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Concentration-dependent Half-Lives of Polychlorinated Biphenyl in Sera from an Occupational Cohort

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Highlights
1. This is the largest and longest studied cohort of workers exposed to PCBs for whom serum values are available
2. We present PCB half-life estimates using sera from four time points
3. PCB half-life estimates are for two commercial PCB mixtures (Aroclor 1254 and 1242)
4. Two serum PCB elimination rates were discovered (rapid and then slow)
5. Gender differences were observed only for Aroclor 1242 in earlier years.
Abstract

Polychlorinated biphenyls (PCBs) are carcinogenic. Estimating PCB half-life in the body based on levels in sera from exposed workers is complicated by the fact that occupational exposure to PCBs was to commercial PCB products (such as Aroclors 1242 and 1254) comprised of varying mixtures of PCB congeners. Half-lives were estimated using sera donated by 191 capacitor manufacturing plant workers in 1976 during PCB use (1946-1977), and post-exposure (1979, 1983, and 1988). Our aims were to: (1) determine the role of covariates such as gender on the half-life estimates, and (2) compare our results with other published half-life estimates based on exposed workers. All serum PCB levels were adjusted for PCB background levels. A linear spline model with a single knot was used to estimate two separate linear equations for the first two serum draws (Equation A) and the latter two (Equation B). Equation A gave half-life estimates of 1.74 years and 6.01 years for Aroclor 1242 and Aroclor 1254, respectively. Estimates were 21.83 years for Aroclor 1242 and 133.33 years for Aroclor 1254 using Equation B. High initial body burden was associated with rapid PCB elimination in workers at or shortly after the time they were occupationally exposed and slowed down considerably when the dose reached background PCB levels. These concentration-dependent half-life estimates had a transition-point of 138.57 and 34.78 ppb for Aroclor 1242 and 1254, respectively. This result will help in understanding the toxicological and epidemiological impact of exposure to PCBs in humans.
1.0 Introduction

Many electrical equipment manufacturing workers in the United States were exposed to polychlorinated biphenyls (PCBs) before their use was banned in 1977. The National Institute for Occupational Safety and Health (NIOSH) is conducting epidemiologic studies of the possible health consequences of occupational exposure to PCBs at three capacitor manufacturing plants (Prince et al., 2006; Rocheleau et al., 2011; Ruder et al., 2006; Silver et al., 2009; Steenland et al., 2006), using job-exposure matrices as a surrogate for PCB body burden.

The PCB body burden (dose levels) over time depends upon toxicokinetics, which includes elimination half-lives (Shirai and Kissel, 1996). Intrinsic human elimination half-lives for PCBs were 10-15 years in a recent study (Ritter et al., 2011), derived from cross-sectional biomonitoring data. In humans with occupational exposure to PCBs, several studies have provided estimates for PCB half-life varying from < 1 year to 71 years (Steele et al., 1986; Phillips et al., 1989; Taylor and Lawrence, 1992; Wolff et al., 1992; Seegal et al., 2011). These previous half-life estimates were usually based on only two measurements. The objectives of the current effort were to develop estimates of the half-lives of commercial PCB mixtures Aroclor 1242 and Aroclor 1254 using all available sera from a select group of workers from one of the three plants, to consider the role of high initial body burden and gender on the half-life estimates, and to compare the results with other published half-life estimates based on occupational exposure. The estimates were adjusted for PCB background levels (Hopf et al., 2009). This is the only study that incorporates four PCB blood measurements over time, allowing us to explore PCB elimination rates.
2.0 Background

Shirai and Kissel (1996) reviewed fourteen studies of humans with occupational, accidental, or experimental exposure to PCBs and concluded that very short (i.e., < 1 year) and very long (i.e., > 10 years) half-lives were probably unlikely. The exponential decay model, assuming first-order kinetics, is given by

\[ X(t) = X(t_0) e^{-\lambda(t-t_0)} \]

where \( X(t) \) is the concentration in the compartment at time \( t \), \( X(t_0) \) is the unknown initial concentration at time \( t_0 \), and \( \lambda \) is the elimination constant which has units of time\(^{-1}\). The half-life, \( t_{1/2} \), is defined as the length of time after which the initial concentration of the chemical is reduced by half, and is equal to the natural logarithm of 2 divided by the elimination constant, or

\[ t_{1/2} = \ln(2) / \lambda \] (Cassarett and Doull, 1986).

