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Half-Life of Polychlorinated Biphenyls in Occupationally Exposed Workers

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ABSTRACT. In 1977 and 1985, serum polychlorinated biphenyl (PCB) concentrations were determined for 58 workers in a Bloomington, Indiana, factory that used polychlorinated biphenyls (PCBs) in capacitor manufacture until 1977. Less chlorinated PCBs were quantitated as Aroclor 1242, and more highly chlorinated PCBs were quantitated as Aroclor 1254. The median half-life was 2.6 y for Aroclor 1242 and 4.8 y for Aroclor 1254. However, the half-life varied inversely with the initial serum concentration. This pattern may be a result of continued low-level exposure, variation in the time of exposure, or enzyme induction by PCBs.

POLYCHLORINATED BIPHENYLS (PCBs) are persistent compounds that have become widely distributed in the environment. From 1959 to 1977,[1] Monsanto Industrial Chemicals Company produced more than a billion pounds of PCBs in the United States. PCBs were produced as mixtures of the 209 possible chlorinated congeners under the trade name Aroclor. These mixtures were characterized and named by their different

degrees of chlorination. The major use of PCBs was in the manufacture of capacitors and transformers. The National Institute for Occupational Safety and Health (NIOSH) estimated that in 1976, as many as 12 000 workers experienced occupational exposure to PCBs.[2]

PCBs are lipophilic, and the main storage depot in the body is adipose tissue, although a dynamic equilibrium is established with the blood and other tissues.[3] Little information is available on the rates of metabolism, excretion, and elimination of PCBs in humans. Steele et al.[4] reported half-life calculations for less chlorinated PCBs (Aroclor 1242) and more highly chlorinated PCBs (Aroclor 1260) in serum from five humans. As in animal metabolism and excretion studies,[5] the less chlorinated PCBs decreased in concentration much faster than more highly chlorinated forms. More data are needed on the change in PCB concentrations in humans following exposure. In this report we describe the changes in PCB concentrations over an 8-y period for a group of occupationally exposed workers and examine how the degree of chlorination and initial serum concentration affect the half-life.

Methods

In 1975, NIOSH began a study of the effects of occupational exposure to PCBs.[6] One group of workers surveyed included 228 active white employees of an electrical equipment manufacturing plant in Bloomington, Indiana. Aroclor 1242, which is 42% chlorine by weight, was used in the production of capacitors at this plant from 1959 to 1971. Aroclor 1016, which is 41% chlorine and similar to Aroclor 1242, was used from 1971 to 1977. At the time of the survey (April, 1977), the use of PCBs was being discontinued at the plant. As part of the NIOSH study, researchers measured less chlorinated PCBs (quantitated as Aroclor 1242) and more highly chlorinated PCBs (quantitated as Aroclor 1254) in serum samples drawn from workers after a 12-h fast. Serum PCB concentrations were considerably higher than in the general population, especially for employees working in or adjacent to the capacitor processing area.[6]

In August 1985, NIOSH conducted a follow-up study by resurveying 60 of these same workers. All 60 were white males and were 32 to 67 y of age at the time of the second survey. In 1977, this group had Aroclor 1242 levels of 2 to 3 300 ppb (μg/l) with a median of 155 ppb, whereas in 1977 they had Aroclor 1254 levels of 5 to 250 ppb with a median of 39 ppb. As in 1977, serum samples were collected after a 12-h fast and analyzed for PCBs (as Aroclor 1242 and 1254). One PCB value obtained in 1977 was invalidated because of clerical errors, and one sample collected in 1985 was of insufficient volume for analysis. In all, there were 58 valid paired PCB levels, one each, for 1977 and 1985.

