Environmental Health Perspectives
Vol. 60, pp. 165-184, 1985

Effects of PCB Exposure on Biochemical and Hematological Findings in Capacitor Workers

by Richard W. Lawton,* Marie R. Ross,† Joseph Feingold‡ and John F. Brown, Jr.*

Certain former operations in capacitor manufacturing resulted in extensive direct contact of the workers with electrical grade polychlorinated biphenyls (PCBs). A study group of 194 such individuals, all exposed to Aroclor 1016 and many previously exposed to Aroclors 1242 and/or 1254, was examined before (1976) and after (1979) discontinuance of PCB use in the operations (1977). At the two examinations, the approximate geometric mean serum levels (in ppb) and 5 to 95% ranges were for lower PCBs (LPCB), 363 (57–2270) and 68 (12–392); and for higher PCBs (HPCB), 30 (6–142) and 19 (4–108), respectively.

The statistical associations among 42 measured clinical chemical and hematological parameters, five different measures of PCB exposure, and seven confounding variables observed in the two examinations were determined by three regression procedures. Similar regressions were performed with DDE, which was present at background levels. The principal statistical findings were a depression in serum bilirubin and elevations in serum GGTP and lymphocyte levels at the time of the first examination, and only an elevation in monocytes at the second. Appraisal of the results suggested an induction of microsomal enzymes which appeared to be subsiding after the cessation of direct exposure to PCBs. The statistical association between serum levels of PCBs and lipids reported by others was confirmed, but shown to be explained by the partitioning behavior of PCB in the body, rather than to changes in liver function. No evidence for health impairment related to PCBs was found, despite the high serum levels of PCBs in the study population.

Introduction

Concern over the human health effects of the polychlorinated biphenyls (PCBs) arises because of the environmental persistence of these substances, which were widely used in the U.S. for nearly 50 years (1929–1978). Several hundred million pounds still remain in existence, either in electrical equipment or in environmental compartments such as landfills, spillage sites or aquatic sediments (*1*), so that the potential for human exposure continues.

The main growth of PCB usage occurred only after early toxicological studies and extensive industrial experience indicated these materials to be of relatively low toxicity (*2–5*). In the 1970s, however, PCBs were linked to an outbreak of severe chloracnegic disease in southwestern Japan in 1968. The outbreak was traced to the ingestion of rice oil (Yusho) that had been contaminated with thermally decomposed PCB. The toxic agents responsible for "Yusho disease" were ultimately identified as 2,3,4,7,8-pentachlorodibenzofuran and other polychlorinated dibenzofurans (PCDFs) (*6*), which are formed from PCBs only at very high temperatures (*7*). Despite contrary evidence, concern has remained that ordinary, unpyrolyzed PCBs, even at residual environmental concentrations, might also produce some human health effects.

In order to identify such effects, a number of epidemiological investigations have been performed on occupationally (*8–19*) or environmentally (*20–22*) exposed populations. All such studies have indicated PCB-related health effects in the human to be uncommon, and the only reasonably consistent findings to be statistical associations between the levels of serum PCBs and those of serum lipids, e.g., triglycerides and cholesterol (*13,15,21,22*). These associations have been interpreted as suggestive of otherwise asymptomatic alterations in liver function.

This interpretation did not recognize that in the body

*General Electric Research and Development Center, P. O. Box 8, Schenectady, NY 12301.
†General Electric Company, Capacitor Products Department, Hudson Falls, NY 12839.
‡Present address: 31 East Street, Fort Edward, NY 12828.

PCBs are partitioned between adipose tissue (the major reservoir) and blood serum in proportion to the lipid content of the serum (*23,24*). Therefore, statistical associations of serum PCBs with serum lipids and any covariant parameters could arise solely from such partitioning. In order to determine whether PCBs actually do have any effect upon serum lipid levels, it would be necessary to examine the dependence of the latter, not upon the levels of PCB in the serum, but instead upon their levels within the body lipids. For lipid-soluble materials, the concentration within the body's lipid phases has long been recognized as the determinant of the pharmacological response (*25*).

In addition to the consistently observed association between the levels of PCBs and lipids in the serum, there have been isolated reports of hypertension (*22*), hepatomegaly (*14*), chloracne (*14,22*), other dermal effects (*12–14*), oxidase induction (*16*), restrictive lung disease (*18*), increased levels of serum γ-glutamyl transpeptidase (*14,15,22*), serum glutamic oxalacetic transaminase (*13–15*), serum glutamic pyruvic trans aminase (*12,14*), serum ornithin-carbamoyl transferase (*14*), or serum pseudocholine esterase (*14*), increased bromsulphthalein retention (*12*), or reduced plasma HDL cholesterol (*15*) in the groups studied. Most such reports, however, either lack consistency with the findings of other investigators, or were observed only in groups that were small, lightly exposed to PCBs, and/or exposed to PCBs in combination with other chemicals.

