples for the initial PBB measurements were obtained from January 1976 to May 1980 and samples for the last PBB measurements were obtained from February 1977 to January 1988.

Information on covariates that were thought to influence elimination of PBBs was obtained primarily from a 1997 telephone interview of participating adult female members of the cohort. The interview included detailed questions on pregnancies and breast-feeding duration. Archived data were used to obtain participant age, height, and weight at initial PBB measurement, as well as smoking status in 1976–1978, 1990–1994, and 1997. BMI (in kilograms per square meter) was used as the measure of adiposity at initial PBB measurement.

PBB measurement. PBBs were measured in human serum using gas chromatography with electron capture detection (*18–20*). The denatured serum sample first undergoes an ether–ethyl or hexane–ether extraction and is then passed through either a Florisil or Florisil and silica gel column (*20*). Quantitation of PBB was based on PBB153. The size of this peak in the serum sample is measured relative to the size of this peak in a control sample containing a known weight of FireMaster (*18*). The methods of PBB detection used in this study have coefficients of variation of 7.1–14.0% and recovery ranges of 80–90% (*18*).

PBB levels < 1.0 ppb, the LOD, were assigned a value of 0.5 ppb. This level was chosen because it is halfway between zero and the LOD and allows for log-transformation of the data. This technique was used previously in a study of PCB-exposed women (*21*) and, in highly skewed distributions (such as the present data), it is an appropriate estimation technique (*22*).

Kinetic estimation. To explore the kinetics of PBB elimination, we used a technique known as the method of residuals or feathering (*23*). We first graphed $\ln PBB_{1 \text{ to } ki}$ against time_{ij}. We then attempted to extrapolate the terminal straight-line portion of the curve back to the *y*-axis. We did this for the serum PBB profiles of women with at least five serum PBB measurements and at least 10 years between the first and last measurements ($n = 16$). Inspection of the graphs for these women did not reveal any evidence for multiple body compartments involved in the elimination of PBB from serum. This is consistent with the data of Wolff et al. (*24*), who showed that equilibrium between serum and adipose tissue was probably reached by 1976—2 years after exposure. All of the serum measurements used in this study were taken at least 2 years after exposure. Because of a lack of multiple measurements on women with low PBB levels, we were not able to graphically assess whether there was a dose-related transition from linear to nonlinear kinetics.

Statistical analysis. Because there was no apparent metabolism of PBB153 and there were no serum measurements taken during the initial distributional phase (*24*), we modeled the entire body as a single compartment for PBB; therefore, assuming a linear one-compartment open model for PBB elimination, the initial and subsequent concentrations of PBB are therefore related by the following formula:

$$C(t) = C_0 e^{-\lambda t},$$

where $C(t)$ represents concentration at time t, C_0 represents PBB concentration at initial time, and λ is the rate of decay. If both sides are log-transformed a linear relationship is obtained: $\ln[C(t)] = \ln(C_0) - \lambda t$. Thus, given a set of successive PBB measurements, i.e., $[C(t_1), \ldots, C(t_k)]$ on a participant at times $[t_1, \ldots, t_k]$, a rate constant, λ, can be estimated from the slope of the linear regression of $\ln[C(t)]$ versus t (*25*). The corresponding half-life is then equal to $t_{1/2} = \ln(2)/-\lambda$, the time after which the original concentration has been halved (*26*).

Using a linear regression of the natural logarithm of all eligible PBB measurements (range 2–9) versus the time since first level, i.e., $\ln PBB_{1 \text{ to } ki} = B_{0i} + B_{1i}(\text{time}_{ij}) + \varepsilon_{ij}$, we estimated the overall decay rate ($\lambda_i = -B_{1i}$) for each woman. Because of its positively skewed distribution, the PBB level was $\log_e$ transformed for use as a continuous variable in the regression analysis.

Table 1. Female participants by inclusion criteria in the Michigan PBB cohort eligible for the serum PBB decay analysis.

No.	Criteria
2,262	Females enrolled in the Michigan PBB cohort
1,407	At least two serum PBB measurements
950	Initial measurement ≥ 2 ppb PBB
943	Initial and last measurements > 6 months apart
737	At least 16 years of age at time of initial measurement
380	Measurements known to not have been taken during pregnancy

Table 2. Characteristics of PBB serum samples included in decay analysis.