In a controlled pharmacokinetic study, the initial concentration of a chemical in a compartment is known and subsequent concentrations are measured at specific time points. In occupational studies, the initial concentration of a chemical in a compartment after first exposure is usually unknown. Also, exposure typically is chronic, not acute, occurring at different rates over different periods of time. However, measurements taken after exposure is known to have ceased can be used to estimate the half-life for elimination of the chemical from the sera compartment.

Estimating the half-life of PCBs in the body using sera from exposed workers is complicated; occupational exposure to PCBs was generally to commercial PCB products comprised of varying mixtures of some of the 209 PCB congeners. Different methods exist for quantifying the level of PCBs in sera (Lawton et al., 1985a). Ideally, congener-specific serum PCB levels would be
measured. However, in the past, results were typically either quantified using an “Aroclor standard” by summing the heights of selected peaks on the gas chromatogram (GC) which correlated with hallmark peaks in a specific Aroclor, or quantified as lower- or higher-chlorinated PCBs (LPCBs or HPCBs) based on the sum of the GC peaks that occurred before or after the retention time of p,p’-dichlorodiphenyldichloroethylene (DDE), universally detected in sera from people in the industrialized world. The two methods of quantifying PCBs in sera are related, with 93% of Aroclor 1242 being LPCBs and 96% of Aroclor 1260 being HPCBs (Lawton et al., 1985b). The range of chlorination of the Aroclors in sera was determined to be Aroclor 1016: 2-5 chlorines, Aroclor 1242: 2-6 chlorines, Aroclor 1254: 4-7 chlorines, and Aroclor 1260: 4-8 chlorines (Lawton et al., 1985b).

In addition to degree of chlorination, several other factors are considered to be related to the half-life of PCBs in humans. Wolff et al. (1992) found PCBs in serum from workers (N=60) in jobs with high and direct PCB exposure had shorter half-lives for lower chlorinated PCBs than PCBs in serum from workers (N=105) in jobs with low and indirect PCB exposure (4.8 versus 17 years, respectively). A follow-up study of some of these workers (N=45) 28 years later (Seegal et al., 2011), showed somewhat longer half-lives than Wolff et al. (1992) had, but showed the same trend with respect to high initial PCB body burden: half-life estimates for lower chlorinated PCBs were 13.5 and 7.3 years and for higher chlorinated PCBs were 32.6 and 12 years for low and high exposed workers, respectively. Factors complicating the estimation of PCB half-life include percent body fat, laboratory measurement error (Caudill et al., 1992), the time interval between measurements (Caudill et al., 1992), and continuing low-level exposure to PCBs (Shirai and Kissel, 1996), such as background levels of exposure (Michalek et al., 1998).
Different statistical methods have been proposed for determining the half-life of a substance in humans from an exposed population. The choice of method often depends on the number of participants and the number of measurements available for each participant over time. Steele et al. (1986) used linear regression to estimate the half-lives of PCBs in the body using sera quantified as Aroclors 1242 and 1260. Five capacitor manufacturing workers at one of the NIOSH cohort plants, selected because of their high probability of PCB exposure, provided sera at two draws separated by 84 months. The analysis produced half-life estimates of 2.0 years for Aroclor 1242, 27.6 years for Aroclor 1260, and 11.5 years for total serum PCBs. The median technique was developed by Phillips et al. (1989) to estimate the half-lives of Aroclors 1242 and 1254 for 60 former capacitor manufacturing workers (at the same NIOSH cohort plant) with two serum draws separated by 100 months. Phillips et al. reported half-life estimates of 2.6 years for Aroclor 1242 and 4.8 years for Aroclor 1254. In addition, they observed a decreasing trend in half-life based on initial concentration of PCBs in 1977, although Shirai and Kissel (1996) showed that this was likely due to confounding by continuing exposure to PCBs. Table 1 gives an overview of previous half-life estimates from US occupational exposed populations and type of statistical methods used to derive these half-lives.