An opportunity to study the effects of unpyrolyzed, electrical grade PCB exposure has been provided at two capacitor manufacturing plants located within a mile of each other along the Hudson River in upstate New York. During their period of PCB use (1946–1977), these plants are believed to have been the largest single U.S. users, consuming about 15% of all U.S. production, and to have had one of the largest PCB-exposed work forces. Between 1946 and 1975, approximately 9500 different employees worked there, and the employment during the 1976–1979 period of this study was between 1500 and 1800.

Previous investigators of this plant population have found its mortality experience (reported as that for "Plant 2" by Brown and Jones) (*19*) to be normal for all major causes of death, and have indicated a general paucity of significant clinical effects in a volunteer sample drawn from the plant population as a whole (*17*). However, only 5 to 10% of the plant employees worked in areas or jobs providing direct, continuing exposure to the dielectric fluids. Thus, it appeared probable that this exposed subpopulation, still a sizeable group, might exhibit considerably greater blood PCB levels and physiological effects than the remainder of the plant population.

Accordingly, a study population was selected, using criteria that were broad enough to include the entire directly exposed group, as well as some less directly exposed individuals, and detailed clinical examinations were performed approximately 16 months before and 29 months after the discontinuance of PCB use in the plant. No attempt was made to establish a comparable age- and sex-matched control cohort, but since the study group itself exhibited a distribution of PCB levels covering over two orders of magnitude, analyses within the group offered adequate prospects for identifying and quantifying physiological effects attributable to the PCBs.

Since it was not possible, initially, to decide which of the many clinically measured varaiables might be affected by PCBs or might confound the study, a three-tiered analysis was used to identify statistically significant associations. In order, these analyses were: (a) a simple linear regression, intrinsically bias-free, for each measured variable or its log transform against each measure of PCB exposure; (b) a multiple linear regression for each of the measured variables against the selected measures of PCB exposure and a series of other independent variables, e.g., sex, age, smoking history, body mass index, etc., believed to have effects on one or more of the clinical variables and (c) a backward stepwise linear regression to remove non significant independent variables. For each regression, statistically significant associations ($p < 0.05$) with the measures of PCB were identified. In addition, the 95% confidence limits of the regression coefficient were used to estimate the significance of the association over the observed range of exposure. Similar regressions were performed for the same measures of p,p'-DDE, which shares with PCBs partitioning behavior in lipids.

Materials and Methods

Description of Environment

In the process used for manufacturing liquid dielectric capacitors, metal foil strips separated by paper layers were wound into tight coils and inserted into metal cans. A cover assembly, having electrical connectors and a port to admit the dielectric fluid, was then sealed to the can. For filling, small capacitors, such as those used in fluorescent light ballasts, were packed onto racks that were placed in large autoclaves, warmed, degassed under vacuum, and then flooded with the dielectric fluid. The racks were then drained, removed, and transported to sealing stations where the port was manually sealed with solder. Large power capacitors were originally filled manually; subsequently, they were filled by an electronically controlled manifold system which reduced spillage and dermal contact. Following sealing, both large and small capacitors were cleaned, degreased, tested, repaired if appropriate, labeled, and packed for shipment. The dielectric fluids were blended with stabilizers, treated with fuller's earth to remove polar impurities, and tested for dielectric properties, thereby producing an "electrical grade" product. The jobs which provided frequent or continuous direct exposure to the dielectric fluids (i.e., direct dermal contact and/or close proximity to a source of vapor) were those associated

with the fluid processing, the handling and sealing of wet capacitors, capacitor salvage and repair, and the quality control laboratory.

Aroclor 1254, a commercial mixture of PCB isomers and homologs having the average molecular composition of a pentachlorobiphenyl, was used initially in the two plants (1946 ff.). During 1953–1955 a transition was made to Aroclor 1242, a PCB mixture having the average composition of a trichlorobiphenyl, for all but a few specialty capacitors. In 1971, all use of Aroclor 1254 was phased out, and Aroclor 1242 was replaced by Aroclor 1016, a PCB mixture that also had the average composition of a trichlorobiphenyl, but which had been redistilled by the manufacturer to remove all homologs containing more than four chlorines per biphenyl. Finally, on June 30, 1977, all PCB use ceased. The stabilizer used with the Aroclor 1254 mixture was β-chloroanthraquinone; that most commonly used with Aroclors 1242 and 1016 was Union Carbide epoxide 4221.

