Great Lakes sport-caught fish are contaminated with various organochlorines (OCs) such as polychlorinated biphenyls (PCBs). Through consumption of these fish, humans are subject to continuing levels of OC contamination. To assess potential adverse effects of past exposure, we compared three different backward extrapolation models. The data originated from OC determinations in a cohort of anglers and their families. Repeated PCB measurements collected in the 1970s, 1980s, and 1990s were used when testing the backward extrapolations. We applied a simple and a complex decay model based on assumptions used in previous studies; a third was a regression model incorporating markers of OC intake and loss. These techniques provided past exposure estimates. Intraclass correlation coefficients (ICCs) were calculated comparing measured and estimated PCB values. ICC values for the regression model equations were 0.77 and 0.89; ICC values for the simple and complex decay models were significantly lower, with ranges of 0.07–0.45 and –0.14–0.69, respectively. Plots showing trends of OC concentrations in fish and humans indicate comparable increases and decreases of PCB in fish and humans, with fish concentrations peaking approximately 10 years before that in humans. Our findings suggest that one should be cautious when using simple backward extrapolation techniques to estimate OC exposure in situations involving changing environmental exposures. Whenever repeated measurements are available, regression analyses seem to produce more accurate backward estimations of exposure. Key words: backward extrapolation, epidemiology, exposure assessment, fish consumption, Great Lakes, organochlorines.

**Environmental Health Perspectives** 112:710–716 (2004). doi:10.1289/ehp.6761 available via http://dx.doi.org/ [Online 4 February 2004]
(years between two PCB determinations) were used in the development of the model.

In this study, we focused on maternal PCB concentrations collected for each of three surveys completed over a 19-year span from 1973 through 1991. We were prompted toward this work because of our interest in adverse reproductive outcomes in the offspring of women who ate fish. Most participants had birth dates between 1950 and 1980. The measurements between 1973 and 1991 do not coincide with the dates of their pregnancies and therefore do not directly reflect the OC concentrations to which their offspring were exposed during pregnancy.

We tested how well the models described above would predict actual OC determinations collected in the past. Repeated OC measurements allowed us to calculate intraclass correlation coefficients (ICCs) comparing actual and estimated values for each of the proposed extrapolation models. This statistic is used to assess how well the backward estimations fit the past OC determinations, thereby determining the efficacy of each model for the backward extrapolation of PCB concentrations involving repeated measurements (Armstrong et al. 1992).

Materials and Methods

Population. In the 1970s, the Michigan Department of Community Health (MDCH) established a cohort of anglers and their families who consumed sport-caught fish, in order to monitor their body burden of PCBs (Humphrey 1983b). To assess the level of PCB contamination in these families due to fish consumption, the MDCH conducted three surveys in 1973–1974, 1979–1982, and 1989–1991, known as the Great Lakes Fish Eaters Studies. MDCH workers recruited anglers and their spouses at sites of fishing activities (e.g., docks, marinas, and bait shops) in 11 Lake Michigan shoreline counties. By the end of the third survey, the cohort totaled 1,177 individuals with PCB determinations, including 419 women.

OC concentrations in fish. In order to determine the degree to which the environmental load of OCs has changed and to compare this change with human data, we gathered information on PCBs in fish from Lake Michigan. Because of similar chemical characteristics and for the sake of comparison, we also collected data on dichlorodiphenyl dichloroethylene (DDE) in fish. PCB and DDE concentrations in fish collected over a range of years were identified through the National Library of Medicine by means of an extensive PubMed literature search [De Vault et al. 1996; Gerstenberger and Dellinger 2002; Great Lakes National Program Office (GLNPO) 2003; Manchester-Neessvig et al. 2001; Neidermeyer and Hickey 1976; Veith 1975; Willford et al. 1975]. We were able to identify fish exposure information from 1929 through 1998. The fish used in the determination of PCB and DDE data for the period of 1929 to approximately 1970 were properly stored in formaldehyde or ethyl alcohol. The OC measurements were then conducted in the 1970s. Exposure levels from different Lake Michigan fish species over this time interval were converted into lipid-based concentrations determined by the percentage of fat recorded for each species of fish used in this process. This conversion eliminated the effect of varying fat content in different fish species. An additional reason for lipid-based determinations is that storage in formaldehyde or ethyl alcohol led to dehydrated fish tissues in some historical samples. The values were then condensed into 5-year intervals.

