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Review

Background levels of polychlorinated biphenyls in the U.S. population

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ABSTRACT

Background: Polychlorinated biphenyl (PCB) exposures are encountered by the general public by eating contaminated food or living near a previously operating PCB factory or hazardous waste site. PCBs affect the immune, reproductive, nervous, and endocrine systems and are carcinogens. PCBs were banned in the United States in 1977. For public health, it is important to be able to estimate individual risk, especially for vulnerable populations, to monitor the decline in risk over time and to alert the public health community if spikes occur in PCB exposures, by measuring serum PCB levels. The historical decline in PCB exposures cannot be documented within a repeatedly tested general population, since there is no such population. Therefore, our aim was to model serum PCB levels in the US general population over time using published data.

Methods: Models were developed based on 45 publications providing 16,914 background PCB levels in sera collected 1963–2003. Multiple linear regression and exponential decay were used to model the summary PCB levels.

Results: Background levels of higher-chlorinated PCBs (five or more chlorines) in sera increased before 1979 and decreased after 1979; a quadratic model was the best fit. However, the exponential decay model explained better the low PCB serum levels still seen in the general population. For lower-chlorinated serum PCBs, no increase or decrease was shown (1.7 ppb for all years).

Conclusions: Limitations for both models were lack of repeated measures, non-randomly selected study participants, selected years, concentration on geographic areas centered on PCB waste sites, lack of adjustment for BMI or for laboratory methods. Despite the limitations, this analysis shows that background PCB levels in the general population are still of concern. Future work should focus on uncertainties governing how to interpret the levels with respect to possible long term health effects.

Contents

1. Introduction

Polychlorinated biphenyls (PCBs) were used in the U.S. as an industrial oil (i.e., Aroclors) from the 1930s until banned in 1977. PCBs are persistent organic pollutants. They are established developmental

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neurotoxicants in humans, associated with thyroid toxicity, effects on immune, reproductive, nervous (Steenland et al., 2006), and endocrine systems, and carcinogens (Agency for Toxic Substances and Disease Registry, 2000).

PCB serum levels have been measured in human population groups without occupational exposures during the years that PCB oils were in use and in subsequent years. Even though PCBs were banned in 1977, more than one million capacitors and 14,000 transformers containing PCBs are still in use in the U.S. (Environmental Protection Agency and Canada, 2004). The transformers are mandated to be inspected every three months for leaks (Environmental Protection Agency, 1985). The total amount of PCBs in registered transformers in the EPA database is $4.7*10^7$ kg ($1.03*10^8$ lb). Primary sources of PCB exposure for the general population include contact with ground water or soil contaminated due to inappropriate disposal of materials containing PCBs (e.g., discarded transformers and capacitors) (Agency for Toxic Substances and Disease Registry, 2000), food contamination from food storage in silos with PCB-coated interiors (Willett et al., 1985), and consumption of fish from contaminated waterways (Humphrey, 1976). Additional sources of PCB exposure are still being identified, including contamination from PCBs in caulking materials used in buildings built or refurbished prior to 1977 (Herrick et al., 2004), PCBs in floor refinishing compounds (Rudel et al., 2008), incineration of municipal waste (Ikonomou et al., 2002), and volatilization from landfills (Faroon et al., 2003).

Methods for determining the levels of PCBs in blood have been reviewed (Cochran and Frame., 1999). Quantification of PCBs in serum is performed with packed column gas chromatography and electron capture detection (GC/ECD) (Needham et al., 1981a). Quantitative methods have been developed and improved over the years (Sawyer, 1978; Mullin et al., 1984). A majority of serum PCB levels analyzed in early 1970 used GC/ECD and methods developed by Webb and McCall (1973). Serum PCB levels have been reported as parts per billion (ppb) of p,p′-dichlorodiphenyldichloroethylene (DDE) (equivalent to nanograms of DDE per milliliter of serum) and as the sum of the higher PCB congeners—compounds with retention times longer than that of DDE (pentachlorobiphenyls, hexachlorobiphenyls and heptachlorobiphenyls) (Wolff et al., 1991, 1993). Quantification of PCBs has used internal homologue standards or PCB mixtures that have been characterized such as Aroclors (Gammon et al., 2002), giving a total PCB concentration calculated as the sum of congeners (Burse et al., 1990b; Dewailly et al., 1994; DeVoto et al., 1997; Greizerstein et al., 1997; Stellman et al., 1998; Laden et al., 1999; Willman et al., 2001; Charlier et al., 2003; Whitcomb et al., 2005). Methods for PCB analyses still represent an active area of research in analytical chemistry, involving GC/ECD and gas chromatography/mass spectroscopy (GC/MS) techniques (Patterson et al., 1987, 1989, 1991; Burse et al., 1990a; Brock et al., 1996; Barr et al., 2003; Rogers et al., 2004).

Weighted samples of the general population have been monitored for serum PCB levels by the National Health and Nutrition Examination Survey (NHANES) since 1999. However, NHANES cannot answer questions regarding historical (before 1999) PCB serum levels important to public health aspects such as 1) performing retrospective exposure assessments or risk assessment for carcinogens, and 2) detecting possible spikes in PCB levels. High PCB levels were recently detected in persons living in houses where floors had just been refinished (Rudel et al., 2008). It turned out that the floors had been coated in the 1950s with a polyurethane finish containing PCBs; refinishing these floors released PCBs. Future environmental sources of lower-chlorinated PCBs may increase due to aerobic and anaerobic microbial degradation as reviewed recently (Field and Sierra-Alvarez, 2008 and Borja et al., 2005), and therefore play a more important role in the future prediction of historical PCB serum levels.

Our objective for this review was to investigate PCB levels within the U.S. adult population without occupational exposure using data from the published literature.