In late 1975, PCB area air levels (reported as Aroclor 1242) around the capacitor filling and sealing area were found to be in the range 200 to 2000 μg/m (geometric mean, 690 μg/m). Subsequent to the cessation of PCB use they dropped steadily to a mean of 16 μg/m in April 1983. The TWA levels indicated by personal air samplers on directly exposed personnel in these areas in early 1977 were reported by Brown and Jones (*19*) to average 168 μg/m (range, 24–393 μg/m), or about half the mean area levels that we measured at that time. These investigators also measured the levels of trichloroethylene (used in degreasing); tin, lead and zinc (soldering operations); aluminum and iron (welding operations); and toluene and methyl isobutyl ketone (painting operations): all were generally within OSHA standards.

Unfortunately, there are no data regarding PCB air levels during the 1946–1974 period. Major changes in plant ventilation and changes in the Aroclors used made it impossible to estimate those levels.

Study Population

The study population was selected in early 1976 to include all those workers (a) whose jobs required direct occupational contact with PCBs in high air level zones, such as those in handling and sealing wet capacitors, and capacitor salvage and repair; (b) whose jobs did not involve direct PCB contact, but were at the periphery of the high exposure zone; and (c) whose duties required brief high exposure and contact, such as maintenance men. At the time of the 1976 examination, this study population included 152 males and 42 females. Of these, 41 had service times beginning during the period when the predominant dielectric fluid was Aroclor 1254, 103 began service when it was Aroclor 1242, and 50 had been exposed only to Aroclor 1016. The mean service times and ages in the study population were 17 years (range, 2–35) and 40 years (range 20–65), respectively. Thirty-three of the 194 were also members of the 326-member volunteer group examined by Fischbein et al. a little later in 1976 (*17*). By the time of our 1979 examination, our directly exposed study group was reduced to 174 workers due to relocation, although still including 14 retired and/or relocated workers who returned for the reexamination.

At the time of the initial population selection an estimate of the relative PCB exposure was made by one of us (M. R.) on the basis of the individual worker's job activities. The estimated exposure categories (abbrevi ated as EXE below) generally corresponded to those used for selection, e.g., "low" for peripherally exposed jobs; "medium" for those with intermittent exposure; and "high" for those with continuous direct exposure. After the serum PCB data became available, analysis showed that the "low" and "medium" categories were statistically indistinguishable in terms of serum PCB means.

Clinical Measurements

The clinical examinations were conventional but relatively complete. They included a medical history, physical examination by the plant physician (J.F.), ECG, chest X-ray, spirometry, 26-parameter biochemical analysis, hematology, and urinalysis. Body weight was measured in light indoor clothing and height measured without shoes. Systolic and diastolic blood pressure were measured in the seated position to the nearest 5 mm. The participants were instructed to be fasting for the preceding 12-hr period with water *ad libitum*.

The decision to measure serum PCB levels in 1976 was made during the course of the study, so that only 41 workers had the blood samples required for the PCB analysis drawn while fasting; the remainder were recalled and sampled in the nonfasting state. All of the 1979 measurements were made on fasting sera.

In 1979, the physical examination, ECG, and chest X-ray were repeated only in special cases, but the medical history was expanded and improved, particu larly in relation to smoking habits. Documentation on alcohol consumption remained incomplete and generally unreliable.

The chest X-rays were read by a local radiologist (R. C. Batt) who coded the findings according to the ILO/UC criteria (CRC/NIOSH (M) 2.8, Rev. 4/80). ECG's were interpreted by one of us (J.F.). Clinical chemical analyses were performed on the serum samples using an SMA-26, and hematological analyses on EDTA venous blood specimens, by Medpath (Teterboro, N.J.). The total serum lipids were measured in 1976 by using the phenol turbidity method, but not in 1979; the method has been criticized (*26*) as unreliable for total serum lipids. In 1979 serum triglycerides were reported numerically up to 400 mg/dL and thereafter as δ 400 mg/dL. WBC differentials were performed manually in 1976 and with the Technicon Hemalog D in 1979. Serum osmolarity was calculated from the electrolytes and crystalloids (BUN, blood glucose) by con-

ventional procedures. The mean corpuscular hemoglobin was calculated from the reported red blood cell count and hemoglobin values in 1976.