For the graphs representing time trends in PCB and DDE concentrations in fish, smooth bands were used to indicate levels of exposure in 5-year intervals during the period from 1929 through 1998. Because of the wide variation in PCB and DDE values in different species of fish, a spline routine was used to develop two smooth lines to represent the minimum and maximum levels of PCB and DDE in fish over each time interval. The area between these two lines was then filled in to produce a smooth band that represented the average amount of PCB and DDE contamination in fish over time.

Using external information on fish as a main source of exposure is comparable with the exposure assessment used in other locations, such as Seveso, Italy. Needham et al. (1999) proposed the development of several indices through measurements obtained from source emissions, the environment, and subjects in the chemical plant’s surrounding area, around the time of the explosion. We used corroboration data regarding fish contamination to investigate whether the time trend of PCB contamination in sport-caught fish and anglers is comparable.

PCB determinations in human serum. Analyses of serum specimens were performed by the MDCH Health Risk Assessment Laboratory (Lansing, MI) using a modified Webb-McCall packed column gas chromatography technique to measure serum PCB levels in each study participant. The methodology for this laboratory analysis has been previously reported (Hovinga et al. 1992; Humphrey 1983a; Price et al. 1986). To compare PCB exposures, we used measurements based on the Aroclor 1260 standard that measures the more highly chlorinated PCB congeners. The technical detection limit for PCBs was 3 µg/kg in all three surveys.

Backward extrapolation models. Various assumptions and equations were proposed to account for changes in exposure and reduction of PCBs in the backward extrapolation models (Table 1). We applied these models to determine the extent to which estimated PCB levels concur with PCB concentrations measured in the past.

The decay model of Weisskopf et al. (2003) only included a term for the natural decay of the measured OC exposure. PCB half-lives of 4.6, 8.7, and 11.6 years, corresponding to the suggested decay constants of 0.06, 0.08, and 0.15, were applied.

Rylander et al. (1998) proposed a more complex decay scenario. The authors used different PCB half-lives of 1.5, 10, 15, and 20 years. Other assumptions were the 25, 33, 50, and 67% loss in PCB body burden at each lactation period, and a yearly reduction of the PCB concentration in fish of 1, 3, 5, 8, and 10%. However, Rylander et al. (1998) did not provide an average intake of PCB from fish. Hence, we additionally included an estimated average PCB intake from fish for each participant based on PCB concentrations in frequently consumed fish (2 µg/ounce), number of servings consumed, an 87% loss in PCB contamination due to trimming and cooking techniques used during food preparation to reduce the amount of fatty tissue consumed (multiplier of 0.13) (Zabik et al. 1995), and an absorption of PCB from fish equal to 50% (Bund/Länder-Arbeitsgruppe Dioxine 1991).

For each of these models, we tested two backward extrapolation equations, one for the period from 1991 through 1979 and one from 1982 through 1973.

Linear regression modeling. Serum samples were collected and PCB concentrations were determined in 1973–1974, 1979–1982, and 1989–1991. We developed two models that regressed participants’ PCB determinations from one survey (T) period back to the preceding survey period (T – 1), whenever measurements for both periods were present. Because of the presence of a skewed distribution for the PCB determinations at the 1989–1991 survey period, log10 PCB concentrations were used for this variable in the
regression modeling. The PCB determinations from the 1973–1974 and 1979–1982 surveys followed normal distributions; therefore, the original PCB concentrations were preserved in the regression modeling. As potential predictors, we employed the PCB concentration at \( T \), the interval between the two PCB determinations, total years of fish consumption, amount of fish meals consumed, number of pregnancies and lactation periods between two measurements, maternal age, and birth year of the mother. This information was collected in the surveys that accompanied the PCB determinations.

The regression equations were used to calculate the participant’s level of PCB exposure for the preceding survey period. We compared the estimated PCB concentration at \( (T − 1) \) with the measured concentration at \( (T − 1) \) using the ICC. To achieve a most parsimonious explanatory model, we then used the ICC to determine whether we could eliminate predictors that did not explain the earlier PCB concentrations.