Lawton et al. (1985b) initiated a research study in 1976 to study the possible health effects of PCB exposure in workers at another capacitor manufacturing plant (also in the NIOSH cohort) with two facilities in upstate New York. Aroclor 1254 was used at this plant from 1946-1954, Aroclor 1242 from 1954-1971, and Aroclor 1016 from 1971-1977 (Lawton et al., 1985b). In 1976, 194 employees, selected because their jobs “required direct contact with PCB in zones of
high air concentration, were in the immediate periphery of the high exposure zone, or had high
but intermittent exposure”, underwent examinations that included the collection of blood sera
from most (n=191). This first examination was approximately one year prior to the termination
of PCB use at the plant. Serum draws were repeated in 1979, 1983, and 1988 for subsets of the
191 participants. Taylor et al. (1992) used measured serum PCB levels from 148 of the workers
who provided sera in both 1979 and 1983 to produce half-life estimates of 1.8 years (95%
confidence interval (CI) =1.7 – 1.9) for Aroclor 1242, 3.3 years (95% CI=3.0 – 3.8) for Aroclor
125
126
127
128
3.0 Materials and Methods
129
The basis for the Aroclor half-life estimates were the Aroclor 1242, 1254, and 1260 serum levels
calculated by Lawton et al. (1985). According to study plant records, the use of PCBs in the two
facilities ended 30 June 1977. Time intervals from last exposure were measured from that date.
Specific dates of the serum draws were not known, but estimated as 15 March 1976, 15
November 1979, 15 November 1983, and 1 November 1988 since it is known that PCBs were
“still in use during the first 1.3 years after the first examination” (Brown et al., 1989); the second
serum draw was in November 1979 (Brown et al., 1984); the third serum draw was 48 months
after the second (Taylor et al., 1992); and the fourth serum draw occurred in 1988.
A majority of the 191 participants in the Lawton study provided sera at four time points
(122/194, 63%). Thirty-five participants provided sera at three time points, 19 at two, 15 at one,
and three did not provide sera at any of the time points. Therefore, our statistical analysis was
performed using results of 191 workers. PCB serum levels were quantified for 185 participants
in 1976, 173 in 1979, 150 in 1983, and 138 in 1989. Most participants were male (152/194, 78%).

The methods for quantifying PCB levels (packed column GC with electron capture detector) in the serum have been described (Lawton et al., 1985a). Aroclor standards were used to calculate PCB levels in terms of “Aroclor 1242” and “Aroclor 1254”. Serum PCB levels were quantified by summing peak heights with relative retention times of 37, 70, and 84 as Aroclor 1242 and with relative retention times of 125, 146, 160, and 184, as described in Lawton et al (1985a) as Aroclor 1254 (Brown et al., 1989). (Peak 184 differed from the relative retention time of 174 described in the Webb-McCall method (Webb and McCall, 1973).

Although PCB exposure was ongoing at the time of the first serum measurement, it might be possible to use data from the 1976 serum draw to estimate the half-life for Aroclor 1254 (Brown et al., 1989) since Aroclor 1254 was only used from 1946-1954 at the study plant (Lawton et al., 1985b). Other than gender, information on factors known to affect half-life such as age and percent body fat was unavailable. All statistical analyses were performed using SAS 9 Software (SAS Institute Inc., Cary, NC).