Serum PCB and DDE Measurements

The PCB determinations upon both the 1976 and 1979 serum samples were performed by Hazelton Raltech (Madison, WI) using conventional PCB extraction, packed column gas chromatographic, and data reporting procedures, which are discussed in detail elsewhere (*27*). These procedures also provided data on the levels of DDE present. The observed distributions of PCB isomer peaks in the capacitor workers' chromatograms are also described elsewhere (*27*); they differed markedly from those in the Aroclor 1016, 1242 and 1254 standards because of metabolism and elimination of all of the mono- and dichlorobiphenyl isomers, most of the tri-and tetrachlor, and many of the pentachloro isomers as well.

The serum PCB levels were reported by the analyst in 1976 as levels of Aroclors 1242 and 1254, and in 1979 as Aroclors 1242, 1254, and 1260. These were calculated from the observed chromatograms by ratioing the sums of certain selected peak heights to those of the corresponding peaks in Aroclor standards. The selected peaks were, for Aroclor 1242, those having retention times (relative to that for DDE, times 100) of 37, 70 and 84; for Aroclor 1254, those at 125, 146, 160 and 186; for Aroclor 1260, those at 125, 146, 160, 186, 197, 294 and 372. Because of the differences in PCB composition between the serum samples and the standards, such values overstate the amounts of PCB actually present. The latter are now more commonly described in terms of values for LPCB ("lower PCBs," i.e., all isomers having gas chromatographic retention times on silicone less than that of DDE, which comes in the middle of the pentachlorobiphenyl range), and HPCB ("higher PCBs," i.e., those with retention times > DDE) with the sum of LPCB and HPCB representing the total PCB present (TPCB). We have shown elsewhere (*27*) that for our more heavily exposed subjects the factor for converting a reported serum Aroclor 1242 value to LPCB is 0.237; for Aroclor 1260 to HPCB, 0.71. The factor for converting the 1976 Aroclor 1254 values to HPCB was estimated from the chromatograms as 0.35.

In 1980 it was found that the individual 1979 values of Aroclor 1242, Aroclor 1254 and DDE, relative to the population means, were highly correlated with the corresponding values in 1976, but that the 1979 values were generally several times higher, despite the limited exposure to either PCB or DDE during the intervening period, indicating that one of the data sets contained a systematic error. Review of the methodology and tests on control samples confirmed the validity of the 1979 procedure (*27*); however, the standardization error in the 1976 data could not be identified after the 4-year time lapse, and the analyst could not verify the 1976 serum PCB and DDE measurements. Accordingly, we have reported here all such data as the originally reported numerical quantity times a correction factor x.

Determination of the value of x was not required for the statistical association studies, but was for estimates of actual PCB levels and clearance. To estimate x, we used the DDE peak on the chromatograms as an internal standard; there had been no more than background exposure of the study group to this substance, which is highly persistent in the body, during the 1976–1979 period. The geometric mean DDE value for 1979 was calculated directly from the reported data; that for 1976 using the maximum likelihood estimate for censored data (*28*), since 87 of the 140 1976 values for p,p'-DDE had been reported as $\leq$ 1 ppb. The resulting values (10.2 and 1.18 ppb, respectively) indicated the mean value of x to be about 10, suggesting a possible decimal point error in 1976.

Lipid PCB Determinations

Serum cholesterol lipids (free cholesterol plus cho lesterol esters) were estimated from normal values (*26*) as 1.50 times the clinically reported serum cholesterol (i.e., cholesterol equivalent) values. Total serum neutral lipids were calculated as the sum of the clinically reported serum triglycerides plus the serum cholesterol lipids. Serum lipid PCBs were calculated as the gross serum PCBs divided by serum neutral lipids. It is shown elsewhere (*23,24*) that PCBs partition between serum and adipose tissue fat in direct proportion to the content of neutral lipids as specified by this procedure; thus, this measure of the serum lipid PCB level is approximately equal to the PCB level in adipose tissue fat. However, the regression results were not particu larly sensitive to the exact procedure used for calcu lating serum lipid phases and comparable findings were obtained when they were calculated instead as simply the sum of the serum triglycerides and the serum cholesterol.

Statistical Analyses

Statistical analyses were performed on a Honeywell 600/6000 computer, using STATPAC (*28*), a versatile general statistical program with many of the capabilities of the more widely used BMDP series (*29*), for the distribution plotting; simple, multiple and stepwise linear regression; and maximum likelihood estimates for censored data.