2. Methods

2.1. Study population

Scientific literature providing data on background levels of serum PCBs was identified in several ways. The PubMed database was searched using the following terms: PCB, serum/sera, human and background/environmental exposure. References cited by Kreiss (1985), which contains a concise summary of background levels of PCBs, were also considered. Other publications, including book chapters and local health department reports, were identified by references in papers. Publications describing non-US cohorts and publications describing only lipid-adjusted serum levels or levels in tissue were excluded, as were publications that described only persons with occupational exposure to PCBs. Study populations considered for the assessment of PCB background levels included control groups without occupational exposure to PCBs and fish-eater cohort members who ate fish “never” or “infrequently”. Many study populations were evaluated in more than one of the identified publications; therefore, an effort was made to include only those publications providing unique information. Table 1 provides information from the literature resulting from the search.

2.2. Statistical analysis

The literature database included information from 51 publications containing background PCB serum levels spanning the years 1963–2003. Generally, these publications gave the year of the serum draw, the analytic method, and the arithmetic mean PCB serum level and sample size; some publications reported geometric means, medians, or ranges instead of or in addition to the arithmetic mean. A total of 83 summary levels were reported with sample sizes ranging from 2 to 1631 (median 105). Most of the summary levels were for total serum PCB levels (50/83) and many of the summary levels were not sex-specific (33/83).

Multiple linear regression and exponential decay were used to model the PCB serum levels, weighted by sample size, as a function of year and sex. Higher order terms, including an interaction term for year and sex, were considered. In most cases, the outcome variable was the arithmetic mean (56/83); where the arithmetic mean was not reported the geometric mean (13/83), median (12/83), or midpoint (2/83) was used. A majority of the publications reported arithmetic mean PCB levels; however, some reports that they only reported geometric means. Rather than combine arithmetic and geometric means in a single model, for the few publications that only reported a geometric mean PCB level, an arithmetic mean level was estimated. Geometric means were converted to arithmetic means using the standard conversion (assuming log-normality) when the geometric standard deviation (GSD) was provided (4 of 13 studies; GSD range 1.74–1.92); when the GSD was not provided, an estimated GSD of 2.0 was used. Consequently, the models examined the association of the arithmetic mean PCB level with calendar time. The distribution of the arithmetic mean higher-chlorinated PCB levels was approximately normally distributed. Sex was specified using indicator variables (for female and male, relative to unspecified) and year was relative to 1977 (the year PCBs were banned in the US). For studies that reported summary levels over a range of years, the midpoint year was used. In one instance where the sample size was not provided, the sample size was estimated to be 10 based on personal communication.

Most publications summarized in Table 1 reported serum PCB levels using the method of Webb and McCall with packed GC/ECD, capillary GC (CGC)/ECD, or high-resolution CGC (HCGC) with ECD or mass spectroscopy (MS) to obtain congener-specific data. Serum PCB levels reported as Aroclor 1242, Aroclor 1016 or pre-DDE were considered “lower-chlorinated PCB levels” because Aroclors 1242 and 1016 consist mostly of di- (17–19%), tri- (51–56%) and tetra-chlorinated (21–25%) biphenyls; serum levels reported as Aroclor 1254, Aroclor 1260 or post-DDE were considered “higher-chlorinated PCB levels” because Aroclor 1254 consists mostly of tetra- (19%), penta- (53%), hexa- (22%) and

hepta-chlorinated (5%) biphenyls (Hutzinger et al., 1985). Where Aroclor 1242 or Aroclor 1254 concentrations were not given, but congener-specific serum concentrations were provided, we allocated the congeners to Aroclor 1242 or Aroclor 1254 according to congeners typically found in one type of Aroclor, as described in Burse et al. (1990b) to best estimate Aroclor-specific means where this was not provided. Where both total PCB serum levels and congener-specific serum levels were reported in the same publication or separately in multiple publications, we used the more specific results.

Separate models considered the two dependent variables: higher-chlorinated and total PCB serum levels (to estimate background levels of Aroclor 1254) and lower-chlorinated PCB serum levels (to estimate background levels for Aroclor 1242). All statistical analyses were performed using SAS® 9 Software (SAS Institute, Inc., Cary, NC).

3. Results

A scatter plot of the higher-chlorinated serum PCB levels versus calendar time (Fig. 1) and residuals from initial models (not shown) indicated six potential outliers in levels reported by Baker et al. (1980), Burse et al. (1994), Humphrey (1976), Kreiss et al. (1981a), Orloff et al. (2003) and Wolff et al. (1982). These studies reportedly excluded persons with occupational PCB exposure; however, it is possible that serum levels reflected some participant exposures related to proximity to PCB sources and therefore were not typical of background levels. Serum PCB levels in Baker et al. (1980) were obtained on sera collected from residents of Bloomington, Indiana with "no known unusual exposures to PCBs"; however, Bloomington was the location of a large electrical capacitor manufacturing plant that used PCBs from1957 to 1977 (Ruder et al., 2006) and an ATSDR PCB toxic waste site. Serum PCB levels in Burse et al. (1994) were obtained on sera collected in 1984 from residents of New Bedford, Massachusetts, with no reported occupational exposures to PCBs; however, New Bedford was the site of two large electrical capacitor manufacturing plants that used PCBs from 1939 to 1977 (Prince et al., 2006). PCB-contaminated waste water from these plants was directly discharged into the harbor sediment and defective capacitors were also deposited in the estuary (Agency for Toxic Substances and Disease Registry, 1995). In addition, New Bedford is a coastal community and residents were known to have consumed fish and shellfish contaminated with PCBs. Serum PCB levels in Humphrey (1976) were obtained on sera collected in 1973–1974 from residents of 11 communities along the shores of Lake Michigan. Kreiss et al. (1981a) reported serum PCB levels obtained from a community-wide study in Triana, Alabama, where residents likely consumed fish from Wheeler Reservoir, which may have been contaminated with PCBs (US Army Aviation and Missile Command, 2009). PCB levels in Orloff et al. (2003) were from sera collected in 2000 from adults living within a half-mile radius of a chemical plant that had manufactured PCBs. These six studies (Baker et al., 1980; Burse et al., 1994; Humphrey., 1976; Kreiss et al., 1981a; Orloff et al., 2003; Wolff et al., 1982) were excluded from further analyses because they did not appear to meet the study inclusion criteria of excluding occupational and significant adjacent environmental PCB sources.

