Mortality in Male and Female Capacitor Workers Exposed to Polychlorinated Biphenyls

Renate D. Kimbrough, MD
Martha L. Doemland, PhD
Maurice E. LeVois, PhD

A mortality study was conducted in workers with at least 90 days' exposure to polychlorinated biphenyls (PCBs) between 1946 and 1977. Vital status was established for 98.7% of the 7075 workers studied. In hourly male workers, the mortality from all cancers was significantly below expected (standardized mortality ratio [SMR] = 81; 95% confidence interval [CI], = 68 to 97) and comparable to expected (SMR = 110; 95% CI, 93 to 129) in hourly female workers. No significant elevations in mortality for any site-specific cause were found in the hourly cohort. All-cancer mortality was significantly below expected in salaried males (SMR = 69; 95% CI, 52 to 90) and comparable to expected in salaried females (SMR = 75; 95% CI, 45 to 118). No significant elevations were seen in the most highly exposed workers, nor did SMRs increase with length of cumulative employment and latency. None of the previously reported specific excesses in cancer mortality were seen. This is the largest cohort of male and female workers exposed to PCBs. The lack of any significant elevations in the site-specific cancer mortality of the production workers adds important information about human health effects of PCBs.

Polychlorinated biphenyls (PCBs) are complex mixtures of 209 different chlorinated biphenyl congeners. They were used extensively in the United States from the 1930s through 1977 in a variety of industrial applications. PCB mixtures have several chemical and physical properties that made them extremely versatile, including resistance to acids and bases as well as oxidation and reduction; compatibility with organic materials; and thermal stability and nonflammability. The major volume usage of PCBs was in capacitors and transformers as dielectric fluids, but they were also used as lubricants and sealants; as additives in paint, plastics, newspaper print, and dyes; as extenders in pesticides; and as heat transfer and hydraulic fluids. More than 95% of the liquid-filled electrical capacitors and transformers produced before the early 1970s contained PCBs. PCBs are persistent chemicals and have bioaccumulated in the environment. They continue to be detected in air, soil, water, and sediment. Trace amounts are also present in the tissues of wildlife, domestic animals, and humans;[1] however, the levels of PCBs in the environment are declining.

The potential for adverse human health effects of PCB exposure has been a concern since the early 1970s and resulted in the Environmental Protection Agency's ban of the production of PCBs in 1978. Current knowledge regarding the human health effects of PCBs is limited, inconsistent, and difficult to interpret. Occupational mortality studies of capacitor workers have reported

From the Institute for Evaluating Health Risks, Washington, DC.

Portions of this study were presented in poster form at the 1997 North American Congress of Clinical Toxicology Annual Meeting, September 11–16, 1997.

Address correspondence to: Renate D. Kimbrough, MD, Institute for Evaluating Health Risks, Suite 402, 1629 K Street, NW, Washington, DC 20006.

higher than expected rates of melanoma[2] and cancer of the liver,[3,4] rectum,[3] gastrointestinal tract,[5] brain,[2] and hematopoietic system.[5] The site-specific elevations, however, have not been observed consistently across studies. More importantly, many of the elevated cause-specific standardized mortality ratios (SMRs) reported in the various studies were not correlated with higher and/or longer exposures to PCBs or longer latency periods, which would be suggestive of a dose-response relationship.

We conducted a retrospective cohort mortality study of 7075 workers exposed to PCBs during the capacitor manufacturing process. The cohort represents all hourly and salaried workers from two plants in upstate New York who were employed for 90 days or more from 1946, when capacitor manufacturing began, through June 15, 1977, when PCB use was completely phased out. A cohort of the same workforce was previously assembled by other investigators[6,7] but was incomplete because it did not include approximately 850 workers. A portion of the highly exposed male workers in this study were also included in the cohort assembled by Brown and Jones.[3]

Methods

Study Purpose

The purpose of this study was to further explore previously reported excesses in cancer-specific mortality in capacitor workers exposed to PCBs. Six a priori cancers that were previously reported as being elevated were the primary focus of this study (melanoma, liver, rectum, gastrointestinal tract, brain, and hematopoietic cancers).

Study Population

All hourly and salaried workers employed for at least 90 days between January 1, 1946, and June 15, 1977, in two capacitor manufacturing plants in upstate New York were included in the cohort. Salaried personnel were included in the cohort because they were often involved in the manufacturing process and all personnel were housed in the same building. Personal identifiers, including Social Security number, demographics, and each worker's job history information, were abstracted from employment records that had been microfilmed by the company. Completeness of the cohort was established by our reviewing all available company records, such as pension rosters and the quarterly earning reports of the Social Security Administration (SSA, 941 forms; the complete payroll record for every employee that was ever paid by the company, by plant and location).

Vital Status Determination

The National Death Index and the Equifax Nationwide Death Search tapes were matched against our cohort to identify deceased cohort members through December 31, 1993. A match was considered to exist when at least six digits of the Social Security number, the date of birth, and the first and last name for men and first name for women matched. Death certificates were obtained from the state where death occurred and were coded by a certified nosologist. The underlying cause of death was coded using the International Classification of Diseases (ICD) revision in force at the time of death.[8]

Significant effort went into establishing the vital status of workers not identified as deceased, working, or receiving a pension. Company files were used to identify workers still employed in 1994 and retired workers receiving a pension. The locating services of Equifax were used to establish "alive" status for cohort members that were separated from employment at the time of vital status determination. This was done primarily through the identification of cohort members involved in activities such as insurance underwriting and claims and financial transactions, such as mortgage applications. Computerized county voter registration lists and annual R.L. Polk and Haines City Directories were also used and matched against the cohort list to establish alive status. When employees could not be identified as alive by the above sources, direct contact with neighbors or relatives was attempted to verify vital status. A private investigator was employed to locate difficult-to-find former employees. Long-term workers who were currently employed also assisted us in locating former employees. Workers with unknown vital statuses were considered to be "lost-to-follow-up" and were observed through their last date of employment.