Background PCB levels might contribute to the length of the half-life estimates; therefore an adjustment for PCB background levels for the years 1976, 1979, 1983, and 1988 was needed. No national statistically based cross-sectional data concerning historical serum PCB levels exist for the U.S. population by year. Therefore, we estimated the background PCB serum levels for
these four time points based on the scientific literature (Hopf et al., 2009). The background PCB levels were estimated to follow negative exponential "die away" curves;

- for Aroclor 1242; corr_pcb = pcb - 4.18*exp(-0.088*(year-1977));
- for Aroclor 1254; corr_pcb = pcb - 8.5788*exp(-0.0569*(year-1977));

where corr_pcb represents the serum PCB levels (ppb) corrected for background, and pcb is the uncorrected values. Adjustments for PCBs background serum levels were performed by subtracting the estimated background population serum PCB concentrations from the measured serum PCB concentrations prior to log transformation.

Quantile-quantile plots of natural-log-transformed serum PCB levels (ln(PCB)) versus standard normal quantiles indicated that the data were lognormally distributed (not shown). Figures 1 and 2 depict the individual profiles of the log-transformed serum PCB levels over time, for Aroclors 1242 and 1254, respectively. Vertical reference lines indicate the times of the serum draws relative to the end of PCB use, and average trend lines were fit using a smoothing routine for females and males. The quadratic term for time was statistically significant for fitting a linear model for all years, indicating that the assumptions of a first-order kinetic model were violated. From the graphs it was apparent that the decrease in earlier years was faster than in later years. This bi-phasic elimination was consistent with elimination patterns from high initial body burden of other chlorinated persistent chemicals such as TCDD (Aylward et al. 2005). Therefore, a linear spline model with a single knot (Keele 2008; Altshuler 1981) approach was used to demonstrate that there were two slopes underlying the die-away curve. This model fit the data well; a linear equation was fitted for the 1976 and 1979 data (Equation A), and a second linear equation was used to fit the 1983 and 1988 data (Equation B) using PROC MIXED. The equality
of the slopes estimated over the two time periods was tested by analyzing all the data in a single model which included the interaction between periods with slope. The dependent variables were the natural log transformed PCB Aroclors ln(PCB).

The point (transition point) where Equation A and Equation B intersected was estimated by determining the year during which the two regression equations for equations A and B provided the same estimate for PCB concentrations. Other parameters besides background PCB levels affecting elimination such as additional elimination mechanisms (PCB fecal elimination of unchanged compound through lipid partitioning into the large intestine) were unknown and could not be included in the model; hence our model estimates half-life elimination rates based on PCBs (not metabolites) circulating in the blood. The transition point indicating a possible change in elimination rate from rapid to slow was calculated.

4.0 Results

Aroclor 1242 quantified measurements increased in five participants from 1976 to 1979, in four participants from 1979 to 1983, and in 32 participants from 1983 to 1988. Likewise, Aroclor 1254 quantified measurements increased in 49 participants from 1976 to 1979, in 16 participants from 1979 to 1983, and in 50 participants from 1983 to 1988.

Detailed work histories, available for 192 of the 194 participants, described 2,684 years of employment at the study plant during the era of PCB exposure (January 1, 1946 – June 30, 1977). The median year first employed was 1965 (range 1946 – 1974) and the median duration of employment was 11 years (range 1 – 30 years).
Summary statistics for the measured serum PCB levels, quantified as Aroclors 1242 and 1254 in parts per billion (ppb) with and without corrections for background serum PCB levels, are provided in Table 2. Measured serum PCB levels were highly variable within a given year. The difference between corrected and uncorrected serum PCB levels was minimal in earlier years due to the high serum PCB levels (e.g. 1976: GM was 1,521 ppb) compared to the value used to adjust for background levels.

The year Equation A and Equation B intersected (transition point) for Aroclor 1242 was 1980 and for Aroclor 1254, 1982. We did not find a statistical significant difference in half-life estimates between genders for Aroclor 1254. This was also true for Aroclor 1242 in later years (Equation B). However, the Aroclor 1242 half-life estimate for equation A (1976-1979) was significantly longer in females (half-life of 2.15 years, 95% confidence interval [C.I.] 1.7 – 2.9 years) as compared to males (1.7 years, 95% C.I. 1.4 – 2.2 years, t=2.21, p<0.03).