### Table 1. Overview of backward extrapolation equations, assumptions, and variables.

| Extrapolation equations | Model assumptions and variables |
|------------------------|--------------------------------|
| Weijskopf et al. (2003) | Assumptions of modified complex decay model |
| \( (OC)_i = (OC)_m * e^{\lambda * t} \) | a) Fish OC decay constants of 0.06, 0.08, and 0.15 (Weijskopf et al. 2003) |
| **Simple decay model** | Variables of modified complex decay model |
| \( pcb_{80}(\text{estimated}) = pcb_{90} * e^{\lambda * t} \) | a) \( pcb_{90} = \text{measured PCB concentration at 1989–1991 survey} \) |
| \( pcb_{70}(\text{estimated}) = pcb_{80} * e^{\beta * \phi} \) | b) \( pcb_{80} = \text{measured PCB concentration at 1979–1982 survey} \) |
| **Complex decay model** | c) \( e^{\lambda * t} = \text{OC decay rate over time} \) |
| \( (OC)_i = A_{ij} * (1 - e^{\beta * \phi}) \) | Assumptions of modified simple decay model |
| **Assumptions** | a) Great Lakes fish PCB concentrations follow first-order kinetics |
| \( \alpha = 0.13 \) | b) Fish OC decay constants of 0.06, 0.08, and 0.15 (Weijskopf et al. 2003) |
| **Needham et al. (1999)** | Variables of modified simple decay model |
| Used age and sex-delineated data to produce accurate exposure indices | a) \( pcb_{90} = \text{measured PCB concentration at 1989–1991 survey} \) |
| | b) \( pcb_{80} = \text{measured PCB concentration at 1979–1982 survey} \) |
| | c) \( e^{\lambda * t} = \text{OC decay rate over time} \) |
| Assumptions of modified complex decay model | Assumptions of modified simple decay model |
| \( (OC)_i = A_{ij} * (1 - e^{\beta * \phi}) \) | a) \( pcb_{90} = \text{measured PCB concentration at 1989–1991 survey} \) |
| \( (OC)_i = A_{ij} * \) | b) \( pcb_{80} = \text{measured PCB concentration at 1979–1982 survey} \) |
| \( \sigma = \text{number of fish servings consumed} \) | c) \( e^{\lambda * t} = \text{OC decay rate over time} \) |
| **Proposed regression model** | Assumptions of modified complex decay model |
| \( PCB_{70}(\text{estimated}) = \text{estimated PCB concentration at 1970s survey} \) | a) \( pcb_{90} = \text{measured PCB concentration at 1989–1991 survey} \) |
| \( PCB_{80}(\text{estimated}) = \text{estimated PCB concentration at 1980s survey} \) | b) \( pcb_{80} = \text{measured PCB concentration at 1979–1982 survey} \) |
| \( PCB_{70}(\text{estimated}) = \text{measured PCB concentration in 1979–1982 survey} \) | c) \( PCB_{80} = \text{measured PCB concentration in 1979–1982 survey} \) |
| \( \sigma = \text{number of fish servings consumed} \) | d) \( \omega = \) no. of years eating fish before 1st PCB determination |
| \( \omega = \) no. of years eating fish before 1st PCB determination | e) \( \omega = \) no. of years eating fish before 1st PCB determination |
| \( \epsilon = 2 * \alpha * 0.13 \) | f) \( \psi_{70} = \text{participant’s weight at 1973–1974 survey} \) |
| \( \epsilon = 2 * \alpha * 0.13 \) | g) \( \psi_{80} = \text{participant’s weight at 1979–1982 survey} \) |
| \( \epsilon = 2 * \alpha * 0.13 \) | h) \( \beta = \text{reduction in body burden due to breast-feeding} \) |
| \( \epsilon = 2 * \alpha * 0.13 \) | i) \( \gamma = \text{yearly reduction of PCB in fish} \) |
Validity of the backward extrapolation models. To estimate agreement, there are several approaches to compare extrapolated values with a gold standard. In our case, the actual PCB measurements are considered to be the gold standard. Correlation coefficients between the estimated values and actual measurements determine whether the rank order within the extrapolations was preserved. However, even if the rank order remains the same, the actual and estimated values could be extremely different; Bland and Altman (1986) suggested using the mean difference plotted over the average of two determinations. Using the ICC combines both of the above approaches (Armstrong et al. 1992). The ICC is defined as:

$$\text{ICC} = \frac{(\text{between-subject mean square} - \text{within-subject mean square})}{\left[\frac{1}{k} \left(\text{between-subject mean square}\right) \times \text{within-subject mean square}\right]}$$  

where $k$ is the number of subjects.