Exposure Assessment

Capacitors were produced by assembling the capacitor canisters, filling them with PCBs, heating them to achieve better impregnation, and closing, soldering, and cleaning them. Capacitors were also repaired, which entailed removing the cover, draining the PCBs, repairing the unit, and re-constructing the capacitor.

From 1946 through 1971, the Aroclor™ mixtures (the tradename for Monsanto [St. Louis, MO] PCB products) 1254 and 1242 were predominantly used. Aroclor 1254 was phased out after 1954, and Aroclor 1242 was used until 1971. From 1971 until 1977, Aroclor 1016 was used. Aroclor 1016 was similar to Aroclor 1242 but with lower environmental persistence, which was accomplished by the removal of higher chlorinated homologs.

All jobs were classified according to their levels of PCB exposure prior to the determination of vital status. Jobs with direct PCB contact (dermal contact and/or inhalation exposure to high PCB air levels) experienced while filling, impregnating, repairing, or moving PCB-filled capacitors were classified as high-exposure jobs. In the areas of filling and impregnating, air levels ranged from 227 to 1500 $\mu g/m^3$ in 1975,[9] and in

the spring of 1977, when PCB use had declined substantially, air levels ranged from 170 to 576 μg/m³.[10] Work operations in which no PCBs were used, such as the winding, can, and cover manufacture and the assembly and shipping department, were tested in the spring of 1977, and air levels ranged from 3 to 50 μg/m³.[10] These jobs were classified as low exposure, and workers in these areas primarily had inhalation exposure to the background levels of PCBs in the plant. There were jobs for which the PCB exposure of the worker varied depending on the location where the individual was performing the task. Insufficient information was provided in the worker history records to determine the location of these jobs, and it was therefore not possible to assign exposure classifications for them. These jobs were classified as undefinable.

Between 1976 and 1979, the general population had average serum PCB levels on a wet-weight basis of approximately 5 to 7 parts per billion (ppb; measured in ng/mL), with levels ranging from nondetectable to 20 ppb (ng/mL),[1] with occasional higher levels.[11] In a population of 290 self-selected employees from this plant, the PCB levels measured in serum on a wet-weight basis ranged from 6 to 2530 ppb (ng/mL) for the lower chlorinated compounds and ranged from 1 to 546 ppb (ng/mL) for the higher chlorinated PCBs.[12] In 1976, Lawton et al[13,14] found similar high levels in a group of 190 workers who had been selected because of their estimated high exposures, establishing the extensive exposure to PCBs.

Exposure to other chemicals in these plants was limited. A small number of workers were exposed to low concentrations of toluene in the painting area, with air levels from nondetectable to 21.4 μg/m³ (time-weighted average = 188 mg/m³). Trichloroethylene levels in the degreasing area ranged from 3.7 to 321 μg/m³ (time-weighted average = 269 mg/m³). Low air levels of lead, aluminum, and iron were also reported in the soldering area.[10]

Statistical Analyses

The mortality experience of the cohort is expressed as the SMR (number of observed deaths in the cohort divided by the number of expected deaths derived from the comparison population). Age-, sex-, race-, and calendar-specific mortality rates for the US population and the regional population from the eight counties surrounding the plants (Franklin, Essex, Warren, Saratoga, Washington, Hamilton, Clinton, and Herkimer counties) were used to calculate the expected number of deaths. The US mortality rate tables were provided by the National Institute of Occupational Safety and Health and comprised 92 causes of death for the years 1946 through 1993 for white and nonwhite males and females in 5-year age and calendar time periods.[15] The regional mortality rate tables were obtained from the Mortality and Population Data System[16] and comprised 62 causes of death for the years 1950 through 1989 for malignant neoplasms and the years 1962 through 1989 for nonmalignant causes. The regional rates were also provided for white and nonwhite males and females in 5-year age and calendar time periods. Person-years were accumulated beginning on the 91st day of employment and continued to December 31, 1993, or the date of death, whichever came first. Person-years for workers lost to follow-up were calculated through the last date they were known to be alive, which was typically their last date of employment. Person-years were combined into 5-year age-, sex-, race-, and calendar-specific categories and multiplied by the corresponding age-, sex-, race-, and calendar-specific US mortality rates (or regional rates) to yield the expected numbers. Calculations were performed using OCMAP (Occupational Cohort Mortality Analysis Program).[17] The statistical significance of the differences between the observed and expected numbers was tested assuming a Poisson distribution for the observed deaths, using a two-sided test of significance.[18] SMRs were calculated for all 92 underlying causes of death; however, only selected causes of death, including all causes, all cancers, all site-specific cancers, the major cardiovascular diseases, diabetes, cirrhosis of the liver, and accidental causes are shown.

Presentation of the exposure-specific analysis is confined to those workers who had the greatest potential for exposure, which was defined in three ways: (1) all hourly workers who ever worked in a high-exposure job; (2) all hourly workers who had worked for at least 6 months in a high-exposure job; and (3) all hourly workers who worked for at least 1 year in a high-exposure job. Only 112 male and 12 female workers were exclusively employed in high-exposure jobs, thereby restricting our ability to analyze them as a separate group.

In addition to the overall SMRs, the impact of PCB exposure on mortality in both the total cohort and the high-exposure cohort was examined by categories of cumulative length of employment (<1 year, 1 to <5 years, 5 to <10 years, and ≥10 years) and years of latency. Two latency categories were defined: one as less than or equal to 20 years since first exposure, and the other as greater than 20 years since first exposure. SMRs were calculated for each category of cumulative length of employment by latency for all-causes, all-cancers, and specific causes for which there was an elevated total SMR with two or more observed deaths and for which the lower boundary of the 95% confidence interval (CI) was 90 or above. This analysis examined the trend across categories of increasing length of employment and latency. The purpose was to determine whether the SMRs increased over the length of employment and latency

TABLE 1
Demographic Characteristics of 4,062 Male and 3,013 Female Workers

Characteristic	Hourly Workers		Salaried Workers		Total (mean)
	Male	Female	Male	Female	
Number of workers	2,984	2,544	1,078	469	7,075
Number of person-years	85,991	75,674	34,755	16,358	212,778
Number of deaths	586	380	177	52	1,195
Number of missing death certificates	20	4	9	4	37
Number lost to follow-up	33	52	7	3	95
Mean age started work	26	29	29	25	(27)
Mean time employed, years	6.2	5.8	5.7	4.8	(5.6)
Mean age stopped working	33	35	35	31	(34)
Mean age at death	61	64	62	61	(62)
Mean age for workers alive on December 31, 1993	53	57	60	59	(57)
Mean follow-up time, years	28	30	32	34	(31)
Percentage who attended college	15	7	73	26	(30)

categories, which would suggest a trend consistent with a dose-response effect.