The transition point concentration for Aroclor 1242 and 1254 were 138.57 and 34.78 ppb, respectively. The elimination kinetics of PCBs were concentration dependent with faster rates observed at higher concentrations (>138.57 ppb for Aroclor 1242 and >34.78 ppb for Aroclor 1254 ppb) and the transition to slower rates occurring below this concentration.

Results of the repeated measures regression models and subsequent half-life estimates are provided in Table 3. In the linear spline model with a single knot, the first slope using the first two serum draws (Equation A) produced an estimated half-life of 1.74 years for Aroclor 1242
(95% CI = 1.60 – 1.89 years) and 6.01 years for Aroclor 1254 (95% CI = 4.53 – 8.93 years).

Using the last two serum draws (Equation B) to model the second slope produced an estimated half-life of 21.83 years for Aroclor 1242 (95% CI = 16.92 – 30.76 years) and 133.33 years for Aroclor 1254 (95% CI = 52.88 – ∞ years). The slopes estimated for the two time periods were significantly different (p<0.0001).

We compared the geometric means (cGM) of predicted values of Aroclor 1242 with actual cGM for 1976 (predicted 1503: actual 1528), 1979 (predicted 274: actual 280), 1983 (predicted 115: actual 125), and 1988 (predicted 91: actual 92); and for Aroclor 1254: 1976 (predicted 78: actual 85), 1979 (predicted 48: actual 55); 1983 (predicted 28: actual 35), and 1988 (predicted 27: actual 32).

5.0 Discussion

Estimates of the half-lives of PCBs were based on sera drawn from the same individuals at up to four time points. The half-life, defined as the change in concentration in the body over time is the net result of elimination from the body, changes in the body composition, and intake from the environment. Factors affecting elimination are age, smoking, initial body burden, body fat, and gender (Milbrath et al 2009). Although the gender of each participant was known, age and body mass index data were not available; therefore, it was not possible to adjust for covariates other than gender.

Half-life estimates for sera from female participants were generally longer than half-life estimates for sera from male participants, although the gender difference was only statistically
significant for Aroclor 1242 in the earlier years (equation A). This gender difference in half-life estimates was also seen in Seegal et al., (2011) not only in lower but also higher chlorinated PCBs. PCBs are known to be stored in adipose tissue, therefore half-life estimates are potentially confounded by percent body fat in addition to the rate of PCB migration to the blood (Brown, 1994) or hormonal differences (Kang et al., 2008; Cerna et al., 2008). No clear explanations for this gender-related difference exist, and further investigation is needed.

High initial PCB body-burden showed a concentration-dependent biphasic elimination rate, which has been identified in related compounds such as 2,3,7,8-tetrachloro-p-dibenzo-dioxin (TCDD) and penta-chlorodibenzofuran (PeCDF) in cases of acute poisoning (Abraham et al. 2002), Seveso incident (Aylward et al 2005; Michalek et al 2002) in children (Kerger et al 2006), Yusho and Yu-Cheng rice oil poisoning (Leung et al 2007; Ryan et al 1993), but has until now not been reported in workers with chronic high exposures. This non-linear behavior might be due to possible enzyme induction similarly to that seen in TCDD and pentaCDF, as enzyme induction has been observed previously in animals exposed to PCBs (Emond et al, 2005).

Not adjusting for background PCB levels did not have an impact on equation A (half-lives not corrected for background levels: Aroclor 1242: 1.75 years and Aroclor 1254: 6.8 years). The half-life estimates for uncorrected serum PCB levels using equation B were shortened; giving Aroclor 1242 an half-life of 20.4 years and statistically significantly shortened half-life for Aroclor 1254 of 69.5 years. Since most of these individuals continued to live in the vicinity of the plant they would have an ongoing environmental exposure as would eating contaminated fish
in the 1980s. Accounting for background PCB levels will give a more realistic estimate of the
half-life.