The mean squares are derived by dividing each sum of squares by their corresponding degrees of freedom. The ICC shows perfect agreement if the estimation equals the measurement for each subject (Armstrong et al. 1992). In this case, the within-subjects mean square (Equation 1) becomes 0 and the ICC is a ratio of two identical between-subject mean squares. A perfect agreement is defined as equal to 1.

To accurately interpret ICC results, it is necessary to have normal distributions for the variables included in the ICC calculation. To fulfill this requirement, we used log-transformed human PCB concentrations from the 1989–1991 survey.

We used the ICC to determine which of the backward extrapolation models predicted the best. For the regression models, we provide the estimated ICC and its lower 5% confidence limit; an upper confidence limit is not defined. For the simple and complex decay models, we calculated ICCs for the various assumptions suggested for the simple and complex decay models and provide ICCs for best- and worst-case scenarios, thus developing a range of ICCs for both extrapolation models. The correlation coefficients provided for each model were used to investigate whether the rank order was preserved. We also calculated absolute differences between estimated and measured PCB values for each extrapolation model.

Linear regression, the decay models, and the calculation of the ICC were performed using SAS statistical software (version 8.02; SAS Institute, Inc., Cary, NC).

**Results**

**OC concentrations in fish and humans.** Human PCB determinations presented in Figure 1 show a curvilinear trend. Also, the minimum and maximum PCB concentrations in fish, plotted in Figure 2, show a curvilinear pattern. The peak PCB contamination level in Great Lakes fish (~1970) occurred nearly a decade before the peak PCB concentrations in Great Lakes fish eaters (1979–1982; Figure 1, Table 2). This may be due to the time it takes for PCB contamination in fish to be biomagnified and passed on to humans. Overall, both the time trends in fish and humans present a corresponding increase that is followed by a decline. In Figure 2, for the sake of comparison, we also included information on trends of DDE contamination in fish.

**Characteristics of the female fish-eater population.** Of 419 female fish eaters with PCB determinations, 8 were deceased, 120 could not be contacted, 11 gave no consent, and 9 were nuns and were not eligible for the study on reproductive events. This left us with a study population of 271; the proportion of participation is 66.1% (271 of 410). The PCB serum concentrations in female anglers and partners of male anglers increased between 1973 and 1979/1982 and decreased thereafter (Table 2, Figure 1). The average fish consumption went down during this period from 5.0 meals/month to 1.63 meals/month. Two hundred fifty-one women had a pregnancy. However, most of the female fish eaters were born before 1950, and only a few gave birth from 1973 through 1991.

**Comparison of backward extrapolation models.** The ICCs of the simple decay backward extrapolation were the lowest of the three backward estimation models (ICC for the 1980 values, 0.07–0.39; ICC for the 1970 values, 0.27–0.45; Table 3). When longer half-lives were used in the simple decay model, the resulting estimations provided better predictions, thus increasing the ICC.

The complex decay model based on Rylander et al. (1998) included several assumptions for the reduction of PCBs over time. High levels of PCBs in fish over recent years (1980–1990) led this model to produce several negative estimations for past PCB concentrations. In particular, for the half-life of 1 year, the within-subject mean squares were equal to 1.
larger than the between-subject variation, which also produced negative ICC values (Table 3). With longer half-lives, the complex decay models revealed a best ICC between 0.43 and 0.69 for estimated 1980 and 1970 values, respectively.

The regression models led to the best fit of estimated and measured PCB values. The backward assessment of estimated values for the 1980s was based on 159 female participants with measurements in both surveys (1989–1991 and 1979–1982). The backward estimation for the 1970s included 22 women with measurements in both the 1973–1974 and 1979–1982 surveys. We identified two halves of a curvilinear trend: increasing PCB concentrations from the 1960s back to the 1980s and decreasing PCB concentrations from the 1980s back to the 1970s. Regression models were used to estimate the two separate portions of the overall curvilinear trend. The resulting equations are presented in Table 1.

Regarding changes between 1989–1991 and 1979–1982, we achieved a good predictive model by combining three variables: the log-transformed PCB concentration from the last survey (1989–1991), the length of the interval between the two PCB determinations, and the number of pregnancies that occurred within the two survey periods (Table 1). The PCB levels from 1989–1991 significantly predicted the values in 1979–1982. Pregnancies led to reductions in the estimated PCB concentrations. The time interval showed a positive sign, indicating higher estimated PCB values in the 1979–1982 survey compared with that of 1989–1991 (Table 1).