The individual category-specific SMRs are not particularly relevant, and, because of the small number of deaths, the rates are unstable. Trend analysis using the Mantel-Cox chi-square test[19] with one degree of freedom was done to determine the significance of the trend among the observed over the expected rates within the subpopulation of women who died of intestinal cancer.

Results

Description of the Cohort

The cohort consisted of 2984 hourly white male, 2544 hourly white female, 1078 salaried white male, and 469 white salaried female workers (Table 1). Hourly male and female workers contributed 85,991 and 75,674 person-years of observation, respectively, and salaried male and female workers contributed 34,755 and 16,358 person-years. Only 1.1% of the hourly male, 2% of the hourly female, and less than 1% of the salaried workers were lost to follow-up. The average age at entry for the different groups, the mean time employed, and the mean follow-up time are also shown in Table 1. The mean age at the end of employment for the four subgroups ranged from 31 to 35 years. The mean age of the 5880 cohort members alive at the end of the follow-up period was 57 years, while the mean age at death was 62 (Table 1). Among the salaried male cohort, 73% ever attended college, while in the hourly male cohort only 15% ever attended college. Among salaried female workers, 26% ever attended college, and among the hourly female workers, 7% ever attended college.

There were 586 deaths among the hourly male workers, and 380 deaths among hourly female workers. There were 177 deaths among the salaried male workers and 52 deaths among the salaried female workers. For 38 workers, the cause of death was not known, either because the death certificate could not be located or because the cause of death was not provided on the death certificate.

In Table 2 the length of employment and years of follow-up for the cohort are shown. Over one third of hourly male and female workers and nearly one third of the salaried male cohort worked less than 1 year, and nearly one third of hourly and salaried male and female employees worked 5 years or more. The distribution of follow-up time for the cohort is also presented and indicates that follow-up time for the majority of the cohort exceeded 25 years. The distribution of length of employment by years of follow-up (not shown) illustrated that follow-up time was longest for the long-term workers (ie, those with the longest overall exposure times were observed for the longest period of time).

In Table 3 the distribution of exposure type by gender and pay status is presented. Females primarily held jobs with low exposures (97% of women); they were engaged in the winding operation, which was done in a separate "clean" room, or they held clerical salaried jobs. The distribution of exposure type presented in Table 3 indicates that workers, especially hourly male workers, experienced different exposures throughout their employment. For example, in the hourly male cohort, 27% of men had jobs with high, low, and undefinable exposures during their employment (not shown), and 66% of the male hourly cohort held a job with undefinable exposure sometime during their employment.

The observed deaths, expected deaths, SMRs, and their 95% CIs for selected causes of death for the cohort by subgroup are presented in Table 4. All malignant neoplasms, the major cardiovascular diseases, diabetes, cirrhosis of the liver, and accidental causes of death are presented. Causes with only one death are not presented, nor are irrelevant causes with small numbers of deaths (ie, mental disorders). The expected numbers were calculated from the

TABLE 2
Length of Employment and Follow-Up Time

Characteristic	Hourly Workers (%)		Salaried Workers (%)	
	Male	Female	Male	Female
Length of employment, years				
<1	1066 (35.7)	842 (33.1)	343 (31.8)	106 (22.6)
1 to <5	864 (29.0)	902 (35.5)	341 (31.6)	216 (46.1)
5 to <10	381 (12.8)	251 (9.9)	177 (16.4)	83 (17.7)
10 to <15	212 (7.1)	208 (8.2)	87 (8.1)	130 (5.8)
≥15	461 (15.4)	341 (13.4)	130 (12.1)	37 (7.9)
Years of follow-up				
<10	61 (2.0)	28 (1.1)	11 (1.0)	0
10 to <20	383 (12.8)	333 (13.1)	67 (6.2)	32 (6.8)
20 to <25	656 (22.0)	626 (24.6)	156 (14.5)	33 (7.0)
25 to <30	830 (27.8)	487 (19.1)	206 (19.1)	72 (15.4)
30 to <35	267 (8.9)	240 (9.4)	159 (14.7)	51 (10.9)
≥35	787 (26.4)	830 (32.6)	479 (44.4)	281 (59.9)

TABLE 3
Distribution of Exposure Types

Characteristic	Hourly Workers		Salaried Workers	
	Male	Female	Male	Female
Number ever highly exposed (%)	1268 (42.4)	352 (13.8)	87 (8.0)	10 (2.1)
Median years in high exposure	1.7	1.6	3.2	2.0
Number ever undefinably exposed (%)	1984 (66.4)	379 (14.8)	407 (37.7)	15 (3.1)
Median years in undefinable exposure	1.8	1.5	2.4	1.4
Number ever low exposed (%)	2343 (78.5)	2468 (97.0)	831 (77.0)	459 (97.8)
Median years in low exposure	6.5	6.5	5.0	4.9

mortality rates of the US population. Among the hourly workers, the all-causes mortality was significantly lower than that of the US population (SMR = 84, 95% CI, 77 to 91 for males; SMR = 90, 95% CI, 82 to 100 for females). The all-cancers mortality was also significantly lower than that of the US population in hourly male workers (SMR = 81; 95% CI, 68 to 97). In hourly female workers, the all-cancers mortality rate was comparable to the US rate (SMR = 110; 95% CI, 93 to 129).

In the male hourly cohort no significant elevations in the six a priori cancers of interest (cancers of the rectum, liver, gastrointestinal tract, melanoma, brain, and hematopoietic system) were noted. Several causes of death had SMRs above 100; however, none of them were significantly elevated (Table 4).