Serum levels were reduced by approximately 90% and 50% between the first and third serum
draws for Aroclors 1242 and 1254, respectively, but increased between the third and fourth
serum draws for 23% and 36% of the participants. By the fourth serum draw, serum PCB levels
had fallen to much lower levels and were possibly approaching the levels of those in the general
population who have somewhat elevated environmental exposures. The reasons for the increases
in serum PCB levels between consecutive serum draws seen in some workers are not known.
Possible explanations are de-chlorination of congeners to lower chlorinated PCB; where
particular congeners would be quantified as Aroclor 1254 in earlier serum draws, and as Aroclor
1242 in later serum draws. Continued occupational exposures were possible for those workers
who dismantled the plant, and as mentioned above living in the vicinity could give higher
environmental exposures. Other factors that could lead to increases in PCBs in these workers are
laboratory measurement error, increased release of PCBs into the blood from body fat storage, or
a combination of factors. These factors could lead to unrealistic long half-life estimates.

Dioxin-like (DL) PCBs (PCB77, PCB 81, PCB 126, PCB 169, PCB 105, PCB 114, PCB 118,
PCB 123, PCB 156, PCB 157, PCB 167, PCB 89) are tetra-, penta-, and hexa-chlorinated
congeners. A complete PCB congener distribution of Aroclor mixtures has been published
(Frame et al 1996), and the weight% of DL-PCB congeners for Aroclor 1016, Aroclor 1242, and
Aroclor 1254 were 0%, 1.95%, and 23.58%, respectively. Therefore workers in the early time
period exposed to Aroclor 1254 (before the 1960s) had higher DL-PCB exposures compared to
workers who were only exposed to Aroclor 1242 (~1960-1970) and Aroclor 1016 (in the 1970s) used in later time periods. DL-PCBs in workers’ blood samples can be estimated from Seegal et al 2011; they re-analyzed stored blood samples previously determined as lower (LPCBs; peaks eluding before DDE in the chromatogram) and higher (HPCBs; peaks eluding after DDE in the chromatogram) PCBs, and found four DL-PCBs congeners (118, 105, 167, 156); all present in peaks quantified as HPCBs.

Shirai and Kessel (1996) reasoned that half-lives longer than 10 years were probably the result of confounding by additional exposure. Wolff et al. (1992), on the other hand, observed long half-lives which they attributed to the presence of congeners with relatively longer half-lives in the sera compared to the distribution of congeners in the Aroclor mixtures. The explanation we can offer is that elimination of PCB congeners with shorter half-lives (generally, lower chlorinated biphenyls) from high initial PCB serum levels is estimated with Equation A, while Equation B is an estimate of the elimination of PCB congeners with long half-life as described by Wolff et al (1992) with continuous exposure to PCB background levels as described by Shirai and Kessel (1996). Researchers who have continuously monitored PeCDF in a group of Yusho patients, poisoned by PCB contaminated rice bran oil, have recently reported that these patients maintain a high level resulting in an infinite half-life (Matsumoto et al 2009). The authors suggested that a more complicated model to explain excretion in humans were needed.

One of the strengths of this study was that PCB measurements were available at up to four time points per participant, and a linear spline model with a single knot was used to estimate PCB half-lives. Advantages of the linear spline model with a single knot include generalizability to
any number of repeated measures, the ability to handle varying numbers of repeated measures per participant, and the ability to adjust the half-life estimate for covariates such as gender by adding the appropriate terms and interactions to the model.