Regarding changes between 1979–1982 and 1973–1974, the most parsimonious model was achieved by including the PCB serum concentrations from 1979–1982, the interval between the two PCB determinations, and the total years of fish consumption until 1973–1974. PCB levels in 1979–1982 were strongly associated with preceding values in 1979–1982. The individual years of fish consumption led to increases in the PCB concentration estimates for 1973–1974. The interval between the two PCB determinations had a negative sign, indicating that the levels were lower in 1973–1974.

The estimated ICCs for the regression models were 0.77 for 1973–1982 and 0.89 for 1979–1991 (Table 3). Even the lower 5% values of the ICC (0.71 for the period from 1982 through 1973, 0.80 for the period from 1991 through 1979) are higher than the best predictions of the two other approaches.

When comparing rank correlations between predicted values and actual measurements, the correlations for the 1979–1982 measurements did not differ substantially (our model: \( r_{\text{Spearman}} = 0.82, p < 0.0001 \); simple decay model: \( r_{\text{Spearman}} = 0.74, p < 0.0001 \); complex decay model: \( r_{\text{Spearman}} = 0.78, p < 0.0001 \)). However, for the backward extrapolation from 1979–1982 to 1973–1974, we found important differences (our model: \( r_{\text{Spearman}} = 0.91, p < 0.0001 \); simple decay model: \( r_{\text{Spearman}} = 0.27, p = 0.22 \); complex decay model: \( r_{\text{Spearman}} = 0.12, p = 0.61 \)).

To further investigate the significant correlations for the 1979–1982 measurements, we calculated the differences between estimated and measured values for each of the three backward estimation models (Tables 4 and 5). The mean difference was detected for the regression model (3.78 µg/L), and the highest for the simple decay model (13.14 µg/L). Additionally, five randomly selected observations along with their measured and estimated PCB concentrations for this survey period are presented to demonstrate the variability of results obtained through each model.

The estimated values based on the simple decay model, including only a decay component, led to higher concentration estimates for the past. The regression model used to backward extrapolate PCB exposures from 1982 to 1973 was directed toward lower PCB exposure values because the interval between the two PCB determinations had a negative sign (Table 1). Overall, the simple decay model estimated increased PCB concentrations in the past, whereas the regression model indicated predominantly lower PCB concentration estimates for the 1973–1974 survey period.

### Table 2. Characteristics of the study population.

| Characteristic | No. or frequency | Median (5–95% limit), mean, or percentage |
|---------------|-----------------|----------------------------------------|
| PCB concentration (µg/L, no./median) | 1973–1974 | 30 | 5.0 (1.0–22.0) |
| | 1979–1982 | 237 | 9.1 (1.5–34.6) |
| | 1989–1991 | 178 | 8.0 (0.0–28.0) |
| Fish consumption (meals; no./mean) | 1973–1974 | 27 | 5.01 (0.0–16.7) |
| | 1979–1982 | 240 | 2.41 (0.0–8.0) |
| | 1989–1991 | 197 | 1.63 (0.0–7.3) |
| Fish consumption (years; no./mean) | 1989–1991 | 149 | 33.48 (10.0–70.0) |
| Maternal age (years; no./mean) | At birth of child | 251 | 29.41 (21.0–39.0) |
| Birth year of the mother (frequency/percentage) | Before 1930 | 71 | 28.2 |
| | 1930–1939 | 61 | 24.2 |
| | 1940–1949 | 79 | 31.4 |
| | 1950 and after | 41 | 16.2 |
| No. of pregnancies (frequency/percentage) | 1973–1974 to 1979–1982 | 0 | 170 | 98.9 |
| | 1 | 1 | 1.2 |
| | 2 | 1 | 0.6 |
| | 1975–1982 to 1989–1991 | 0 | 158 | 91.3 |
| | 1 | 11 | 6.4 |
| | 2 | 4 | 2.3 |
| No. of breast-feeding periods (frequency/percentage) | 1973–1974 to 1979–1982 | 0 | 171 | 98.9 |
| | 1 | 1 | 0.6 |
| | 2 | 1 | 0.6 |
| | 1979–1982 to 1989–1991 | 0 | 158 | 91.3 |
| | 1 | 9 | 5.2 |
| | 2 | 6 | 3.5 |