Serum samples (n)[a]	Samples (frequency)	Samples (%)	Mean initial PBB level (ppb)	Mean time between first and last PBB level (years)
2	240	63.2	6.7	2.7
3	84	22.1	13.9	6.3
4	35	9.2	33.8	6.7
5	14	3.7	106.7	9.2
6	2	0.5	396.5	10.2
7	2	0.5	56.5	6.5
8	2	0.5	321.8	10.8
9	1	0.3	933.0	10.2
Total	380	100	20.9	4.2

[a]Per individual.

To evaluate the predictive value of covariates, the covariates were regressed against the subject-specific decay rates (λ_i) using multiple linear regression. Participants who were missing information on any one of the covariates were excluded from the analysis (n = 41), resulting in a total of 339 women for the multivariate analysis. The mean PBB level among those participants with values for all potential predictor variables was virtually identical to the mean PBB among those participants missing at least one predictor variable (5.52 vs. 5.75 ppb, t-test p = 0.84). The covariates examined were initial PBB level (continuous and tertiles); age at initial measurement (continuous and categorized as < 18, 18–50, and > 50 years of age); BMI at initial measurement (continuous, median, and tertiles); smoking history between first and last measurement (ever- versus non-smoker); number of full-term pregnancies between first and last measurement (continuous and categories of 0, 1, and ≥ 2); and total breast-feeding duration in months between first and last measurement (continuous and tertiles). The total duration of breast-feeding was calculated as the number of months the child was fed mainly breast milk plus half the number of months the child was breastfed with supplementation. This equation was based on work by Rogan et al. (*27*) and Wickizer and Brilliant (*28*).

All main-effect variables were included in the initial model. All biologically plausible two-way interaction terms were added to the initial model to assess effect modification. These terms included age × smoking status, age × breast-feeding, age × initial PBB, BMI × pregnancy, BMI × initial PBB, and breast-feeding × initial PBB. We used $\alpha = 0.05$ as a cutoff for retaining variables in the model. Covariates that altered the estimate for PBB exposure by > 10% were retained in the model as confounders. Alternate regression models (e.g., second-order and spline models) were fitted to determine whether they were more appropriate than a straight-line model. Splines have been defined as segmented (piecewise) polynomials of order r, which agree up to derivatives of order 0, to r - 2 at points where they join; the abscissas of these joints are called knots or break points (*29,30*). Splines allow modeling of two or more lines or two or more parabolas in the same regression model. In this analysis, splines are used to describe the kinetics of low PBB doses and to describe the possible departure of the higher PBB dose kinetics (*31*). Knots for this analysis were based on visual inspection of plots of mean decay versus PBB level (i.e., the rate of decay increase was roughly constant until it reached approximately the initial PBB level of 10 ppb, at which point there was slowing of decay). Partial F-tests and adjusted R^2 comparisons were used to assess whether alternative regression models were more appropriate than a straight-line model. Collinearity and regression diagnostics were performed on the multivariate models of decay rate. Diagnostics included plots of both studentized and jackknife residuals versus the predicted value of decay rate. The residual plots revealed eight gross outliers that were more than 3 SD from the mean of the residuals. These outliers were determined not to be data entry errors and were removed from the multivariate analyses. Plots of the residuals versus predicted value of decay rate did not reveal any gross violations of homoscedasticity. We analyzed Cook's distances and leverage values (h_i) for influential predictor values. We also assessed delta betas (the difference in the parameter estimate on deletion of the corresponding observation) of high leverage values. Variance inflation factors and condition indices did not reveal collinearity problems. The main effect covariates (age, BMI, smoking status, breast-feeding duration, and number of pregnancies) were kept in the final model presented here because their influence on elimination, regardless of significance, was a primary objective of this analysis. All analyses were performed using SAS 6.12 (*32*).

Results

Descriptive PBB measurement information for the 380 females in the study group is shown in Table 2. Mean initial serum level was 20.9 ppb (SD 78.7) and mean time between first and last measurement was 4.2 years (range 0.5–11.1 years). A total of 140 (37%) of the 380 women had three or more measurements. The mean age at the time of the initial PBB sample was 33.7 years (range 16.0–75.2). Women with higher PBB levels had a greater number of measurements.