Models were based on data from 16,914 sera collected by 45 studies over 41 years (1963–2003). After exclusion of the six studies that appeared not to meet the criterion of limiting participation to individuals whose lifestyles and locations would not have increased their PCB exposure above background PCB levels, higher-chlorinated serum PCB levels appeared to decrease with calendar time (Fig. 2). Parameter estimates and standard errors for the linear and quadratic regression models are provided in Table 2. Residuals from the linear regression model indicated non-linearity and the quadratic term for year was statistically significant (p-value < 0.0001) in the quadratic model. The use of the quadratic term improved model R-squared values from 0.22 for the linear model to 0.41. The addition of terms describing sex did not improve the model over the quadratic model. In these models, each observation was weighted by the sample size associated with the sample mean (or summary level); results were similar in un-weighted analyses (not shown). The quadratic regression was the best fit model for the current data; however, this model indicates a zero level for higher-chlorinated PCB serum levels 25 years after 1977 or 2002. Due to the continued PCB exposures in the environment, the exponential decay model fit to the post-1977 studies provided a 2002 PCB concentration of 2.07 ppb. The geometric mean PCB concentration in whole blood for the 2003–2004 NHANES study population was 0.820 ppb (Patterson et al., 2009), which falls between the two estimates using the quadratic and exponential decay models. The equations for the three models were: Linear model: $6.173 - 0.128 * \text{YEAR\_1977}$, Quadratic model: $6.352 + 0.0397 * \text{YEAR\_1977} - 0.0111 * (\text{YEAR\_1977})^2$, Exponential decay model: $8.5788 * \exp(-0.0569 * (\text{year-1977}))$, where YEAR_1977 is the year of data collection variable centered at 1977.

Lower-chlorinated serum PCB levels did not appear to change with calendar time (Fig. 3). The coefficient for year did not significantly differ from 0 in either weighted or un-weighted regression models. Since the number of observations for lower-chlorinated PCBs was low, additional analyses were not performed. For lower-chlorinated serum PCBs, no increase or decrease was shown (1.7 ppb for all years).

When the analyses were repeated, including the six studies defined as not meeting the inclusion criteria and their 1639 participants with possible occupational exposure or exposure through eating contaminated fish, both the quadratic and exponential decay models changed, but not radically (results not shown).

4. Discussion

Serum background PCB levels were calculated using regression models, based on 45 published studies with a total of $n = 16{,}914$ samples over 41 years (1963–2003). A quadratic relationship with calendar year was observed for higher-chlorinated serum PCBs; no relationship with calendar year was observed for lower-chlorinated serum PCBs, although data was somewhat limited.

Three of the four largest studies were breast cancer case–control studies of mostly older women (50 years or older at the time of the blood draws in 1995–1997). The calculated overall mean PCB serum background level might not be appropriate for younger persons' PCB serum levels because i) younger persons born after 1977 would have had less environmental PCB exposure, and ii) younger persons have had less time to accumulate PCBs in their bodies (Kreiss, 1985).

Most of the studies were in geographic areas surrounding plants formerly manufacturing or using PCBs (MA, AL, IN), in hospitals to obtain sample sizes >150 (NY, CT), or in fish-eating communities (MI). Including the six excluded studies of 1639 people with possible occupational or environmental exposure to above-average levels of PCBs changed the quadratic and exponential decay models only slightly. In addition, three of the four largest studies focused on residents of the east coast of the United States (MD, NY, and CT), who may not be representative of the entire country.

The methods for quantitating PCBs in serum varied widely across studies. The unavoidability of treating results of all methods as equally valid is a limitation of this study. However, quantifying Aroclor 1260 in human sera by either capillary or packed column GC gave no difference in a small comparison study (Burse et al., 1990a). There is insufficient information in the literature to permit quantitating the differences between analytical methods for human serum PCB levels. Only one study (Orloff et al., 2003) used MS detection but this study was excluded from the analysis because it did not meet the inclusion criteria. There were four studies where chemical analytical methods were not reported; excluding their 1154 participants changed the models only slightly.

Especially limiting were unreported laboratory factors: limit of detection (LOD), possible modifications over time in the analytical method, and quality assurance procedures, if any. The reporting of

Table 1
Studies reporting serum PCB levels among United States residents with no occupational exposures to PCBs.