### Table 3. Calculated ICCs for proposed models.

| Extrapolation equations | ICCs |
|-------------------------|------|
| Simple decay model (minimum–maximum) | Estimation of 1980s values from 1980s values | 0.07–0.39 |
| | Estimation of 1970s values from 1980s values | 0.27–0.45 |
| Complex decay model (minimum–maximum) | Estimation of 1980s values from 1990s values | 0.12–0.69 |
| | Estimation of 1970s values from 1980s values | 0.14–0.43 |
| Proposed regression model | Estimation of 1980s values from 1990s values | 0.89 (lower 5% limit, 0.80) |
| | Estimation of 1970s values from 1980s values | 0.77 (lower 5% limit, 0.71) |
To predict the PCB concentration in women at the time of delivery, we used different time factors (decay constants, half-lives, or regression factors) in the projected models (Table 1) and multiplied these with the time difference between the participant’s last PCB determination and their date of birth. These products were then plotted against the calendar period (Figure 3). Figure 3 includes the original PCB measurements from the three survey periods completed from 1973 through 1991 and the PCB values predicted by the simple decay model and by our regression model for each participant’s date of birth.

The three repeated human PCB concentrations and the PCB concentrations collected in fish were used to develop graphs to represent trends in human and fish PCB levels over time (Figures 2 and 3).

**Discussion**

Exposure assessment using backward extrapolation can result in extremely different estimations. Persistent chemicals, such as PCBs, have the characteristic of long half-lives. However, changes in environmental conditions and subsequent changes in intake can result in misleading exposure assessments when relying solely on current measurements and persistence. Our setting focuses on fish contamination in the Great Lakes and corresponding PCB levels in anglers and their spouses. PCB fish contamination was low from 1920 through 1950, increased dramatically thereafter, and declined again in the 1970s (Figure 2). Using measurements from the 1990s, a simple decay model leads to large overestimations of past exposures (Weisskopf et al. 2003). The backward exposure assessment that employed changing fish PCB levels and reduction due to breast-feeding as proposed by Rylander et al. (1998) produced an acceptable fit in the presence of long half-lives. Our regression model based on repeated measurements leads to the best overall PCB estimations at each survey period.

For the period between 1979 and 1991, our model is based on PCB concentrations from 139 female fish eaters with determinations in both surveys. However, a limitation of our results is the limited number of repeated measurements comparing the 1970s with later measurements in the 1980s (n = 22). It may be that these 22 women do not represent changes typically found between 1970 and 1980. However, we have also found a similar trend in male fish eaters (Karmaus et al. 2002).

Using correlation coefficients comparing estimated values and actual measurements, we would not have identified differences for the backward estimations for 1979–1982. Nevertheless, large disagreements were discovered through comparing absolute differences for each model (Table 4). This discrepancy was explained in 1986, when Bland and Altman (1986) showed that, although correlations are significant and rank orders are preserved, this does not mean that the estimated and measured individual values will be comparable. The results show that the ICC is superior in determining agreements because it takes both correlation and difference into account.

For the backward estimations for 1973–1974, the rank orders for the simple decay and the complex decay model are not preserved (simple decay model: \( r_{\text{Spearman}} = 0.27, p = 0.22 \); complex decay model: \( r_{\text{Spearman}} = 0.12, p = 0.61 \). The reasons for these are that the actual measurements were lower before 1979 (Figure 1) and both decay models resulted in higher backward estimates, illustrated for the simple decay model in Figure 3.

The results show that we estimated two different trends, an increase in PCB concentrations from 1973 through 1982, and a decrease from 1979 through 1991. For our regression-based backward assessments, the comparison of PCB concentrations presented in Figures 2 and 3 suggests a similar trend between fish and humans. There is an increase in PCB exposure concentrations closely followed by a corresponding decrease in PCB exposure levels. This is suggestive of PCB fish concentrations being transferred up the food chain and resulting in similar trends in humans, however, with a delay of approximately 10 years. We did not include changing fish concentrations in our models. However, the trend in PCB concentrations in fish as an external criterion supports our findings of suggested lower human levels in the past. Rylander et al. (1998) also incorporated declines in fish concentration in the range of 1–10%; however, the PCB levels in Lake Michigan fish indicate a much stronger decline of approximately 90% since the 1970s (Figure 2).

Based on the ICC values calculated for the simple decay model (Table 3), we suggest that this type of model is too simple to obtain an accurate backward estimation of OC contamination in humans. This approach does not contain variables necessary to model changes in OC concentrations in the environment, such as fish contamination levels or consumption of sport-caught fish.