A total of 109 females (29%) did not have a reduction in serum PBB over time. This was not a phenomenon restricted to the lower concentrations, as might be expected due to greater measurement error near the LOD. The proportion of women with no decay based on their initial PBB level were as follows: ≤ 4 ppb, 32.2%; 5–10 ppb, 23.2%; 11–20 ppb, 35.5%; 21–100 ppb, 18.7%; and > 100 ppb, 23.1%.

The decay rate was slower, resulting in a longer half-life, with higher initial PBB levels (Table 3). Characteristics of the study population for multivariate analyses are shown in Table 4. Table 5 shows results for the final multivariate model. Models with linear and quadratic splines (with knots at 10 and/or 90 ppb) did not improve the fit of the model (data not shown). A second-order polynomial model of initial PBB level was more appropriate than a straight-line model. We found a slower PBB decay rate in women with an initial BMI above the median (p = 0.03). The number of pregnancies was of borderline significance (p = 0.06). A comparison of the number of pregnancies as a continuous variable from 0 to 4 and as a continuous variable by collapsing women

Table 3. Decay rates and corresponding half-life estimates for all eligible females by initial PBB level.

		Decay rate (years^{-1})		PBB half-life (years)			
Initial PBB	No.	Mean	Median	Mean	CI	Median	CI
2–4 ppb	205	-0.155	-0.086	4.5	3.5–6.2	8.1	5.1–infinite
5–10 ppb	99	-0.099	-0.069	7.0	4.6–15.0	10.1	7.2–13.5
11–20 ppb	31	-0.052	-0.032	16.2	7.3–80.1	29.8	16.2–infinite
21–100 ppb	32	-0.032	-0.023	21.6	17.4–28.5	30.8	14.7–73.5
> 100 ppb	13	-0.040	-0.026	17.5	9.5–106.7	27.2	12.1–212.3
Total	380	-0.118	-0.051	5.9	4.8–7.7	13.5	10.5–23.2

Table 4. Characteristics of serum PBB decay study participants included in multivariate regression models.

Variable	No.	%
Age		
< 18 years	47	12.4
18–50 years	278	73.1
> 50 years	55	14.5
BMI		
< 23.0	188	49.9
> 23.0	189	50.1
Smoker		
Never	324	85.3
Ever	56	14.7
Months breast-feeding		
< 3 months	314	92.4
3–9 months	13	3.8
> 9 months	13	3.8
Pregnancies		
0	292	76.8
1	63	16.6
2	18	4.7
3	5	1.3
4	2	0.5

Table 5. Results of the multivariate analysis of predictors of serum PBB decay.

Predictor variable[a]	Parameter estimate	SE	p-Value
Intercept	-0.227	0.044	0.001
Initial PBB level	0.031	0.028	0.269
(Initial PBB level)^2	-0.002	0.005	0.663
BMI[b]	0.050	0.023	0.032
Pregnancies	0.038	0.021	0.064
Age (years)	0.001	0.001	0.122
Ever smoker[c]	-0.031	0.029	0.288
Breastfed (months)	-0.003	0.004	0.463

Effect of predictors on serum PBB yearly decay.
[a]Variables continuous if not noted. [b]BMI (0, < median; 1, ≥ median). [c]Ever smoked (0, no; 1, yes).

with ≥ 2 pregnancies (0–2) showed that most of the effect of this variable on decay rate is in women who had 3 or 4 pregnancies. The effects of BMI and pregnancy were the same regardless of the model fitted. Neither age nor smoking was associated with serum decay of PBB.

Weighting the estimates based on the number of measurements per woman did not substantially alter overall parameter estimates. A sensitivity analysis of the full model that excluded females < 18 years of age (n = 293) at the time of initial PBB measurement did not result in appreciable differences in parameter estimates; however, BMI was only of borderline significance (p = 0.09), with a reduction from 0.050 in the full model to 0.040 in the age-limited model. The estimate for ever-smoking also changed from -0.031 in the full model to -0.043 in the age-limited model. To separate the effects of pregnancy and breast-feeding, we analyzed separately the data for women who did not breast-feed. The analysis of women who did not breast-feed (n = 295) resulted in similar directionality of effect for each of the parameters; however, the parameter estimate was slightly reduced for pregnancies from 0.039 (p = 0.06) in the full model to 0.033 (p = 0.18) in the stratified data.