In the hourly female cohort, there were no significantly elevated SMRs for any of the six a priori cancers of interest. SMRs for several other cancer sites were elevated, although none were significantly elevated (Table 4).

SMRs for deaths from diseases other than cancer were also not significantly elevated in either hourly male or female workers. The SMR for diabetes, however, was significantly lower than expected in hourly male workers (four observed and 10.5 expected; SMR = 38; 95% CI, 10 to 97).

Overall, among salaried male workers, a striking healthy worker effect was observed (Table 4). The all-causes SMR for salaried male workers was 54 (177 observed and 328 expected; 95% CI, 46 to 62) and the all-cancers SMR was 69 (56 observed and 81 expected; 95% CI, 52 to 90). None of the a priori cancers of interest were elevated in the salaried male workers. The lung cancer rate was significantly lower than expected, with an SMR of 41 (12 observed and 29.6 expected; 95% CI, 21 to 71), as was ischemic heart disease, with an SMR of 45 (44 observed and 97.5 expected; 95% CI, 33 to 61), and cerebrovascular disease, with an SMR of 20 (three observed and 15.2 expected; 95% CI, 4 to 58).

The female salaried workers (Table 4) also demonstrated a marked healthy worker effect, with an all-causes SMR of 69 (52 observed and 75 expected; 95% CI, 52 to 91) and an all-cancers SMR of 75 (19 observed and 25 expected; 95% CI, 45 to 118). The only significant finding in the salaried female workers was that for cancer of the connective tissue, with an SMR of 1290 (two observed and 0.2 expected; 95% CI, 156 to 4659). However, one of the connective tissue tumors was a pericytoma, a lesion of borderline malignancy.

The age-, sex-, race-, and calendar-specific mortality rates for the hourly workers, compared with the regional population (eight counties surrounding the plants), were similar to the SMRs calculated using the US rate tables (not shown). None of the a priori cancers of interest in either males or females were significantly different than expected.

SMRs by Length of Employment and Latency Categories

There was no trend of increasing SMRs over length of employment and latency categories for all causes or all cancers in either male or female hourly workers. The data for all cancers are presented in Tables 5 and 6.

The only site-specific cause of death that met the a priori criteria for analysis by cumulative length of employment and latency (ie, greater than two observed cases and CIs with a lower boundary >90) was intestinal cancer in female hourly workers. As listed in Table 6, the

TABLE 4

Observed and Expected Deaths[a] in 2984 Hourly Male Workers,[b] 2544 Hourly Female Workers,[c] 1078 Salaried Male Workers,[d] and 469 Salaried Female Workers[e]

	Hourly Workers[f]				Salaried Workers[f]			
	Males		Females		Males		Females	
Cause of Death	Obs/Exp	SMR (95% CI)	Obs/Exp	SMR (95% CI)	Obs/Exp	SMR (95% CI)	Obs/Exp	SMR (95% CI)
All causes	586/699	84** (77–91)	380/420	90* (82–100)	177/328	54** (46–62)	52/75	69.0** (52–91)
All cancers	128/158	81* (68–97)	150/136	110 (93–129)	56/81	69* (52–90)	19/25	75 (45–118)
MN[g] of tongue	1/0.9	103 (3–576)	2/0.4	483 (59–1745)	0/0.1	—	1/0.07	1346 (34–7498)
MN of buccal cavity	2/1.1	178 (22–642)	2/0.5	365 (44–1317)	0/0.5	—	1/0.1	1021 (26–5690)
MN of pharynx	4/2.0	199 (54–509)	2/0.8	253 (31–915)	0/1.0	—	0/0.1	—
MN of esophagus	5/3.8	131 (42–304)	1/1.1	87 (2–482)	1/2.0	49 (1–272)	0/0.2	—
MN of stomach	4/5.9	68 (18–173)	4/3.0	132 (36–339)	1/2.7	36 (0.9–200)	0/0.5	—
MN of intestine	8/14.0	57 (25–112)	20/12.7	157 (96–242)	7/7.1	98 (40–203)	1/2.2	44 (1–247)
MN of rectum	3/3.4	87 (18–255)	4/2.3	169 (46–434)	3/1.6	185 (38–540)	0/0.4	—
MN of biliary passages and liver	2/2.5	80 (10–289)	2/2.2	89 (11–321)	1/1.2	79 (2–439)	0/0.3	—
MN of pancreas	9/7.8	115 (53–219)	7/5.9	117 (47–241)	6/3.9	150 (55–327)	0/1.1	—
MN of larynx	3/2.0	147 (30–428)	1/0.4	215 (5–1198)	0/1.0	—	0/0.1	—
MN of trachea, bronchus and lung	42/54.5	77 (56–104)	32/25.2	127 (87–179)	12/29.6	41** (21–71)	5/4.7	104 (34–244)
MN of breast	—	—	25/30	82 (53–121)	—	—	6/5.7	104 (38–226)
MN of cervix uteri	—	—	6/4.7	126 (47–277)	—	—	1/0.9	112 (3–622)
MN of other parts of uterus	—	—	5/3.8	130 (43–305)	—	—	0/0.6	—
MN of ovary, tube and broad ligament	—	—	8/9.3	85 (37–168)	—	—	2/1.7	115 (14–415)
MN of prostate	12/10.9	110 (57–192)	—	—	3/5.3	56 (5–136)	—	—
MN of kidney	3/4	75 (15–219)	2/2.1	94 (11–341)	0/2.1	—	—	—
MN of bladder and other urinary tract	3/3.8	77 (16–226)	2/1.3	151 (18–545)	1/1.8	54 (1–299)	0/0.2	—
MN of skin (melomonas)	5/3.8	130 (42–303)	3/2.0	144 (30–421)	4/1.9	210 (57–538)	0/0.4	—
MN of brain and nervous system	2/5.1	39 (5–140)	2/3.7	53 (6–192)	4/2.5	156 (42–398)	0/0.7	—
MN of connective tissue	0/0.9	—	1/0.8	125 (3–694)	1/0.4	229 (6–1275)	2/0.2	1290* (156–4659)
Other and unspecified cancer	6/10.3	58 (21–126)	3/8.6	35 (7–101)	3/5.4	55 (11–161)	0/1.5	—
Lymphosarcoma	2/2.1	92 (11–331)	1/1.5	65 (2–364)	0/1.0	—	0/0.2	—
Leukemia and aleukemia	4/6.3	63 (17–162)	4/4.3	93 (25–238)	5/3.0	166 (54–387)	0/0.8	—
Other lymphatic and hematopoietic	5/5.7	87 (28–202)	5/4.7	105 (34–245)	4/3.0	131 (36–336)	0/0.8	—
Cirrhosis of the liver	13/18	72 (39–124)	6/9.2	65 (24–142)	3/9.1	33* (7–96)	1/1.7	57 (1–318)
Diabetes	4/10.5	38* (10–97)	9/10.3	87 (40–165)	5/5.1	97 (32–226)	0/1.8	—
Ischemic heart disease	182/205	89 (76–103)	71/87	81 (64–103)	44/97.5	45** (33–61)	8/14.3	56 (24–110)
Hypertension with heart disease	5/5.8	86 (28–201)	2/4.4	45 (6–164)	0/2.5	—	0/0.7	—
Other diseases of the heart	34/34.7	98 (68–137)	18/21.4	84 (50–133)	16/18.2	88 (50–143)	1/3.8	26 (0.7–146)
Cerebrovascular disease	26/34.9	74 (49–109)	27/30	89 (59–130)	3/15.2	20** (4–58)	6/5	120 (44–260)
Arteries, veins, pulmonary circulation	19/17.0	112 (67–174)	10/11	95 (46–175)	4/8.0	50 (14–128)	1/1.8	56 (1–310)
Transportation accidents	29/34.7	84 (56–120)	14/9.1	153 (84–257)	3/12.6	24** (5–69)	3/1.9	156 (32–455)
Other accidents	10/14.4	69 (33–127)	5/3.1	158 (51–369)	3/5.9	51 (11–148)	1/0.6	159 (4–886)
Suicide	14/21.3	66 (36–110)	3/6.8	44 (9–128)	2/8.6	23* (3–84)	2/1.4	140 (17–507)
Homicide	3/8.4	36 (7–104)	2/2	96 (12–345)	0/3.0	—	0/0.4	—