To evaluate the distributions of the dependent variables, probability plots of both the measured and logarithmatically transformed data were prepared and compared for linearity. The choice for a number of the distributions seemed equivocal, with the arithmetic and geometric means approximately equal. We generally selected the distributions yielding the highest F-ratios in the regressions, or the distributions which tended to produce normal residuals. Partial residual plots were prepared and examined in cases where there was a significant PCB association. Outliers were not removed. The residuals from the regression appeared to be normally distributed with only a few exceptions (blood, glucose, red cell indices), in which cases the distribu tions were not improved by data transformation.

The independent variables used in the multiple and stepwise regressions, as identified from preliminary studies, were as follows:

- Sex (SEX). Workers were coded as males = 1 and females = 2 so that a positive association represented an attribute of females.
- Age (AGE). The numerical age to the nearest year in 1976 was used. Service time and age covaried (r = 0.75).
- Urinary Specific Gravity (SPG). A number of variables appeared sensitive to the degree of hydration in these fasting subjects, principally the crystalloids (blood glucose, blood urea nitrogen).
- Disease Status (DS). Thirteen workers were iden tified as having significant conditions bearing upon the analysis. They included diabetics (*5*), those with alcohol problems (*3*), nonfasting at examination time (*3*), one worker who was post-pituitary surgery, and one worker with epilepsy taking Dilantin. A dummy variable was created (disease absent = 0, disease present = 1) to identify these cases.
- Nonfasting PCB Measurement (FNF). In the 1976 data individuals whose serum PCB levels were obtained in the nonfasting state were coded as 0; fasting measurements were coded as 1.
- Smoking (SC). Smokers and ex-smokers were coded as 2, nonsmokers as 1.
- Job Status (JS). For the 1979 analysis, workers continuing in employment were coded as 0, separated or retired workers as 1.
- Body Mass Index (BMI). The body mass index (W/H) was calculated for each individual in 1976 and 1979 and used as an independent variable.

In the stepwise regressions, the criterion for adding an independent variable was an F value of 3.0; that for removing a variable was 4.0. The numbers of subjects in the stepwise regressions were only 159–166, rather than the 189–194 used in the simple regressions, because of incomplete data. In addition, 41 cases had missing hematological data in 1976 (Table 1) yielding an N of 128 for these analyses.

Because half of the 1976 gross serum DDE values were reported only as $\leq 1x$ ppb, a dummy variable ($\leq 1x$ ppb = -1, $> 1x$ ppb = $+1$) was used in the regressions, and no attempt was made to estimate serum lipid DDE values. The 1979 gross serum DDE and serum lipid DDE levels were expressed in the same terms as the corresponding measures of PCB.

Results

Clinical Characteristics of the Study Population

The medical history and physical examination of the study population revealed a variety of clinical conditions and health-related practices.

Sixty-five percent of the population were smokers or ex-smokers, and 26 workers (17%) showed obstructive patterns on repeated spirometric testing. There were six chest X-ray reports of possible emphysema.

Fifty percent of the population was overweight [>1.2 times the "desirable" weight by 1959 standards (*30*)] and many were frankly obese. Hypertension histories were obtained on 11.3%. Elevated diastolic pressures (>90 mm Hg) were found in 19.6% of the population at examination in 1976 as compared to 14.7% at the time of employment. Reported urinary tract problems included renal stone or "gravel" in 8 subjects; surgically corrected congenital obstruction in one; bladder, kidney, or prostatic infection in 14; and one benign bladder tumor.

Forty-five workers showed one or more elevated fasting blood glucose values between 1976 and 1979. Of these, 5 were known diabetics, 30 were found to give normal postprandial values, and the remainder showed normal fasting values when retested.

A review of the medical dispensary records of all PCB-exposed employees between 1960 and 1975 revealed 49 visits for contact dermatitis attributed to the dielectric fluid. There were an additional 16 visits for nausea, dizziness, or eye or nasal irritation following short initial exposure to the workplace. In all cases the conditions subsided with removal from exposure. Chloracne was never observed in the plant work force.

Clinical Laboratory Findings

The distributions of clinical chemical and hematological values observed in the study population are described in Table 1, along with the normal ranges unadjusted for sex and age, and asterisks indicating variables having values outside these rough reference ranges.

The numbers of individuals reported by the clinical laboratory to be outside its internal age- and sex- adjusted standards (based on ± 2 standard deviations from mean values) are listed for each reported parameter in Table 2. If the parameters were normal and normally distributed, one would expect four or five cases to fall along each tail of these distributions, making a total of eight to ten.