Study	Cohort	Year	*N*	Sex [a]	Age (years)		PCB (ppb)						Laboratory methods [b]
					Range	Mean	Type	Mean	GM	Median	SD	Range	
Anderson et al. (1998)	Comparison group to Great Lakes sport fish consumers	1996	41	NR	NR	NR	Aroclor 1242 Aroclor 1254 Total PCBs [c]	0.409 1.321 1.2				0.46–2.9	Patterson et al. (1987), Burse et al. (1990b, 1994) GC/ECD. Aroclor 1242 estimated as sum of congeners 28/31, 52, 56/60, 66/95, 74, 101, 132/153/105. Aroclor 1254 obtained by summing congeners 99, 118, 138/163, 145, 132/153/105, 167, 170/190, 172/197, 177, 178, 180, 182/187, 194, 195/208, 201, 203/196, 206.
Baker et al. (1980) Landrigan et al. (1979) cited in ATSDR (2000)	Community residents with no known unusual exposures to PCBs in a study of contaminated sludge users and occupational exposure	1977	22	NR	NR	NR	Aroclor 1242 Aroclor 1254 Total PCBs [c]	11.6 12.8 24.4				11–79	GC/ECD. Used Aroclor 1242 and 1254 standards; total PCBs sum hallmark peaks before and after DDE
Berkowitz et al. (1996)	Control group to pregnant women with preterm birth	1996	20	F	NR	25.9 ± 5.0	HPCB			1.70		0.08–5.30	Wolff et al. (1993) HPCB (BZ# 82/151, 118, 153, 141, 138, 187, 183, 174, 156, 180, 170, 203)
Brown et al. (1991)	Office workers Connecticut	1976	NR	NR	NR	NR	Aroclor 1242 Aroclor 1254		6.7 10				GC/ECD. Used Aroclor 1242 and 1254 standards
Burse et al. (1994)	Residents with no occupational exposure New Bedford, MA	1984	2 4	F M	50–54 36–56	52 48	Aroclor 1242 Aroclor 1254 Aroclor 1242 Aroclor 1254	8.3 34.4 30.5 83.6					Burse et al. (1989) GC/ECD
Charlier et al. (2004)	Female controls for PCBs and breast cancer case–control study	2004[d]	60	F		54.8	Total PCBs	5.10			5.15		Charlier et al. (2003) GC–MS. Summed congeners 28, 52, 101, 118, 138, 153, 180
Chase et al. (1982)	Workers without PCB exposure Railroad passenger car and locomotive maintenance facility	1979	19	M		30.7	Total PCBs	12.0				10–27	GC/ECD. Webb and McCall (1973)
Condon (1983)[e], as cited in ATSDR (2000) (Agency for Toxic Substances and Disease Registry, 2000)	Volunteers Canton, MA Norwood, MA	1980 1983	10 990	NR			Total PCBs Total PCBs	7.1 4.9	5.2 4.2		5.2 3.5	1–18 2–30	Not available
DeVoto et al. (1997)	Female controls for breast cancer case–control study	1993–1995	68	F	28–74	52.3	Total PCBs			1.8			GC/ECD LOD = 0.025 ppb/c
Drotman et al. (1983)[e]	Packing house workers, Billings, MT Volunteers, Franklin, ID	1979 1979	17 105	NR			Total PCBs Total PCBs	7.5	5.8		6.8	2–30 ND–5	Not available
Emmett et al. (1988)	Workers without PCB exposure Transformer repair workers in a switchgear shop	1980	54	M		38	Total PCBs		4.6	6		ND–15	GC/ECD. Webb and McCall (1973) using Aroclor 1260 standard.
Finklea et al. (1972)	Volunteers Charleston County, SC	1968	178 163	F M	20–60+ 20–60+		Total PCBs Total PCBs	2.51 2.76					GC/ECD using Aroclor 1254 and 1260 standards
Gammon et al. (1997)	Female volunteers without occupational PCB exposures	1995	30	F	45–81	58.7	Total PCBs	4.24			2.72		Wolff et al. (1993) GC/ECD LOD = 2 ng/ml
Gammon et al. (2002)	Female controls for breast cancer case–control study (Long Island, NY)	1996–1997	423	F	20–65		Total PCBs		2.45		1.76 GSD		Brock et al. (1996) solid phase extraction then GC/ECD. Summed congeners 118, 153, 138, 180. LOD = 0.07 ppb/c
Hanrahan et al. (1999)	Infrequent GL fish consumers GLSCF Cohort	1994–1995	57 42	M F	25.0–71.8 29.1–56.6	48.2 40.7	Total PCBs Total PCBs		1.5 0.9			0.5–9.7 0.5–3.3	Burse et al. (1990b) CGC/ECD. Summed 62 congeners.
He et al. (2001)	Non-fish-eaters GLSCF Cohort	1973–1974 1979–1982 1989–1993	27 52 202 283 135	M F M F M			Aroclor 1260 Aroclor 1260 Aroclor 1260 Aroclor 1260 Aroclor 1260	12.1 5.9 10.1 8.3 8.2		10 5.0 8.1 6.0 6.8	8.6 3.9 7.9 7.7 6.2	6.0–15.0 4.0–8.0 5.6–11.5 3.9–10.1 4.3–10.4	Hovinga et al. (1992) GC/ECD. Webb and McCall (1973)