* Significant at $P < 0.05$.

** Significant at $P < 0.01$.

[a] Expected numbers for selected causes of death based on age-, sex-, race-, and time-specific US rates coded according to the rules of the International Classification of Diseases coding in force at the time of death. ICD code groupings are shown as listed in Steenland et al.[15]

[b] 85,991 Person-years of observation.

[c] 75,674 Person-years of observation.

[d] 34,755 Person-years of observation.

[e] 16,358 Person-years of observation.

[f] Obs/Exp, observed/expected; SMR, standardized mortality ratio; CI, confidence interval.

[g] MN, malignant neoplasms.

TABLE 5
Mortality by Length of Employment and Latency from All-Cancers for Hourly Male Workers

	Length of Employment (years)									
	<1		1 to <5		5 to <10		≥10		Total	
Cause/Latency	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR
All cancers, *n*										
<20	8	81	8	79	9	105	10	89	35	89
≥20	19	74	14	59*	12	108	48	78*	93	78*
Total	27	76	22	65*	21	107	58	81*	128	81*

* $P < 0.05$.

TABLE 6
Mortality by Length of Employment and Latency from All-Cancers and Intestinal Cancer for Hourly Female Workers

	Length of Employment (years)									
	<1		1 to <5		5 to <10		≥10		Total	
Cause/Latency	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR
All cancers, *n*										
<20	9	84	13	90	8	106	8	107	38	95
≥20	31	145	30	117	13	120	38	100	112	96
Total	40	124	43	107	21	114	46	101	150	110
Intestinal cancer, *n*										
<20	0	—	0	—	1	154	1	147	2	62
≥20	4	198	5	208	5	458*	4	100	18	189*
Total	4	142	5	143	6	345*	5	106	20	157

* $P < 0.05$.

intestinal cancer SMRs occurred primarily in women with greater than 20 years of latency; however, the deaths distributed evenly through the length-of-employment categories. While some of the category-specific SMRs for intestinal cancer were significantly elevated in and of themselves, they were calculated using small numbers and were therefore unstable.

To further evaluate any increased risk of mortality from intestinal cancer with increasing length of employment, an internal analysis for trend was calculated. The observed over the expected rates calculated by length of employment and the associated trend were tested for statistical significance using the Mantel-Cox chi-square test for trend. The observed over expected rates for employment time of less than 1 year, 1 to less than 5 years, 5 to less than 10 years, and 10 years or greater were 5.07, 1.27, 2.26, and 0.40, respectively. The chi-square was significant at $P < 0.001$; however, the trend of the observed over the expected rates did not increase but rather decreased with length of employment.

Exposure-Specific SMRs

Mortality in the 1268 hourly male and 362 hourly female workers who worked for at least 1 day in a high-exposure job was compared to the mortality experience of the US population. The 1268 ever-high-exposed hourly male workers contributed 37,739 person-years of observation. The all-causes SMR was significantly lower than expected (SMR = 82; 95% CI, 72 to 93), and the all-cancers SMR was 77 (95% CI, 57 to 101). The 362 ever-high-exposed hourly female workers contributed 10,584 person-years of observation. Both all-causes and all-cancers mortality in the ever-high-exposed hourly female workers did not deviate from that expected (all-causes SMR = 96, 95% CI, 75 to 123; all-cancers SMR = 100, 95% CI, 63 to 152). There were no significant differences in any of the site-specific SMRs for either male or female ever-high-exposed hourly workers.