Assessment of breast-feeding duration as ever/never or tertiles of duration did not appreciably alter the results. The parameter estimates for breast-feeding (ever/never) was 0.0303 (p = 0.49). The parameter estimates for the middle and upper tertiles of breast-feeding duration were 0.0014 (p = 0.98) and -0.0469 (p = 0.45), which were consistent with the lack of effect on serum decay observed with the continuous variable.

Half-life estimates of serum PBB in women with various scenarios are shown in Table 6. Two parts per billion is shown because it reflects the median initial PBB level among women actively participating in the Michigan cohort in 1997.

Discussion

We estimated the decay rate of serum PBB among women with multiple serum PBB determinations between 1976 and 1988. Thirty-seven percent of women had ≥ 3 serum PBB measurements and 29% of women did not have a reduction in their PBB values over time. Women with an initial PBB level < 10 ppb had a median half-life for PBB of approximately 12.9 years and women with an initial PBB level > 10 ppb had a median half-life of approximately 28.7 years. We found that PBB decay was significantly slower, resulting in a longer half-life, in women with an initial BMI at or above the median for this population (BMI ≥ 23). A borderline significant effect was observed for the number of pregnancies. PBB decay was slower and was inversely related to number of pregnancies. No significant change in the decay estimate was observed with age, smoking history, or breast-feeding duration.

Table 6. Estimates of half-life in years for serum PBB in women with various scenarios.

Initial serum PBB (ppb)	Initial BMI	Decay rate/ years	Half-life (years)
2	< 23	-0.169	4.10
5	< 23	-0.082	8.45
2	≥ 23	-0.119	5.82
5	≥ 23	-0.032	21.7

The fact that a proportion of participants showed no decline in measured PBB over time is not surprising given the errors in measurement and other unmeasured contributors to decay. These sources of unmeasured error in our study include changes that could result in a lack of serum decay over time. These include changes in an individual's weight, the lack of lipid adjustment or the fact that the serum samples might not be fasting, continued exposure to PBB, medication use by participants, and age-related changes including lipid concentrations and hepatic enzyme induction. We cannot eliminate the possibility that some individuals received continued exposure to PBB despite public health interventions (e.g., manure from some of the exposed cows could have been left on the fields, leading to potential subsequent exposure of replacement herds).

The unmetabolized PBB153 and its analogous PCB congener have an average half-life of at least 10 years (*13,33*). PBB, like other highly persistent chemicals, is therefore assumed to be in equilibrium among the organs and tissues before substantial amounts are eliminated (*34*) and was likely in equilibrium before the first serum measurements were taken in participants of the PBB registry (*24*). Wolff et al. (*24*) suggested that PBB equilibrium should have been achieved in the Michigan cohort by November 1976. Consistent with equilibrium, graphs of log-transformed serum PBB concentration versus time in years (in candidate women) did not suggest multicompartment effects; therefore, a simple exponential decay model was used in the current analysis. That longer half-lives were found with higher initial PBB levels suggests that PBB elimination may be a saturable process at higher exposures resulting in different distribution patterns or, more likely, that there are unmeasured sources of variability. In the latter case, there are examples where nonlinearity may be difficult to distinguish from experimental variability (*23*).

We do not believe that greater measurement error near the LOD accounts for the shortened half-life in women with low initial PBB levels because the coefficients of variation over a range of PBB concentrations appear to be similar (*18,19*). Specifically, Needham et al. (*18*) found coefficients of variation for PBB of 8.4–13.8% for a target value of 10 ppb, 14.0% for a target value of 41 ppb, 8.7% for a target value of 164 ppb, and 7.1% for a target value of 484 ppb. In an interlaboratory comparison of PBB detection in human serum, Burse et al. (*19*) reported that the Michigan Department of Public Health (the agency that performed the PBB measurement in the current study) had the following coefficients of variation for serum PBB: 3.2% for a target value of 5 ppb, 3.6% for a target value of 25 ppb, 2.2% for a target value of 50 ppb, 3.1% for a target value of 500 ppb, and 2.4% for a target value of 1,000 ppb.