			181	F			Aroclor 1260	7.6		6.0	6.7	4.2–9.0	
Helzlsouer et al. (1999)	Female controls from	1974	235	F		51+	Total PCBs	4.7		4.2	2.3		Brock et al. (1996) solid phase extraction then
	Breast cancer case–control study (CLUE I)	1989	105	F		61+	Total PCBs	2.2		1.7	1.9		GC/ECD
	Breast cancer case–control study (CLUE II)												
Hoppin et al. (2000)	Controls	1996–1998	82	C	32–85	65.7	Total PCBs	1.9		1.9	1.3	ND–7.2	Brock et al. (1996) solid phase extraction then GC/ECD.
	Pancreatic cancer case–control study												Summed congeners 28, 52, 74, 105, 118, 138, 153, 170, 180, 194, 203.
													LOD = 0.2 ppb/c
Hovinga et al. (1992)	Controls, <6 lb annual fish consumption	1979–1982	419	C		44.1	Total PCBs	7.2					Needham et al. (1981a), Sawyer (1978) GC/ECD.
	GL fish-eaters and non-fish-eaters cohort	1989	95	C			Total PCBs	6.8					Webb and McCall (1973) using Aroclor 1260 standard.
Humphrey (1976)	Controls, no fish consumption	1973	16	C			Total PCBs	17					GC/ECD using Aroclor 1254 and 1260 standards.
	Pilot study of GLSCF Study	1974	10	C			Total PCBs	16					
Humphrey (1983)	Farm residents in Iowa	1976–1977	803	C			Total PCBs			5		5–50	Landrigan et al. (1979)
	Farm residents in Michigan	1976–1977	1631	C			Total PCBs			6		<5–57	GC/ECD
Humphrey (1988)	Controls, infrequent fish consumption	1979–1982	419	C			Total PCBs			6.6		<3–59.5	Needham et al. (1981b)
	GLSCF Cohort												GC/ECD. Webb and McCall (1973) using Aroclor 1260 standard.
Humphrey et al. (2000)	Michigan residents of 11 shoreline communities	1993–1995	78	C	≥50		Aroclor 1242	0.24					Mullin et al. (1984)
							Aroclor 1254	4.31					CGC/ECD. Aroclor 1242 estimated as sum of congeners 74, 105; Aroclor 1254 estimated as sum of congeners 99, 118, 138/163, 146, 153, 171, 172, 177, 179/190, 180, 182, 183, 187, 193, 194, 195, 196/203, 199, 206, 208; total PCBs summed all 19 congeners and 3 coeluting congener pairs
							Total PCBs [c]	4.55					
James et al. (2002)	Pregnant women	1963–1967	399	F			Aroclor 1242	0.802		4.75	2.31		Willman et al. (2001) GC/ECD. Aroclor 1242 estimated as sum of congeners 101, 105; Aroclor 1254 estimated as sum of congeners 110, 118, 137, 138, 153, 156, 170, 180, 187; total PCBs summed congeners 105, 110, 118, 137, 138, 153, 170, 180, 187
	Child Health and Development cohort						Aroclor 1254	5.108					
							Total PCBs [c]	5.42					
													LOD = 1 ppb
Kreiss et al. (1981a)	Community-wide study	1979	458	C	<9–70+		Total PCBs	22.2		17.2	20.8	3.2–157.9	GC/ECD. Webb and McCall (1973) using Aroclor 1260 standard
	Triana, AL												LOD = 3 ppb
Kreiss et al. (1981b)	Community residents	1979	17	NR	NR		Total PCBs	7.5				2–30	Not reported
	Billings, MT												
Kreiss et al. (1982)	Michigan residents	1978–1979	855	M	<9–70+		Total PCBs		7.1				GC/ECD. Used Aroclor 1254 standard
			776	F	<9–70+		Total PCBs		5.6				
Krieger et al. (1994)	Female controls for	1964–1971	150	F			Total PCBs	4.8			2.5		Wolff et al. (1991, 1993)
	Breast cancer nested case–control study												LOD = 2 ppb
	San Francisco Bay area												
Laden et al. (2001)	Female controls for	1995–1997	502	F			Total PCBs			4.07			(Zheng et al. (2000) GC/ECD. Summed congeners 118, 138, 153, 180
	Breast cancer case–control study												
	Connecticut (Yale)												
	(First reported as lipid-adjusted serum levels in Zheng et al., 2000)												
Laden et al. (2001)	Female controls for	1989–1990	372	F	43–69		Post-DDE			3.79			Wolff et al. (1991, 1993)
	Breast cancer case–control study												GC/ECD
	Nurses Health Study												
	(First reported with $n = 230$ in Hunter et al., 1997)												
Louis et al. (2005)	Female controls for	1999–2000	52	F	18–40		Total PCBs					0.19–5.58	Whitcomb et al. (2005) GC/ECD. Used standards (congener 30 and 204).
	Environmental PCB exposure and risk of endometriosis study												
Meeker et al. (2007)	Men in subfertile couples	2000–2003	341	M	20–54	36	Total PCB		1.08[f]	1.06			57 PCB congeners
	Boston, MA												GC/ECD
Miller et al. (1991)	Residential area	1984–1987	391	M	18–64		Aroclor 1254	5.9	4.3	3.9		0.5–60.9	Burse et al. (1983) GC/ECD
	New Bedford, MA	1984–1987	449	F	18–64		Aroclor 1254	5.7	4.2	3.9		0.38–154	
Millikan et al. (2000)	Female controls	1993–1996	270	F			Total PCBs	2.56		1.97	2.3		GC/ECD
	Breast cancer case–control study	1993–1996	389	F			Total PCBs	1.89		1.63	1.2		Summed congeners 74, 99, 101, 105, 114, 118, 137,

(continued on next page)

Table 1 (*continued*)