Unlike all previous half-life estimates reported in the scientific literature, ours is based on serum draws from four time points, which allowed us to explore more than one linear regression PCB elimination rate. A single linear regression using all four time points did not achieve as good a fit as did the linear spline model with a single knot. We did not try more than a single knot as based on the data; the linear slope for decline appeared much steeper between the first 2 occasions than the latter two. This bi-phasic decay was also observed by Brown and Lawton (2001) who tried to fit a pseudo-first order elimination to their studies’ three serum draws. Other studies (Phillips et al., 1989; Taylor and Lawrence, 1992; Brown et al., 1989; Wolff et al., 1992) estimated half-lives based on serum draws at only two time points, which resulted in shorter half-lives (Table 1). The half-life estimates using the linear spline model with a single knot were somewhat shorter for Equation A and longer for Equation B than estimates previously published, because it incorporates high initial PCB body burden (Equation A) and low body burden (Equation B). The equation A estimated half-life of 1.8 years for Aroclor 1242 was 31% shorter than the 2.6-year estimate by Phillips (1989), 81% shorter than the 9.6-year estimate by Seegal et al. (2011), but the same as the estimate by Taylor et al. (1992). Equation B estimated an half-life of 21.8 years for Aroclor 1242, 2.3, 7.4, and 11.1 times longer than the estimates by Seegal et al. (2011), Phillips (1989), and Taylor et al. (1992), respectively. Likewise, Equation A estimated a half-life of 6.01 years for Aroclor 1254, which was 42 and 106% longer than the estimates by Phillips (1989) and Taylor et al. (1992), respectively; and 90 and 62% shorter than the estimates
PCB Half-Lives in Occupational Cohort Sera

by Wolff et al (1992) and Seegal et al (2011). Equation B estimated half-life of 133.33 years for
Aroclor 1254 was 27, 40, 1, and 7.5 times longer than estimates by Phillips (1989), Taylor et al.
(1992), Wolff et al. (1992), and Seegal et al. (2011), respectively. The half-life estimates using
the linear spline model with a single knot were consistent with elimination rates computed by
Phillips et al., 1989; Taylor and Lawrence, 1992; Brown et al., 1989 for the fast elimination rate
(Equation A) for a high internal dose, and by Wolff et al 1992, Shirai and Kissel 1996, and
Seegal et al. 2011 for the slow elimination rates (Equation B) for a low internal dose approaching
background PCB levels.

Major limitations of this study include not being able to estimate PCB congener-specific half-
lives because congener-specific serum data were not available. The PCB half-life estimates
would have improved if we could have adjusted for body mass index and age that are known to
affect PCBs half-lives. Strengths of these half-life estimates include a relatively long 13-year
sampling period, a large study population (191 participants), one to four serum draws per
participants, and three sampling points after occupational exposure ended. In addition, these
half-life estimates are for individuals with high initial body burdens, which we show here result
in concentration-dependent PCB half-lives. Attempts to back-calculate body burden in highly
exposed workers based on assumption of uniform half-lives will greatly underestimate dose and
overestimate potency as shown for TCDD (Aylward et al 2005).

6.0 Conclusion

Our PCB half-life estimates using the linear spline model with a single knot take into account
high initial body burden, ongoing environmental exposure, low serum levels, and congeners with
very long half-lives. The estimated half-lives during a period of high internal dose were 1.74
years for Aroclor 1242 and 6.01 years for Aroclor 1254, modeling elimination using sera from
the first two serum draws. Half-lives during a period of low internal dose were estimated to be
21.83 years and 133.33 years for Aroclor 1242 and Aroclor 1254, respectively, using the final
two serum draws. The transition point for Aroclor 1242 was 138.57 ppb and for Aroclor 1254
was 34.78 ppb. The high internal dose estimates are in general agreement with the half-life
estimates reported in Phillips et al. (1989) and Brown and Lawton (2001), and the low dose
estimates are in agreement with Wolff et al. 1992 and Seegal et al. 2011. These half-life
estimates may aid in assessing PCB exposures retrospectively and reconstructing PCB dose
estimates for persons on whom biological monitoring was performed only once, which may in
turn help in understanding the toxicological and epidemiological impact of exposure to PCBs in
humans.

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