In the 723 hourly male workers, with 22,217 person-years of observation, who were engaged in a high-exposure job for at least 180 days, the all-causes SMR was 87 (95% CI, 74 to 102) and the all-cancers SMR was 82 (95% CI, 58 to 114). In the 184 hourly female workers, with 5783 person-years of observation, the all-causes SMR was 92 (95% CI, 65 to

TABLE 7
Mortality by Length of Employment and Latency from All-Cancers for Hourly Male and Female Workers Highly Exposed for 180 Days or More

	Length of Employment (years)									
	<1		1 to <5		5 to <10		≥10		Total	
Cause/Latency	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR
Males										
All cancers, *n*										
<20	1	116	4	164	3	121	5	140	13	140
≥20	1	45	6	108	2	53	14	67	23	67
Total	2	64	10	125	5	80	19	82	36	82
Females										
All cancers, *n*										
<20	0	—	2	193	1	98	0	—	3	86
≥20	0	—	1	102	1	110	6	82	8	87
Total	0	—	3	149	2	103	6	70	11	87

TABLE 8
Mortality by Length of Employment and Latency from All-Cancers for Hourly Male and Female Workers Highly Exposed for 1 Year or More

	Length of Employment (years)							
	1 to <5		5 to <10		≥10		Total	
Cause/Latency	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR	No. of Deaths Observed	SMR
Males								
All cancers, *n*								
<20	0	—	3	146	4	143	7	107
≥20	4	121	1	30	11	60	16	64
Total	4	83	4	75	15	71	23	73
Females								
All cancers, *n*								
<20	1	170	0	—	0	—	1	40
≥20	1	213	0	—	4	65	5	69
Total	2	189	0	—	4	56	6	61

127) and the all-cancers SMR was 88 (95% CI, 43 to 155). There were no elevated site-specific SMRs above the expected number.

The all-causes SMR for the 479 hourly male workers who had worked for at least 1 year in a high-exposure job was 89 (95% CI, 74 to 107; 15,181 person-years of observation) and the all-cancers SMR was 73 (95% CI, 46 to 109). In the 122 hourly female workers who worked in a high-exposure job for at least 1 year, the all-causes SMR was 81 (95% CI, 53 to 119; 4047 person-years of observation) and the all-cancers SMR was 61 (95% CI, 23–134). No site-specific elevations were seen in either males or females.

In Tables 7 and 8, the results of the SMR analysis by length of employment and latency are presented for all-cancers for hourly male and female workers highly exposed for at least 180 days (Table 7) or for at least 1 year (Table 8). Because of the small number of site-specific cancers, analysis by cumulative length of employment and latency category was not feasible. There was no consistent trend across the length-of-employment categories and/or latency categories in either males or females that would suggest an association between PCB exposure and increased mortality (Tables 7 and 8).

Comment

The lower-than-expected mortality seen in this cohort has been reported in other PCB mortality studies[2–6] and is consistent with the healthy worker effect often observed in employed populations.[20] The lower all-cancers SMR seen in hourly male

workers is, however, unusual and raises the question of whether cancer deaths have been sufficiently ascertained in this cohort. This discrepancy was not seen in the female cohort, and a systematic underascertainment or ICD coding problem related to gender is unlikely.

The excess cancer mortality related to PCB exposure that has been reported previously in the literature was not replicated in this study. However, the capacitor workers in prior studies were exposed to the same mixtures of PCBs at similar concentrations, since the production process in different plants was the same. The significant excess of liver cancer reported by Brown[4] was not observed in this cohort. SMRs for liver cancer for both males and females in our cohort were similar to those of the US population, with SMRs below 100 (SMR = 89 for hourly female and SMR = 80 for hourly male workers). Brown and Jones[3] also reported a significant increase in mortality from rectal cancer in women, with three observed deaths and 0.50 expected; however, the excess was no longer significant in Brown's follow-up study of the same cohort.[4] Among hourly female workers in our cohort, there were four observed deaths from rectal cancer and 2.3 expected, a nonsignificant increase (SMR = 169; 95% CI, 46 to 434). All four women who died of rectal cancer held only low-exposure jobs during their employment. Length of employment in the four women ranged from 6 to 22 years, with a mean of 10 years. Years since first exposure in three of the deaths exceeded 20. Known risk factors for rectal cancer include smoking[21] and family history.[22] Occupational risk for rectal cancer in females has been reported for women involved in the furniture-making industry, with an SMR of 3.2 (95% CI, 1.3 to 4.5).[23] Occupational history before and after employment the capacitor plants was not available for members of our cohort and could not be evaluated.

In the Bertazzi et al[5] cohort of 2100 workers, a significant excess of total cancers and cancers of the gastrointestinal tract (ICD codes 150 to 159) among males was reported (six observed vs 1.7 expected, SMR = 346; 95% CI, 141 to 721). In contrast to the Bertazzi et al[5] cohort, hourly male workers in our cohort had lower than expected numbers of both intestinal and rectal cancers, although not significantly lower (cancer of the intestine SMR = 57, 95% CI, 25 to 112; cancer of the rectum SMR = 87, 95% CI, 18 to 225). Hourly female workers in our cohort had nonsignificantly elevated SMRs for intestinal and rectal cancer (cancer of the intestine SMR = 157, 95% CI, 96 to 242; cancer of the rectum SMR = 169, 95% CI, 46 to 434). In the Bertazzi et al[5] cohort, the numbers of lung cancer and hematological neoplasms were also elevated in males, but the excesses were not statistically significant. In our cohort, neither the numbers of lung cancer nor neoplasms of the hematopoietic system were elevated.

The 1556 females in the Bertazzi et al[5] cohort experienced higher than expected all-causes mortality, when compared with the Italian national population, and significantly higher than expected all-cancers mortality and mortality related to hematological neoplasms, when compared with the local population. In our cohort the all-causes mortality in females was significantly lower, the all-cancers mortality in females was comparable to the expected number, and no elevation in hematological neoplasms was observed.

In the cohort of 3588 male and female capacitor workers examined by Sinks et al,[2] a significant increase in mortality from melanoma and a nonsignificant increase in mortality from cancers of the brain and nervous system was observed. In our cohort the numbers of cancers of the brain and nervous system were lower than expected for both males and females. Mortality from melanoma was similar to the expected number in both males and females (five observed and 3.8 expected deaths in males, and three observed and 2.08 expected deaths in females). None of the five males with melanoma had worked for longer than 2 years at the plants, and two of them had less than 20 years of latency. Of the three women with melanoma, one had worked for 1 year, one for 3.4 years, and one for 12 years at the plants; all three held only low-exposure jobs. Exposure to the sun is the major risk factor for melanoma and accounts for 65% of melanomas worldwide[24]; melanomas represent almost all fatal skin cancers.