Study	Cohort	Year	*N*	Sex [a]	Age (years)		PCB (ppb)						Laboratory methods [b]
					Range	Mean	Type	Mean	GM	Median	SD	Range	
Millikan et al. (2000)	Carolina Breast Cancer Study												138, 141, 146, 149, 153, 156, 157, 158, 167, 170, 171, 172, 174, 177, 178, 180, 182, 183, 185, 187, 190, 195, 196, 197, 200, 201, 203
Moysich et al. (1998, 1999, 2002)	Healthy, postmenopausal women Western New York State	1986–1991	192	F	45–85		Aroclor 1242 Aroclor 1254 Total PCBs [c]	0.91 3.69 4.12			2.24		Greizerstein et al. (1997) GC/ECD. Aroclor 1242 estimated as sum of congeners 6, 7/9, 15/17, 16/32, 18, 19, 22, 25/50, 31/28, 33, 40, 44, 45, 47/48, 49, 52, 55, 59/42, 60, 66/95, 70, 77/110; Aroclor 1254 estimated as sum of congeners 87, 97, 99, 101, 105/132, 118, 128, 129, 134, 135, 136, 138, 141/179,147, 149, 151/82, 153, 171/156, 172, 174/181, 176, 177, 180, 183, 185, 187, 188, 194, 195, 200, 203/196, 205, 206; total PCB congeners includes 23, 64, plus all congeners above except 44,105/132 varied by congener.
Orloff et al. (2003)	Adults living in a 0.5 mile radius of a chemical plant that formerly manufactured PCBs, AL	2000	43	C			Aroclor 1242 Aroclor 1254 Total PCBs [c]	2.6 11.6 14.3		2.2		ND–210	Patterson et al. (1991) HRGC/ID-HRMS Aroclor 1242 estimated as sum of congeners 28, 52, 49, 44, 74, 66, 101, 99, 87, 110, 118, 105; Aroclor 1254 estimated as sum of congeners 151, 149, 146, 153, 138/158, 128, 167, 156, 157, 178, 187, 183,177, 172, 180, 170, 189, 201, 196/203, 195, 194, 206, 209.
Persky et al. (2001)	Comparison group to sport fish consumers. Non-Great Lake sport fish consumers.	1993	9 28	F M		44.6 47.7	Total PCBs Total PCBs			0.9 1.4			Burse et al. (1990b) CGC/ECD. Summed 89 congeners (62 peaks).
Reid and Fox (1982)[e], cited in ATSDR, 2000 (Agency for Toxic Substances and Disease Registry, 2000)	Volunteers Old Forge, PA	1981	138	NR			Total PCBs	3.6				<3–43	Not available
Ritchie et al. (2005)	Male controls Prostate cancer case–control study	2000–2001	99	M	44–85	63.1	Total PCBs			0.3		0.05–2.46	Ritchie et al. (2003) GC/ECD. Summed congeners 99, 101, 105, 110, 118, 138, 146, 153, 156, 170, 172, 177, 178, 180, 183, 187, 189, 193.
Rogan et al. (1986)	Mothers (white) participating in a lactation study in North Carolina [g] At birth At six weeks	1978–1982	872 802	F	16–41	27 [h]	Total PCB			9.06 6.98	NR	NR [i]	McKinney et al. (1984) GC/ECD
Sahl et al. (1985)	Pre-employment screen of utility company workers	1982–1984	738	NR	NR	NR	Total PCBs [c] Pre-DDE Post-DDE	5 3 3		4 2 2	4.37 2.76 2.74		Needham et al. (1981a,b) GC/ECD. Webb and McCall (1973) using Aroclors 1242, 1254 and 1260 as standards.
Schwartz et al. (1983)	Mothers, none-moderate fish consumption Michigan Fish-eater Cohort	1980–1982	190 196	F F			Aroclor 1016 Aroclor 1260	1.6 5.5		0.8 4.6	4.5 3.7		Needham et al. (1981a) GC/ECD. Webb and McCall (1973) using Aroclor 1016 and 1260 standards.
Stehr-Green et al. (1986)	Unexposed group Study of persons exposed to PCB-contaminated waste sites, Bloomington, IN	1984	8	NR		35.6	Total PCBs			5.87		4.0–13.0	Needham et al. (1981a) GC/ECD

Tee et al. (2003)[j]	Non-fish-eater controls	1980	78	NR	<50–69		Total PCBs	9.1					GC/ECD. Webb and McCall (1973)
	Michigan Fish-eater cohort	1990	78		(in 1980)		Total PCBs	8.6					LOD = 3 ppb
		1994	78				Total PCBs	6.9					
Vernon (1981)[e], as cited in ATSDR, 2000 (Agency for Toxic Substances and Disease Registry, 2000)	Volunteers Newton, KS	1979	7	NR			Total PCBs	4.9	4.2		3.1	2–11	Not available
Weisskopf et al. (2005)	Mothers, infrequent fish consumption GLSCF Cohort	1994–1995	24	F			Total PCBs		0.85	0.81		0.53–1.66	Burse et al. (1990b) CGC/ECD
Welty (1983)[e], as cited in Kreiss (1985)	Volunteers	1983	59	NR			Total PCBs	5.8	4.4		6.5	1–45	Not available
	Jefferson, OH	1983	40				Total PCBs	6.7	5		5.3	1–23	
	Fairmont, WV												
Wolff et al. (1982)	Residential population, Michigan	1978	963	NR			Total PCBs	9		7			HRGC/ECD-MS, GC/ECD. Webb and
	Michigan residents, not Muskegon County	1978	69				Total PCBs	21		18			McCall (1973) pre and post-DDE.
	Muskegon County residents												
Wolff and Schecter (1992)	Hospital controls for a study of workers after an electrical transformer explosion	1987	37	NR		41	Total PCBs	3.5		3.0	2.0	1–9	GC/ECD using Aroclor 1254 standard.
Wolff et al. (1993)[k]	Female controls for breast cancer nested case–control study New York University Women's Health Study	1985–1991	171	F	35–65		Total PCBs	6.7			2.9		Wolff et al. (1991) GC/ECD. Webb and McCall (1973) using Aroclor 1260 standard.
Wolff et al. (2000a,b)[k]	Female controls for breast cancer nested case–control study New York University Women's Health Study New York, NY	1987–1992	295	F			Total PCBs		4.97		1.74 GSD		Burse et al. (1990b) GC/ECD. Webb and McCall (1973) using Aroclor 1260 standard.
Wolff et al. (2000a,b)	Benign breast cancer and other hospital controls for a breast cancer case–control study New York, NY	1994–1996	325	F		54.5	HPCB		4.1		1.89		Wolff et al. (1993), Hunter et al. (1997) GC/ECD. HPCB summed congeners 118, 138, 141, 153, 156, 167, 170, 174, 177, 180, 183, 187, 201, 203; LPCB summed congeners 28, 66, 74, 99, 101. LOD = 1 ppb
			275	F		54.5	LPCB		0.75		1.92 GSD		
Wolff et al. (2005)	Pregnant women Children's Environmental Health Study	1998–2001	194	F			Total PCBs			0.79			Gammon et al. (2002) GC/ECD. Summed congeners 118, 153, 138, 180

Abbreviations: GLSCF Cohort, Great Lakes Sport Caught Fish Cohort; CLUE I, Campaign Against Cancer and Stroke conducted in Washington County, MD; CLUE II, Campaign Against Cancer and Heart Disease conducted in Washington County, MD; GC/ECD, gas chromatography with electron capture detection; CGC/ECD, capillary GC/ECD; HRGC/ID-HRMS, high-resolution gas chromatography isotope-dilution high-resolution mass spectrometry; NR, not reported; ND, not detected.