The proposed linear regression modeling for the backward extrapolation of OC exposure turned out to be an accurate method for an exposure scenario with changing environmental conditions (ICC, 0.77–0.89; Table 3). The modeling employs repeated measurements and uses potentially necessary predictors.
needed to properly backward extrapolate exposure. We focused primarily on PCB concentrations in women to model potential exposure levels to which their offspring may be exposed in utero. One limitation of our suggested approach is that the entire basis of the regression model is dependent on having repeated measurements. Without availability of repeated measurements, the complex decay model (Rylander et al. 1998) would generate better results than the simple decay model. Additionally, the complex decay model may be improved by employing measurements that reflect time trends determined in other environmental entities specific to the region of study.

Because other OC exposures such as DDE have properties similar to those of PCBs and also have similar exposure trends in Great Lakes fish (Figure 2), they may also be backward extrapolated through regression modeling.

Conclusion

Backward extrapolation models can provide varying results depending on the assumptions used. We recommend validating backward extrapolation models with past exposure measurements before applying estimated exposure levels in assessment of human health effects. Our results indicate that when repeated exposure measurements are available, backward estimations based on regression models are superior. Results of the simple decay model do not seem acceptable, whereas a complex decay model generated satisfactory results when employing longer half-lives. To obtain valid backward estimations of past human exposure in the absence of repeated measurements, we recommend the use of a complex decay model following the strategies that Rylander et al. (1998) have established through prior analyses. We suggest improving the model by not only including declines in fish PCB concentrations or other environmental toxics but also by taking into account any variations that can be identified through environmental or food measurements.

REFERENCES

Armstrong B, White E, Saracci R. 1992. Principles of Exposure Measurement in Epidemiology. Oxford:Oxford University Press.

Bland J, Altman D. 1986. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1:307–310.

Brown J, Lawton R, Morgan C. 1994. PCB metabolism, persistence, and health effects after occupational exposure: implications for risk assessment. Chemosphere 29:2287–2304.

Bund/Länder-Arbeitsgruppe Dioxine. 1991. UAG II “Richt- und Grenzwerte.” Final Report. Berlin:Bundeseigentumsgesellschaftamt (Federal Health Office).

Cordie R, Locke R, Spring J. 1982. Risk assessment in a federal regulatory agency: an assessment of risk associated with the human consumption of some species of fish contaminated with polychlorinated biphenyls (PCBs). Environ Health Perspect 45:171–182.

De Vauld D, Hesselberg R, Rodgers P, Feist T. 1996. Contaminant trends in lake trout and walleye from the Laurentian Great Lakes. J Great Lakes Res 22:884–895.

Fiore B, Anderson HA, Hanranah LP, Olson LJ, Sonzogni WC. 1989. Sport fish consumption and body burden levels of chlorinated hydrocarbons: a study of Wisconsin anglers. Arch Environ Health 44:92–98.

Gerstenberger S, Dallinger J. 2002. PCBs, mercury, and organochlorine concentrations in lake trout, walleye, and whitefish from selected tribal fisheries in the Upper Great Lakes region. Environ Toxicol 17:513–519.

GLNPO (Great Lakes National Program Office). 2003. Great Lakes Monitoring Program: Toxics in Top Predator Fish. Washington, DC:U.S. Environmental Protection Agency. Available: http://www.epa.gov/gltnp/gltnp/effluents.html [accessed 15 August 2003].

Guo YL, Chen YC, Yu ML, Hsu CC. 1994. Early development of Yu-Cheng children born seven to twelve years after the Tianwan PCB outbreak. Chemosphere 29:2395–2404.

Hovinge M, Soviers M, Humphrey H. 1992. Historical changes in serum PCB and DDT levels in an environmentally-exposed cohort. Arch Environ Contam Toxicol 22:362–366.

Humphrey H. 1983a. Evaluation of Humans Exposed to Water-Borne Chemicals in the Great Lakes. Lansing, MI:Michigan Department of Public Health.

Humphrey H. 1983b. Population studies of PCBs in Michigan residents. In: PCBs: Human and Environmental Hazards (D’Itri F, Kamrin MA, eds). Boston:Butterworth, 20–21.

Karmaus W, Huang S, Cameron L. 2002. Parental concentration of dichlorodiphenyl dichloro- and polychlorinated biphenyls in Michigan fish eaters and sex ratio in offspring. J Occup Environ Med 44:8–13.