Table 2 indicated substantial numbers of individuals with elevations in serum triglycerides, cholesterol, and SGPT in both 1976 and 1979, and in blood glucose and albumin/globulin ratio in 1976. Some elevations in BUN and chloride were found in 1979. In 1976 there were some elevations in total WBCs associated with decreased PMNs and increased lymphocytes, monocytes, and eosinophils. In 1979 there were marginal increases in monocytes and eosinophils, but the WBCs were near normal. Urinalysis in both 1976 and 1979 showed elevated cell counts, but no attempt had been made to obtain a clean catch. Urinary specific gravity and calculated serum osmolarity were both elevated in 1976 and 1979 (Table 1).

The observed distributions of serum triglycerides and serum cholesterol are shown in greater detail in Figures 1 and 2. The cross-hatched bars represent values that

Table 1. Distribution of clinical laboratory finding in study population of PCB-exposed capacitor workers.

Clinical measurements[a]	Units	Dist.	Std. range[b]	1976 (N = 194) Mean	± SD	AM or GM	Percentiles 5th	Percentiles 95th	Missing values	1979 (N = 174) Mean	± SD	AM or GM	Percentiles 5th	Percentiles 95th	Missing values
Serum triglycerides	mg/dL	LN	50–200	2.133	0.224	135.8	58.9	310*	1	2.157	0.225	143.7	61.3	336.9*	
Serum total cholesterol	mg/dL	N	125–300	251.3	55.2	251.3	159.2	342.5*	1	238.1	50.1	238.1	155.7	320.4*	
Serum neutral lipids[c]	mg/dL	N		2.709	0.127	512.1	316	829	1	2.702	0.119	503.3	321	789	
SGOT	IU/L	LN	1–50	1.374	0.152	13.3	23.7	41.9		1.448	0.144	28.0	16.3	48.4	2
SGPT	IU/L	LN	1–55	1.460	0.189	28.9	14.1	58.8*	1	1.537	0.164	34.4	18.5	63*	2
SGGTP	U/L	LN	1–70	1.091	0.266	12.3	4.50	33.8	2	1.198	0.263	15.8	5.82	42.7	
Serum alkaline phosphatase	IU/L	LN	15–55	1.419	0.142	26.2	15.8	43.4		1.465	0.122	29.1	18.4	46.3	
Serum lactic dehydrogenase	IU/L	N	97–250	160.1	28.2	160.1	114.5	205.4		173.6	31.3	173.6	122.1	225.1	
Serum total protein	g/dL	LN	6.2–8.3	0.858	0.079	7.21	6.45	8.04		0.864	0.028	7.30	6.58	8.11	
Serum albumnin	g/dL	LN	3.8–5.1	0.648	0.032	4.44	3.92	5.02	1	0.644	0.036	4.41	3.84	5.05	
Serum globulin	g/dL	N	2.1–4.0	2.77	0.51	2.77	1.93	3.60	3	2.92	0.43	2.92	2.21	3.63	
Albuming/globulin ratio		LN	1.2–2	0.213	0.099	1.63	1.12	2.38*	3	0.182	0.082	1.52	1.11	2.07	
Blood urea nitrogen	mg/dL	LN	7–28	1.185	0.119	15.3	9.72	24.0	1	1.227	0.115	16.9	10.9	26.0	
Serum creatinine	mg/dL	N	0.8–1.8	1.30	0.21	1.30	0.95	1.64	1	1.32	0.20	1.32	0.99	1.65	
Bun/creatinine ratio		LN		1.078	0.124	12.0	7.45	19.10	2	1.112	0.127	12.0	8.00	20.9	
Serum total bilirubin	mg/dL	LN	0.1–1.4	−0.339	0.193	0.46	0.22	0.95		−0.218	0.168	0.61	0.32	1.14	
Serum direct bilirubin	md/dL	N	0–0.4	0.15	0.08	0.15	0.02	0.27	1	0.14	0.07	0.14	0.02	0.26	