Environmental Science and Engineering, Inc. (ESE) (Gainesville, FL) performed the 1977 serum PCB analyses. The methods are described in detail elsewhere.[6-8] ESE employed an electron capture gas chromatographic procedure that used a mixed-phase column. Quantitation was by peak height summation for matching peaks in an Aroclor 1242 standard for less chlorinated PCBs (retention times less than that of DDE) and an Aroclor 1254 standard for more highly chlorinated PCBs (retention times greater than that of DDE). For quality control, two in vitro spiked serum pool specimens and one blind split duplicate were analyzed in each analytical run. The Centers for Disease Control (CDC) laboratory provided one unspiked pool and one pool spiked at 81.1 ppb Aroclor 1242. The mean concentrations for the two laboratories agreed within 10% for the unspiked pool and within 7% for the spiked pool. The recovery for the spiked pool was 92% for ESE and 99% for CDC.

The 1985 serum PCB analyses were performed at the Centers for Disease Control using similar methodology. Electron capture gas chromatography with a mixed-phase column and the same quantitation technique were used to duplicate, as closely as possible, the methodology for the 1977 analyses. Two blind and two nonblind in vivo pool specimens were analyzed in each analytical run for quality control.

We assumed that no further exposure to PCBs occurred after the initial measurement, and that PCBs exhibit first-order kinetics (single exponential decay over time) according to the equation:

$$C_t = C_0 \exp(-\lambda t) \qquad \text{[Eq. 1]}$$

where C_0 and C_t are, respectively, the initial (1977) and final (1985) concentrations, t is the time between measurements (100 mo), and λ is the decay constant. The half-life is defined as the time after which the original concentration has been halved, and in first-order kinetics is computed:

$$\text{Half-life} = (\ln 2)/\lambda. \qquad \text{[Eq. 2]}$$

Half-lives were calculated for each of the 58 pairs of measurements for Aroclor 1242 and 1254. All statistical analyses were done using SAS (SAS Institute, Cary, NC).

Results and Discussion

The paired values for the 1977 and 1985 PCB concentrations are shown in Figure 1. The percentage changes over the 100-mo interval ranged from +22% to −99%, with a median of −89% for Aroclor 1242, and from −25% to −96%, with a median of −70% for Aroclor 1254. The correlations between the paired log values were 0.79 and 0.80 for Aroclors 1242 and 1254, respectively. Figure 2 shows the relationship between the calculated half-life value and the initial (1977) concentration. If the assumptions of no further exposure and exponential decay were true, the estimated half-life should be the same regardless of the starting point. Instead, half-life estimates decreased as initial concentrations increased. The rank correlations (Spearman's rho) between half-life and initial concentration were −0.32

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(p = .0133) for Aroclor 1242 and −0.82 (p < .0001) for Aroclor 1254. Table 1 shows the median half-life estimate for different concentration ranges. For both Aroclors, the median half-life showed an increase between the highest concentration range (100+ ppb) and the lowest range (0–30 ppb). The median of sample half-lives is a relatively unbiased estimator of the mean population half-life under a first-order kinetics model with no further exposure.[9] The median half-life for the less chlorinated PCBs (Aroclor 1242) was consistently shorter than the half-life for the more highly chlorinated PCBs (Aroclor 1254) for all concentration ranges. This is consistent with the results of pharmacokinetic studies in laboratory animals.[5]

We have several possible explanations for the observed inverse relationship between half-life and initial concentration. Negative biases for the 1977 measurements and/or positive biases for the 1985 measurements could result in such a pattern. However, no indication of such patterns of bias between the two laboratories was evident.

Continued low-level exposure to PCBs between 1977 and 1985 would raise the apparent half-life values, especially at low initial concentrations, because small additional doses would represent a larger proportion of the initial body burden. Although the plant stopped using PCBs during the 1977 study, additional exposure is possible through residual PCBs in the workplace or environmental exposure pathways. PCBs were purportedly discharged into the Bloomington municipal sewage system throughout the 18-y period of PCB use.[10] Potential environmental exposure pathways in this community include using PCB-contaminated sewage sludge,[10] scavenging metal from discarded capacitors at local dump sites, swimming in water adjacent to dump sites, and eating fish caught locally.[11] The environmental ubiquity of PCBs and the tendency of body burdens to increase with age in populations without exceptional exposure[12] suggest that low-level exposure may continue to occur.