[a] For sex, M = male, F = female, C = males and females combined, and NR = not reported.

[b] All congener numbers are International Union of Pure and Applied Chemistry (IUPAC) numbers.

[c] Total PCBs not used in the regression models since more specific estimates (e.g., Aroclor 1242 and Aroclor 1254) are available.

[d] Publication year was used as a surrogate for the year of the serum draw.

[e] As cited in ATSDR Toxicological Profiles (2000, Table 6–21).

[f] Table 1 in Meeker et al. (2007) provides the distribution of PCBs in selected percentiles (5th, 10th, 25th, 50th, 75th, 90th, and 95th) with the following values: 0.41, 0.57, 0.74, 1.06, 1.56, 2.27, and 2.65, respectively.

[g] Blood was collected twice from the mothers: once at birth and a second time six weeks after birth.

[h] Median age.

[i] The 95th percentile (maximum) was reported for serum at birth and six weeks: 19.70 (88.80) and 14.60 (44.60), respectively.

[j] Tee et al. (2003) represents the same cohort as for Hovinga et al. (1992) and Humphrey (1988).

[k] We suspect that there is some overlap between the controls in the Wolff et al. (1993) and Wolff et al. (2000a) studies. The 1993 study had 56 cases and 2–4 controls per case (with 7 extra controls) resulting in 171 controls. The 2000a study had additional cases with the additional years of follow-up. The 2000a study had 148 cases and approximately 2 controls per case, randomly selected from the control used in the endogenous hormone/breast cancer study. The extent of the overlap is unclear, but since it is not 100%, we retained information from both studies.

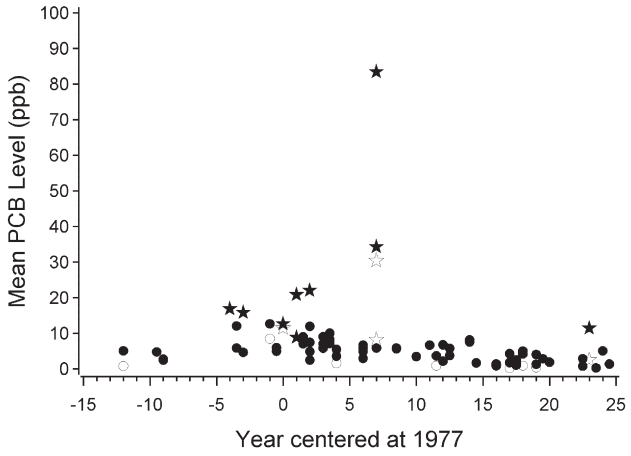

Fig. 1. Scatter plot of summary PCB serum level (ppb) versus time since 1977 for all studies described in Table 1; higher-chlorinated PCBs are marked with solid circle and solid star for nine outliers: Baker et al. (1980) (12.8 ppb), Burse et al. (1994) (34.4 and 83.6 ppb), Humphrey (1976) (1973-study: 17 ppb and 1974-study: 16 ppb), Kreiss et al. (1981) (22.2 ppb), Orloff et al. (2003) (11.6 ppb), Wolff et al. (1982) (9 and 21 ppb); lower-chlorinated PCBs are marked with open circle and open star for the four outliers; Baker et al. (1980) (11.6 ppb), Burse et al. (1994) (8.3 and 30.5 ppb), Orloff et al. (2003) (2.6 ppb).

total PCB serum level, rather than congener-specific levels, was an additional limitation. Adjustments could not be made for age and body mass index (BMI) which could affect measured PCB serum levels. Pre-blood-collection weight loss (not reported) potentially could influence the PCB serum measurement due to PCB partitioning between adipose tissue and serum (Brown et al., 1991; Dar et al., 1992; Pelletier et al., 2003). BMI could potentially have reduced the variability in the model because for each individual the PCB levels would be adjusted to the person's body mass or possible 'storage area' for PCBs. PCBs are stored in the body's adipose tissue and through steady state are released into the blood for metabolism and excretion (Mes et al., 1989). Persons with a large storage area (i.e.; a high BMI) can store more PCBs than a person with less body mass.

Some additional limitations were related to the collection of data from the published literature. Some of the studies overlapped; participants potentially could have been counted twice (Laden et al., 2001). Most of the publications reported arithmetic mean; however some studies reported the geometric mean, median, or midpoint. We converted the geometric means to arithmetic means using the geometric standard deviation, if it was provided, or an assigned GSD (2.0) if it was not; if the actual GSD differed from 2.0 this could have introduced some minor errors into the estimate.

Table 2
Parameter estimates and standard errors (SEs) where observations were weighted by sample size (REG procedure, SAS).

Model	Term	Higher-chlorinated and total PCBs [a] ($N=62$)		Lower-chlorinated PCBs [b] ($N=8$)	
		Estimate	SE	Estimate	SE
1	Intercept	6.2	0.33	1.7	0.53
	Year–1977	−0.13	0.031	0.0042	0.047
	Model R^2	22%		0.1%	
2	Intercept	6.4	0.29		
	Year–1977	0.040	0.048		
	(Year–1977)^2	−0.011	0.0026		
	Model R^2	41%			

[a] Higher-chlorinated PCBs reported as Aroclor 1254, Aroclor 1260, "higher PCBs", post-DDE, or total PCBs in the published literature.
[b] Lower-chlorinated PCBs reported as Aroclor 1016, Aroclor 1242, "lower PCBs" or pre-DDE in the published literature.