Blood glucose	mg/dL	LN	65–130	2.010	0.057	102.4	82.8	126.5	1	1.995	0.056	98.8	79.8	122.3	
Serum uric acid	mg/dL	N	3.3–8.9	5.74	1.25	5.74	3.65	7.80	1	6.01	1.30	6.01	3.88	8.15	
Serum Na	mmole/L	N	134–146	139.5	2.67	139.5	135.1	143.9	2	139.4	2.32	139.4	135.6	143.2	
Serum K	mmole/L	N	3.4–5.4	4.26	0.44	4.26	3.54	4.98	2	4.42	0.46	4.42	3.66	5.17	
Serum Ca	mg/dL	N	8.7–10.5	9.87	0.49	9.87	9.06	10.7*	1	9.67	0.42	9.67	8.97	10.4	
Serum Mg	meq/L	N	1.6–2.3							1.91	0.15	1.91	1.66	2.15	
Serum Cl	mmole/L	N	96–109	102.0	2.93	102.0	97.1	106.8	2	103.8	3.27	103.8	98.4	109.1*	
Serum P	mg/dL	N	1.9–4.3	3.01	0.44	3.01	2.28	3.74	1	2.85	0.44	2.85	2.12	3.58	
Serum osmolarity	mosm/kg	N	280–295	299.0	6.06	299.0	288.9	309.0*	2	299.5	5.37	299.5	290.6	304.3*	
Specific gravity (urine)	g/cm^3	N		1.026	0.005	1.026	1.017	1.035*	5	1.026	0.005	1.026	1.018	1.03*	
Serum iron	μg/dL	N	55–200	112.1	36.1	112.1	53.1*	170.6	2	108.2	29.1	108.2	60.3	156.2	
RBC	10^6/mm^3	N	4.3–6.4	4.94	0.42	4.94	4.24*	5.63	1	5.05	0.39	5.05	4.39	5.70	
HG	g/dL	N	13.0–18.5	14.8	1.67	14.8	12.5*	17.0	1	15.4	1.18	15.4	13.4	17.4	
HCT	%	N	39.5–57.0							46.2	3.55	46.2	40.3	52.1	
MCV	μ^3	N	80–103							91.6	5.18	91.6	83.1	100.0	
MCH[c]	μμg	N	26–33	30.0	1.89	30.0	26.9	33.1	1	30.6	1.61	30.6	27.9	33.1	
MCHC	%	N	30.6–36.0							33.5	2.05	33.5	31.2	35.7	
WBC	10^3/mm^3	N	4.1–11.9	7.02	1.74	7.02	4.21	9.81	2	6.90	1.87	6.90	3.85	9.92	
PMNS	10^3/mm^3	N	1.65–8.33	4.20	1.32	4.20	2.02	6.37	41	4.12	1.46	4.12	1.77	6.45	
# PMNS	% WBC	N	45–77	59.7	9.57	59.7	44.3	74.9	41	59.0	8.65	59.0	44.6	73.2	
Lymphocytes	10^3/mm^3	N	1.05–3.58	2.33	0.76	2.33	1.07	3.57	41	2.09	0.64	2.09	1.03	3.14	
% Lymphocytes	% WBC	N	16–45	33.8	9.64	33.8	18.2	49.2*	41	30.9	7.84	30.9	17.9	43.9	
Monocytes	10^3/mm^3	N	0.06–0.93	0.30	0.17	0.30	0.02	0.59	41	0.48	0.22	0.48	0.12	0.83	
% Monocytes	% WBC	N	0–8	4.38	2.14	4.38	0.87	7.95	41	6.90	2.57	6.90	2.60	11.2*	
Eosinphils	10^3/mm^3	N	0.04–0.42	0.13	0.13	0.13	0	0.32	41	0.16	0.12	0.16	0	0.33	
% Eosinphils	% WBC	N	0–4	1.84	1.73	1.84	0	4.34*	41	2.34	1.78	2.34	0	4.8*	
Basophils	10^3/mm^3	N	0.01–0.15							0.046	0.026	0.046	0.003	0.090	
% Basophils	% WBC	N	0–2							0.68	0.38	0.68	0	1.30	

[a] All blood chemical determinations made on serum: hematology measurements in EDTA venous blood. Abbreviations: SGOT, serum glutamic-oxalacetic transaminase; SGOT, serum glutamic-pyruvic transaminase; SGGTP, serum γglutamyl transpeptidase; LDH, serum lactic dehydrogenase; A/G Ratio, albumin/globulin ratio; BUN, blood urea nitrogen; RBC, red blood cell count; HG, hemoglobin; HCT, hematocrit; MCV, mean red cell corpuscular volume; MCH, mean red cell corpuscular hemoglobin; MCHC, mean red cell corpuscular hemoglobin concentration; WBC, white blood cell count; PMN, polymorphonuclear white cells.