In an exponential decay model, the concentration of a compound is halved after an interval of one half-life regardless of the initial concentration. PCBs, however, are not single compounds but are complex mixtures of congeners with differing rates of metabolic breakdown. If an individual had been exposed several years before the initial blood sample, he would have metabolized many of the less resistant PCB congeners, retaining the more resistant congeners (e.g., more highly chlorinated forms). The half-life for the mixture of congeners that remain would, therefore, be longer than for an individual with a more recent exposure. If the individuals with higher PCB levels in the 1977 study had been more recently exposed that those with lower levels, this could help explain the observed pattern.

In addition, if insufficient time lapsed between exposure and blood sampling for equilibrium between blood and adipose levels to be reached, then blood levels would be artificially elevated.[13] Thus, if individuals with the highest concentrations in 1977 had very recent exposures, their equilibrial serum levels

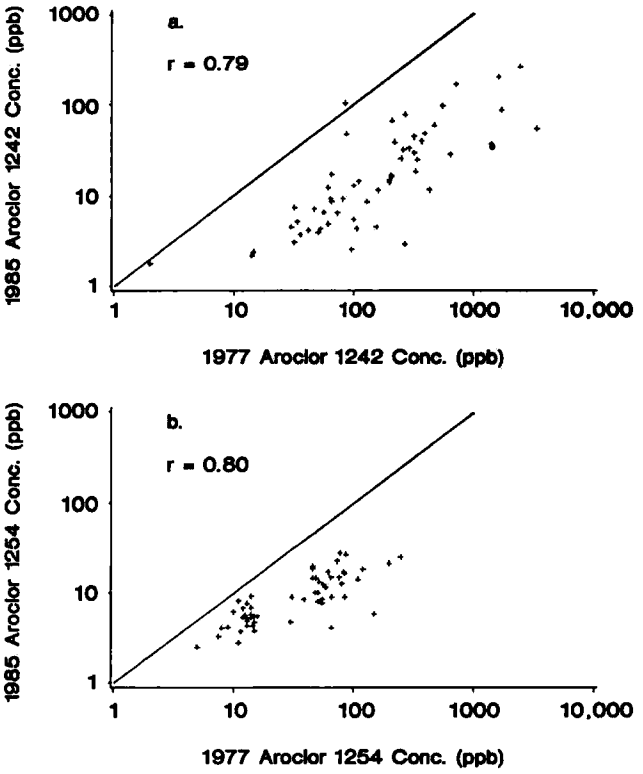

Fig. 1. Log serum PCB concentration (ppb) in 1985 vs. that in 1977: (a) Aroclor 1242; (b) Aroclor 1254. The line of equal concentrations is shown for reference.