Kreiss K. 1985. Studies on populations exposed to polychlorinated biphenyls. Environ Health Perspect 60:193–199.

Manchester-Nevesig J, Valters K, Sonzogni WC. 2001. Comparison of polybrominated dipheny ethers (PBDEs) and polychlorinated biphenyls (PCBs) in Lake Michigan salmonids. Environ Sci Technol 35:1072–1077.

Needham LL, Gerthoux PM, Patterson DG Jr, Brambilla P, Smith SJ, Sampson E, et al. 1999. Exposure assessment: serum levels of TCDD in Sevose, Italy. Environ Res 80A:520–526.

Neidermyer W, Hickey J. 1976. Chronology of organochlorine compounds in Lake Michigan fish, 1929–66. Pesticides Monit J 10:92–95.

Newcombe W, Andrew P. 1993. Organochlorine pesticides and polychlorinated biphenyl congeners in commercial fish from the Great Lakes. J AgriChem 76:707–710.

Phillips D, Smith A, Burse V, Steele G, Needham L, Hannon W. 1989. Half-life of polychlorinated biphenyls in occupationally exposed workers. Arch Environ Health 44:351–354.

Polušák Z, Wasserman D, Wasserman M, Cucos S, Ron M. 1977. Organochlorine compounds in mother and fetus during labor. Environ Res 13:276–284.

Price H, Welch R, Scheel R, Warren L. 1986. Modified multi-residue method for chloroform, toxaphene, and polychlorinated biphenyls in fish. Bull Environ Contam Toxicol 37:1–9.

Rappolt R, Hale W. 1996. p,p’-DDE and p,p’-DDT residues in human placentas, cords, and adipose tissues. Clin Toxicol 1:57–61.

Rylander L, Stromberg U, Dyrenmark E, Ostman C, Nilsson-Ehle P, Hagmar L. 1998. Polychlorinated biphenyls in blood plasma among Swedish female fish consumers in relation to low birth weight. Am J Epidemiol 147:493–502.

Shirai J, Kissel J. 1996. Uncertainty in estimated half-lives of polychlorinated biphenyl in humans: impact on exposure assessment. Sci Total Environ 187:199–210.

Stewart P, Darvill T, Lonky E, Reihlman J, Pagano J, Bish B. 1999. Assessment of prenatal exposure to PCBs from maternal consumption of Great Lakes fish: an analysis of PCB pattern and concentration. Environ Res 85:7–96.

Swain W. 1983. An overview of the scientific basis for concern with polychlorinated biphenyls in the Great Lakes. In: PCBs: Human and Environmental Hazards (D’Itri F, Kamrin M, eds). Boston:Butterworth Publishers, 20–21.

U.S. EPA. 1993. Proceedings of the U.S. Environmental Protection Agency’s National Technical Workshop “PCBs in Fish Tissue,” 10–11 May 1993, Washington, DC: EPA 823-R-93-003, 231. Washington, DC:U.S. Environmental Protection Agency. .

Veril G. 1975. Baseline concentrations of polychlorinated biphenyls and DDT in Lake Michigan fish, 1971. Pesticides Monit J 8:21–29.

Weisskopf MG, Anderson HA, Hanranah LP, for the Great Lakes Consortium. 2003. Decreased sex ratio following maternal exposure to polychlorinated biphenyls from contaminated Great Lakes sport-caught fish: a retrospective cohort study. Environ Health 2:2. Available: http://www.ehjournal.net/content/2/1/2 [accessed 23 March 2004].

Willford W, Hesselburg R, Nicholson L. 1976. An overview of the scientific basis for concern with polychlorinated biphenyls in the Great Lakes. In: PCBs: Human and Environmental Hazards (D’Itri F, Kamrin M, eds). Boston:Butterworth Publishers, 20–21.

Yakushiji T, Watanabe I, Kuwabara K, Tanaka R, Kashimoto T, Kunita N. 1984. Rate of decrease and half-life of polychlorinated biphenyls (PCBs) in the blood of mothers and their children occupationally exposed to PCBs. Arch Environ Contam Toxicol 13:341–345.

Zabik M, Zabik M, Booren A, Nettles M, Song J, Welch R, et al. 1995. Pesticides and total polychlorinated biphenyls in chinook salmon and carp harvested from the Great Lakes: effects of skin-on and skin-off processing and selected cooking methods. J Agric Food Chem 43:993–1001.