In our cohort the SMR for intestinal cancer (large and small intestine) in hourly female workers was elevated and approached statistical significance (SMR = 157; 95% CI, 96 to 242). There were 20 observed deaths and 12.7 expected, using the US rate data. One of the intestinal cancers was a carcinoid originating from endocrine argentaffin cells, representing a tumor with a different etiology but one grouped with intestinal carcinomas in the ICD coding system. In contrast, there were eight observed deaths and 14 expected deaths in the hourly male cohort (SMR = 57; 95% CI, 25 to 113). The SMR for cancer of the large intestine in hourly female workers, using the regional population as the comparison population, was lower (SMR = 120; 95% CI, 74 to 186), with 16.6 deaths expected. Since the incidence of intestinal cancer is greatly influenced by ethnicity and since higher rates are observed among the white population of the northeastern part of the United States, the regional comparison is more representative.[25] The majority of intestinal cancers occurred in women with 20 or more years of latency; however, the cancers were evenly distributed across the length of employment. All of the women worked exclusively in sedentary, low-exposure jobs during their employment. Trend analysis did not reveal any increase but rather a decrease in the observed over the ex-

pected rates by the category length of employment. Known risk factors for intestinal cancer include tobacco use,[26,27] dietary factors,[28] family history,[29] and lack of physical activity.[25] Known occupational risks for intestinal cancer in women are few.[23,30]

The low SMRs in the male salaried cohort may represent a socioeconomic effect. The salaried male workers comprised mostly professional staff, with 73% (792) having attended at least some college and 71% of these 792 employees having graduated from college. In contrast, only 15% of hourly male workers had some college education, and only 13% of them completed 4 years of college.

Overall, the salaried women demonstrated a larger healthy worker effect than did their hourly counterparts. Again, this may reflect a socioeconomic effect, including better education, as 26% (n = 120) of the salaried women ever attended college and 30% of those completed 4 years (n = 36). Low SMRs in salaried employees have been reported in other occupational cohorts.[31] The disparity in mortality between socioeconomic groups has been increasing, and the differences in SMRs between the hourly and salaried workers may reflect this disparity.[32,33]

The exposure-specific analysis for this cohort was limited by the lack of individual dosimetry data. The only available industrial hygiene data consisted of PCB air levels measured in various production areas in 1975 and in 1977.[9,10] Because of the persistence of PCBs and the length of time that a worker had repeated exposures, length of employment was a useful proxy of cumulative exposure. Hourly workers employed in high-exposure jobs represented the most highly exposed group of workers and were grouped by their cumulative time in high-exposure jobs into three groups. None of the six a priori cancer sites of interest, all-cancers mortality, or any site-specific mortality were elevated in either males or females for any of the three groupings of high-exposed workers. There was no consistent trend in any of the tables illustrating SMRs by length of employment and latency for any of the groupings. The number of workers employed in high-exposure jobs for long time periods was small and limited the extent of the analysis; however, the consistent lack of any significant elevation in mortality in any of the groups in either males or females is worth noting. Reliance on categorical exposure assessment may result in misclassification. However, jobs that involved direct dermal and inhalation exposure to PCBs were clearly identified by job code in the worker history records, and the PCB exposure in these jobs was substantial, as indicated by the air-monitoring data and PCB serum and adipose tissue levels measured in selected workers.

While not an a priori consideration, the large cohort of women in this study provided an opportunity to examine the relationship between breast cancer and occupational exposure to PCBs. In our study, mortality from breast cancer among hourly and salaried female workers was not increased over the expected number. Additionally, we had the opportunity to examine a cohort of women, albeit small, who experienced high exposure to PCBs.

In the past, capacitor workers as an occupational group had the highest exposures to PCBs, through the inhalation of PCB vapors and the dermal absorption of PCB liquid. Since PCBs were heated, their volatility was increased, resulting in high air levels. The worker groups such as electric utility workers[34] had poorly defined and definitely lower exposures than the capacitor workers. Such workers did not inhale vapors from heated PCBs nor did they have daily dermal contact with liquid PCBs.

The potential for bias in any observational study is always a concern and must be considered in the study design as well as in the examination of results. Both selection and information bias can be prevented if disease and/or vital statuses are not known when exposure assignments are made. In this study, exposure was assigned on the basis of the historical information related to PCB exposure that was contained in the job codes. The exposure assignment was done before the vital status determination.

In conclusion, this is the largest cohort of workers directly exposed to PCBs that was assembled specifically for the examination of the association between exposure and increased cancer mortality. Extensive effort went into assembling a complete cohort and obtaining vital statuses from over 98% of the cohort. Despite the fact that the cohort is relatively young, 85% of the cohort was observed for at least 20 years, with a mean follow-up time of 31 years. Neither overall cancer mortality nor numbers of any of the a priori cancers of interest previously reported as being elevated were elevated in this cohort. With the exception of intestinal cancer in the hourly female workers, there were few cancer sites whose numbers were elevated, with few cases and wide CIs, and these sites have not been reported in other studies, suggesting that our results were chance findings.

Because of the inherent limitations in any retrospective cohort mortality study, the best way to evaluate the validity of a reported association is to replicate the study in similarly exposed populations. To date none of the reported elevations in cancer mortality have been successfully replicated, even within individual cohorts (eg, Brown[4]). Notwithstanding the bias inherent in retrospective occupational cohort studies, the lack of consistent findings with respect to occupational PCB exposure and mortality in studies conducted to date would suggest a lack of an association.

Acknowledgments

This study was funded by the General Electric Company. The assistance of Mr Yong-Gon Chon in developing our database is appreciated. Dr Kyle Steenland of the National Institute for Occupational Safety and Health provided the US mortality rate tables. We thank the members of our advisory panel: Arthur C. Upton, MD, John E. Vena, PhD, Jack S. Mandel, PhD, Roy E. Shore, PhD, and Gilbert W. Beebe, PhD, for their helpful suggestions and support throughout the study.