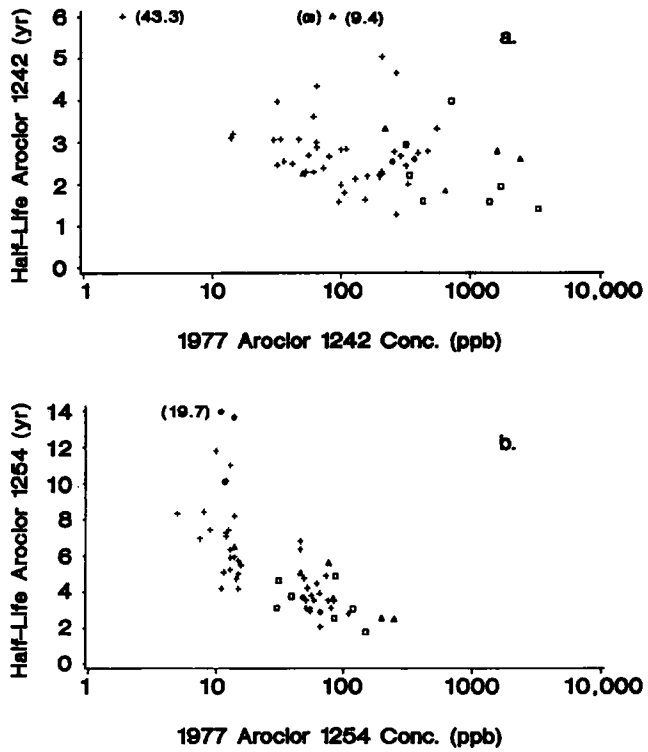

Fig. 2. Half-life (y) vs. log serum PCB concentration in 1977: (a) Aroclor 1242; (b) Aroclor 1254. The symbols represent work areas within the plant: *square* = capacitor processing area; *diamond* = adjacent to capacitor processing area; *triangle* = maintenance (worked throughout plant); and *cross* = other. Off-scale half-life values are shown within parentheses. An infinite half-life value denotes no observed concentration decrease.

Table 1.—Median Half-Lives for Aroclor 1242 and 1254 in Groups with Different Initial Serum PCB Concentrations in 1977

1977 concentration (ppb*)	Median half-life (y)	
	Aroclor 1242	Aroclor 1254
0–30	3.1 (*N* = 4)	6.5 (*N* = 27)
30–100	2.7 (*N* = 21)	3.8 (*N* = 26)
100+	2.4 (*N* = 33)	2.6 (*N* = 5)
All	2.6 (*N* = 58)	4.8 (*N* = 58)

*ppb = μg/l serum.

would be overestimated and their half-life estimates would be too low. Indeed, individuals working directly in and adjacent to the capacitor-processing area and in maintenance (which required work throughout the plant) tended to have the highest 1977 PCB levels and the shortest half-lives (Fig. 2). These individuals worked in areas where daily contact with PCBs was possible and may have had very recent exposure.

Enzyme induction by PCBs may also help explain the relationship between half-life and initial concentration. The cytochrome P-450 monooxygenase system converts PCBs to metabolites that may then either be conjugated and excreted or bound to macromolecules such as proteins, DNA, or RNA. In studies on rats and rabbits, both 3-methylcholanthrene (MC) and phenobarbital (PB) induced forms of cytochrome P-450 that catalyze this process, although the latter was much more effective.[14] PCBs are also powerful microsomal enzyme inducers in the rat, and their effect resembles that of both MC and PB administered simultaneously.[15] Thus, higher concentrations of PCBs in humans could lead to greater microsomal enzyme induction and more rapid metabolism of PCBs.

Steele et al. presented paired data for Aroclors 1242 and 1260 for five workers from the same electrical equipment manufacturing plant in Bloomington, Indiana, which was the focus of this study.[4] These workers had Aroclor 1242 levels ranging from 51 to 320 ppb in 1977. In that study, Aroclor 1242 half-life estimates of 6 to 7 mo were reported using a different half-life estimation procedure. Recalculation of the half-life for each individual, with the present methodology, gives estimates ranging from 1.7 to 2.2 y, with a median of 1.9 y. This is comparable to the median of 2.4 y we found for initial Aroclor 1242 concentrations of 100 ppb or more.

The current data suggest a concentration-dependent decrease in PCB levels over time, but cannot distinguish between continued low-level exposure, variation in the time of exposure, or enzyme induction as the cause. Estimating the persistence of PCBs in human tissues is also complicated by the variety of congeners to which individuals may have been exposed and may retain in their tissues. The use of Aroclor standards provides a convenient way for researchers to summarize overall PCB levels, but it obscures congener-specific differences in rates of metabolic breakdown associated with the degree and position of chlorine substitutions. Further studies incorporating greater numbers of data points for each individual, and, if possible, congener-specific analyses, are needed to more fully understand the dynamics of PCBs in humans.

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