A kinetic study could properly characterize the possible nonlinear elimination, much like that done to assess trichloroethylene (*35*). Previous PBB animal studies have failed to use a range of dosing levels when examining PBB elimination. A pharmacokinetic model in growing rats used a compartmental model to simulate the time course of a dose of 1 mg/kg of PBB in rat tissues and feces (*36*). Tissues examined included adipose, skin, muscle, liver, and blood. Scaling the model predictions to humans, this study estimated a half-life of 6.5 years for humans. In a separate rat study, the concentration of PBB in serum and other tissues was determined in rats given a single dose of PBB (0.5 mg/kg). This study reported that elimination of PBB from fat and serum in the rat followed first-order kinetics (*37*).

Initial BMI values above the median (≥ 23) for the study group was associated with slower PBB decay, suggesting that there is a greater retention of PBBs in women with greater amounts of adipose tissue. Michalek et al. (*38*) noted that this might be explained by the affinity of the chemical for adipose tissue. Rosen et al. (*13*) found an increased PBB half-life with higher BMI in this cohort, and increased PBB half-life with higher BMI has also been found with TCDD, polychlorinated dibenzo-*p*-furans, and polychlorinated dibenzo-*p*-dioxins (*39,40*).

Increasing parity between the first and last PBB measurement was associated with slower decay, but the effect was of borderline significance. Because transplacental passage from the mother to the fetus is expected to be a minor route of PBB elimination, this result was unexpected. It is possible that the redistribution of PBB between organs and serum due to pregnancy results in a period postpartum during which serum PBB may be increased or excretion of PBBs may be reduced. It is also possible that weight gain after pregnancy may increase the reservoir for PBB storage and lengthen half-life. Laden et al. (*41*) found elevated PCB levels

in parous women, regardless of the number of children and age at first birth, as compared to nulliparous women ($p = 0.001$).

Breast-feeding as either a continuous variable or as categorized by tertiles of duration (< 3 months, 3–9 months, or > 9 months) was not associated with decay. Studies of PCBs have found decreases of 20–38% in maternal serum PCBs with each 6-month lactation period (*42,43*). A total of 35 of 85 women (41.2%) who had given birth during the study period reported some amount of breast-feeding between the first and last PBB measurement; however, only 20 (6% of the multivariate study group) reported a breast-feeding duration of at least 6 months.

This study found a median PBB half-life of 13.5 years. Although there is lack of good data on congener-specific PCBs, researchers in one study of 39 occupationally exposed workers in the United States collected serum in 1976, 1979, and 1983 and found a geometric mean serum half-life of 12.4 years for PCB153 (*33*).

One strength of this study is that the results can be generalized to the majority of the female cohort members because we included women at the lower range of the observed dose of PBB; however, there are a number of limitations to our analysis. In our model, processes such as protein binding and induction of cytochrome P450 enzymes were not explicitly incorporated. In addition, 63% of women had only two PBB measurements. Because the majority of women had only two serum draws and some of the determinations were taken at intervals < 1 half-life, the median half-life and its corresponding 95% confidence interval is reported as a possibly less biased estimate (*44*). The broad confidence intervals around the median for women with low initial PBB levels in Table 3 probably reflect the short mean interval for these particular women (Table 2).

Lambert et al. (*12*) showed that among members of the PBB cohort there was substantial variability in enzyme activity among women, as assessed by the caffeine breath test. Much of this variability may be due to polymorphisms of the genes that regulate metabolizing enzymes. In addition, age, nutrition, hormone use, and hepatic disease can affect microsomal substrate metabolism (*45,46*). Studies concerning age and P450 enzyme activity are inconsistent and appear to be substrate specific (*47,48*). Although age was not a significant predictor of PBB decay in our study, Flesch-Janys et al. (*39*) found that increasing age was related to increasing half-life of polychlorinated dibenzo-*p*-dioxins and dibenzofurans. These authors suggest that age affected P450 (specifically CYP1A1 and CYP1A2) induction. We did not have data on nutrition, medication, or oral contraceptive use.