References

1. Kimbrough RD. Polychlorinated biphenyls (PCBs) and human health: an update. *Crit Rev Toxicol.* 1995;25:133–163.
2. Sinks T, Steele G, Smith A, Watkins A, Shults R. Mortality among workers exposed to polychlorinated biphenyls. *Am J Epidemiol.* 1992;136:389–398.
3. Brown DP, Jones J. Mortality and industrial hygiene study of workers exposed to polychlorinated biphenyls. *Arch Environ Health.* 1981;36:120–129.
4. Brown DP. Mortality of workers exposed to polychlorinated biphenyls: an update. *Arch Environ Health.* 1987;42:333–339.
5. Bertazzi PA, Riboldi L, Pesatori A, Radice L, Zocchetti C. Cancer mortality of capacitor manufacturing workers. *Am J Ind Med.* 1987;11:165–176.
6. Taylor PR. *The Health Effects of Polychlorinated Biphenyls* [doctoral thesis]. Boston, MA: Harvard School of Public Health; 1988.
7. Taylor PR, Reilly AA, Stelma J, Lawrence CE. Estimating serum polychlorinated biphenyl levels in highly exposed workers: an empirical model. *J Toxicol Environ Health.* 1991;34:413–422.
8. World Health Organization. *International Classification of Diseases: Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death.* Geneva: World Health Organization; Revisions 5–9, 1940–1993.
9. Lawton RW, Sack BT, Ross MR, Feingold J. *Studies of Employees Occupationally Exposed to PCBs, a Progress Report.* September 18, 1981 (General Electric Report submitted to the US Environmental Protection Agency).
10. Jones M. *Industrial Hygiene Survey.* Washington, DC: National Institute for Occupational Safety and Health; 1983. NIOSH publication 83–137224. Reprinted by the National Technical Information Service.
11. Kreiss K. Studies on populations exposed to polychlorinated biphenyls. *Environ Health Perspect.* 1985;60:193–199.
12. Wolff MS, Fischbein A, Thornton J, Rice C, Lilis R, Selikoff IJ. Body burden of polychlorinated biphenyls among persons employed in capacitor manufacturing. *Int Arch Occup Environ Health.* 1982;49: 199–208.
13. Lawton RW, Ross MR, Feingold J, Brown JF Jr. Effects of PCB exposure on biochemical and hematological findings in capacitor workers. *Environ Health Perspect.* 1985;60:165–184.
14. Lawton RW, Brown JF, Jr, Ross MR, Feingold J. Comparability and precision of serum PCB measurements. *Arch Environ Health.* 1985;40:29–37.
15. Steenland K, Beaumont J, Spaeth S, Brown D, Okun A, Jurcenko L. New developments in the NIOSH life table analysis system. *J Occup Med.* 1990;32: 1091–1098.
16. Marsh GM, Ehland J, Sefcik S. *Mortality and Population Data System (MPDS)* [technical report]. Pittsburgh, PA: University of Pittsburgh, Department of Biostatistics; 1987.
17. Marsh GM, Preininger M, Ehland JJ. *OCMAP PC: A User-Oriented Occupational Mortality Cohort Analysis Program for the IBM PC.* Pittsburgh, PA: University of Pittsburgh; 1989.
18. Bailar JC, Ederer F. Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics.* 1964;20:639–643.
19. Dixon WJ, ed. *BMDP Statistical Software Manual.* Berkeley: University of California Press; 1992.
20. Monson RR. Observations on the healthy worker effect. *J Occup Med.* 1986;28: 425–433.
21. Heineman EF, Zahm SH, McLaughlin JK, Vaught JB. Increased risk of colorectal cancer among smokers: results of a 26-year follow-up of US veterans and a review. *Int J Cancer.* 1994;59:728–738.
22. Burt RW. Familial risk and colorectal cancer. *Gastroenterol Clin North Am.* 1996;25:793–803.
23. Miller BA, Blair A, Reed EJ. Extended mortality follow-up among men and women in a U.S. furniture workers union. *Am J Ind Med.* 1994;25:537–549.
24. Armstrong BK, Kricker A. Skin cancer. *Dermatol Clin.* 1995;13:583–594.
25. Schottenfeld D, Winawer SJ. Cancers of the large intestine. In: Schottenfeld D, Fraumeni JF, eds. *Cancer Epidemiology and Prevention,* 2nd ed. New York: Oxford University Press; 1996:813–840.
26. Slattery ML, Potter JD, Friedman GD, Ma KN, Edward S. Tobacco use and colon cancer. *Int J Cancer.* 1997;70:259–264.
27. Newcomb PA, Storer BE, Marcus PM. Cigarette smoking in relation to risk of large bowel cancer in women. *Cancer Res.* 1995;55:4906–4909.
28. Giovannucci E, Willett WC. Dietary factors and risk of colon cancer. *Ann Med.* 1994;26:443–452.
29. Burt RW. Familial risk and colon cancer. *Int J Cancer.* 1996;69:44–46.
30. Ruder AM, Ward EM, Brown DP. Cancer mortality in female and male drycleaning workers. *Am J Epidemiol.* 1992; 136:389–398.
31. Teta MJ, Ott MG. Mortality in a research engineering and metal fabrication facility in Western New York State. *Am J Epidemiol.* 1988;127:540–551.
32. Pappas G, Queen S, Hadden W, Fisher G. The increasing disparity in mortality between socioeconomic groups in the United States, 1960 and 1986. *N Engl J Med.* 1993;329:103–109.
33. Sorlie PD, Backlund E, Keller JB. US mortality by economic, demographic, and social characteristics: the National Longitudinal Mortality Study. *Am J Public Health.* 1995;85:949–956.
34. Loomis D, Browning SR, Schenk AP, et al. Cancer mortality among electrical workers exposed to polychlorinated biphenyls. *Occup Environ Med.* 1997;54: 720–728.