The overall sample size was reduced because studies that did not report PCB serum levels separately for non-fish-eaters and fish-eaters (Dar et al., 1992) or reported levels that were not lipid adjusted (Ritchie et al., 2003; Rothman et al., 1997; Shadel et al., 2001; Schecter et al., 2001; Sjodin et al., 2004) were excluded because lipid-adjusted and unadjusted serum PCB levels were not directly comparable. Studies reporting serum PCB levels from non-U.S. populations (Sala et al., 1999; Sandau et al., 2000) were also excluded.

Despite these limitations, we can conclude from the analyses of background population PCB serum levels that there was a quadratic trend, with an estimated date of maximum PCB serum levels in 1979. The upward trend can be explained by the onset of PCB use in the early 1930s after they were first synthesized. Throughout the period of use, PCBs generally were not discarded in closed containers but rather to the environment (Agency for Toxic Substances and Disease Registry, 1995). The peak of the parabolic modeled curve is around 1979 when PCB usage was banned. The decline in PCB serum levels after this time is probably driven by the PCB production and use ban but also EPA's Clean Water Act with an enforceable maximum contaminant level for PCBs in public drinking water systems (0.0005 ppm), and the Food and Drug Administration (FDA) tolerance levels for PCBs in food (0.2–3 ppm) resulting in a decline in PCB concentrations in the environmental media (air, soil, water) and foods.

The quadratic model does not account for higher-chlorinated PCB congeners' resistance to metabolism and continued human exposure

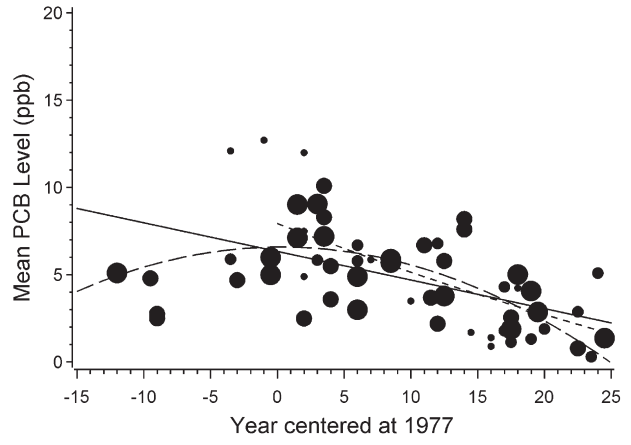

Fig. 2. Scatter plot of higher-chlorinated mean PCB serum level versus time relative to 1977 together with the simple linear (solid) and quadratic (dashed) regression lines, and exponential decay (small dashed). The size of each symbol is indicative of the sample size associated with the reported sample mean PCB serum level. Certain studies were excluded as explained in the text.

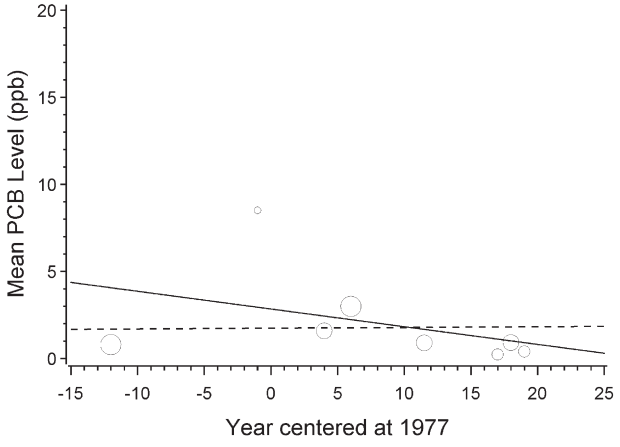

Fig. 3. Scatter plot of lower-chlorinated mean PCB serum level versus time relative to 1977 together with the simple linear regression line (solid line) and the weighted linear regression line (dashed line). The size of each symbol is indicative of the sample size associated with the reported sample mean PCB serum level. Certain studies were excluded as explained in the text.

from contaminated environment and foods. In fact, as long as exposure continues, a true steady state can never be achieved. In the future, the non-creatinine-adjusted NHANES data should be added to the data used in the present analysis; that addition would make the estimate of the decreasing curve considerably better.

The slow reduction in lower-chlorinated PCB serum levels results from the constant feed of degraded and metabolized higher-chlorinated PCBs to lower- chlorinated PCBs in environmental media, and in animal and human systems, resulting in a slight net change with a continuous low level.

Residual PCBs, in the environment, in capacitors and transformers that are still in place (Environmental Protection Agency and Canada, 2004), and in human beings, flora, and fauna are still of concern, especially since we do not know the relationship between PCB serum levels and possible long term health effects (Holoubek, 2001). This information is particularly crucial for the perinatal period where PCB exposure may impair immune system development in children and make diphtheria and tetanus vaccinations less effective (Heilmann et al., 2006).

5. Conclusions

Modeling environmental PCB levels in the general population was possible even with the limitations presented here because PCBs have been extensively studied. The values derived for PCB levels in the general population will be used in a future study estimating PCB half-lives among those occupationally exposed, to adjust for non-occupational PCB exposures.

Future population studies should report participant sex, BMI, and weight changes and any relevant environmental or occupational exposures and should focus on documenting congener-specific PCB exposures and on possible relationships between these and health effects.

This is the first pooled analysis of general population PCB serum levels, providing risk assessors and public health providers a tool to estimate PCB dose over time and to detect spikes in PCB serum levels in the US general population.

Despite the fact that PCBs have been banned for 30 years these once important synthetic industrial chemicals still threaten human health, especially in some regions of the country and within vulnerable populations.

6. Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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