We lacked information on changes in weight over time. When rats are fed a single dose of PCB153 and there is no change in weight, the decay is first-order with reversible storage and total elimination (*49*). In rats with a shrinking adipose compartment, the fecal excretion rate increased up to 10-fold and the skin became an alternative storage depot (*50*). Wyss et al. (*50*) concluded that irreversible storage and limited elimination in the rat was due to steady enlargement of the adipose tissue compartment over time. Because weight was not assessed at each of the serum draws, we only have initial BMI as a measure of adiposity, and we were not able to assess the effect of change in adiposity on decay. It is possible that large fluctuations in adipose tissue mass due to intentional or unintentional weight loss, resulting in redistribution between adipose and serum levels, might result in a lack of serum PBB decline over time. In studies of TCDD, neither reported weight loss nor relative change in percent body fat were associated with serum TCDD levels over time or TCDD decay, respectively (*40*). However, Zober and Papke (*51*) found that after severe weight loss, such as cancer cachexia, blood levels of 2,3,7,8-TCDD increased. At autopsy of dioxin-exposed individuals who died from cancer and had reported weight loss in the months before death, blood levels of 2,3,7,8-TCDD increased from 17 to 32 ppt in one individual and from 518 to 7,482 ppt in another individual. The preautopsy blood levels were taken 5 and 8 months before death, respectively. Because regulation of fat mobilization is not well understood, further study of this phenomenon is needed to determine how organisms handle unmetabolizable and persistent compounds (*52*).

Another possible limitation of the data is that participants were not given instructions about fasting before the serum draw. There is no record of fasting status, and PBB levels were not corrected by total lipids. Phillips et al. (*53*) observed higher nonfasting levels of serum PCBs as compared to fasting serum samples. It is possible that the lack of lipid adjustment is likely to add a small amount of error to the PBB measurement in the current study, potentially resulting in slower or stable half-lifes. That PBB decline was not related to age in our data argues that an age-related lipid effect is extremely small.

The PBB detection methods used in this study have changed over time. During the years 1976–1978, the extraction method was used to detect PBBs. From 1978 to 1982 the dual determination (combined) method was used to detect both PBBs and PCBs. Starting in 1982, the pesticide scan method was used to detect PBBs, DDE, DDT, oxychlordane, *trans*-nonachlor, and mirex. Although the methods have changed over time, Kreiss et al. (*54*), who compared the extraction and dual determination methods, concluded that there was no difference in PBB concentration obtained by the two methods. Specifically, they reanalyzed serum samples collected in 1977 by the combined method (n = 1,622) and serum samples collected in 1978 by the extraction method (n = 609) to determine the comparability of the results obtained. The median difference between the 1,622 paired PBB samples analyzed by the two methods was zero; the median difference in 609 paired PBB levels by extraction and combined method was also zero. The pesticide scan method was used for better separation of DDE from PCBs, with no change in detection of PBB.

We estimated a mean PBB half-life for women in this study with an initial level of 20 ppb as 20.8 years (CI, 14.9–34.6 years) and median half-life as 28.7 years (22.3–41.04 years). Rosen and colleagues (*13*) reported a mean half-life of 13.0 years (CI, 6.3–infinite) and median half-life of 18.5 years (CI 9.5–40.1). Differences in inclusion criteria may account for the differences in half-life found in this study as compared to that found by Rosen et al. (*13*), who used only samples taken before 1983. Rosen et al. (*13*) had a sample size of 51, with a maximum of four measurements for any one participant and a 6-year maximum time between measurements. Rosen's study assessed whether initial PBB level, first year of measurement, BMI, and age were predictors of the decay rate. Only BMI was predictive of decay. The estimated half-life for women in the highest quartile of BMI was infinite. It is not surprising that initial PBB level was not an important predictor in the Rosen et al. (*13*) study because the inclusion criteria limited the analysis to women with an initial PBB level of at least 20 ppb. We found similar half-lives for women with a broad range of initial PBB levels > 21 ppb.

The model developed here may be useful to other researchers who are interested in reconstructing exposure levels to PBBs or to similar organochlorines. In studies of individuals for whom a single serum level is available, the level of chemical at times other than when the serum was collected may be estimated by use of such a model. Because analogous PBB and PCB congeners are expected to have similar toxicokinetics, the results of this study also may be relevant to studies involving the more highly chlorinated PCB congeners, particularly the commonly occurring congener PCB153.

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