[b] laboratory standard ranges unadjusted for sex and age. Asterisk (*) indicates values outside these ranges. Arithmetic (AM) or geometric (GM) means given based on selected distribution (N = normal, LN = lognormal).

fell outside the 95th percentile for age from the Lipid Research Clinics Prevalence Study (*31*). By the LRCP study criteria, the portions of the male population exhibiting elevations in triglycerides in 1976 and 1979 were 5.7% and 12.6%, respectively. This elevation was significant at the 1% level by paired t-test. For females, the elevation in triglycerides was significant at the 5% level but was found in the younger women and appeared to be related in part to obesity and estrogen medication. Of unknown significance were the differences in analytical methodology (fluorimetric method with Technicon Autoanalyser used by LRCPS; enzymatic method with discrete analyser used here). The serum cholesterol values (Fig. 2) were normally distributed. By the LRCPS criteria, the portions of the entire group above the 95th percentile in cholesterol in 1976 and 1979 were 29.4% and 23.3%, respectively.

Measures of PCB Exposure

Table 3 shows the means and ranges for serum PCB concentrations described in four ways: first as the Ar-

Table 2. Numbers of study group members reported by clinical laboratory to have clinical variables outside normal (95%) age- and sex-adjusted ranges.

	1976 (N = 194)				1979 (N = 174)			
Clinical variables[a]	Males	Females	Total	+/– Split[b]	Males	Females	Total	+/–Split[b]
Trigylcerides	36	4	40	*38/2	38	3	41	*41/0
Total cholesterol	27	7	34	*33/1	20	3	23	*22/1
SGPT	15	0	15	*15/0	12	1	13	*13/0
SGOT	6	1	7	*7/0	3	0	3	3/0
GGTP	6	0	6	*6/0	3	0	3	3/0
Alkaline phosphatase	1	1	2	2/0	5	2	7	4/3
LDH	3	0	3	3/0	2	1	3	3/0
Blood glucose	25	4	29	*29/0	3	3	6	*6/0
Uric acid	2	1	3	2/1	3	0	3	3/0
Total bilirubin	0	0	0	0/0	2	2	4	4/0
Direct bilurubin	1	0	1	1/0	1	1	2	2/0
Total protein	4	0	4	4/0	2	2	4	3/1
Albumin	0	0	0	0/0	8	2	10	1/9*
Globulin	9	3	12	7/7	1	2	3	2/1
A/G ratio	12	2	14	*13/1	6	2	8	4/4
BUN	4	2	6	*6/0	6	3	9	*9/0
Creatinine	1	0	1	1/0	1	0	1	1/0
Na	3	2	5	4/1	2	0	2	0/2
K	3	0	3	1/2	5	1	6	5/1
Cl	1	0	1	0/1	9	4	13	*11/2
Ca	1	1	2	0/2	3	2	5	3/2
P	0	0	0	0/0	1	0	1	0/1
Mg					1	0	1	0/1
Iron	5	1	6	5/1	6	0	6	2/4
RBC	2	1	3	1/2	1	0	1	0/1
Hemoglobin	3	0	3	3/0	2	0	2	1/1
Hematocrit	1	0	1	1/0	4	0	4	5/1
MCV					4	0	4	3/1
MCH					10	1	11	*8/3
MCHC					1	0	1	0/1
WBC	11	2	13	9/4	8	3	11	7/4
Differential								
PMNs	7	4	11	2/9*	1	0	1	1/0
Lymphocytes	8	5	13	*11/2	8	2	10	5/5
Monocytes	7	2	9	*9/0	3	3	6	*6/0
Eosinophils	6	1	7	*7/0	4	2	6	*6/0
Basophils								
Urinalysis								
Albumin	3	2	5	5/0	0	1	1	1/0
Acetone	1	1	2	2/0	2	1	3	3/0
Cells	12	12	24	*24/0	4	8	12	*12/0

[a]See Table 1 for abbreviations used.
[b]Asterisk (*) indicates significant probability (95%) of increase or decrease assuming a true binomial proportion of 0.5.

oclor levels reported by the analytical laboratory, based on measurements of selected peak heights; second, as LPCB or HPCB values, representing total PCBs actually present in the specified ranges, determined by applying appropriate conversion factors to each reported Aroclor value (*27*); third, as total PCBs (TPCB), the sum of the LPCB and HPCB values obtained from the Aroclor 1242 and 1260 values, respectively; and fourth, as serum lipid PCB values, obtained by dividing the serum LPCB, HPCB, or TPCB values by the total serum neutral lipid. Also shown are the corresponding data for p,p'-DDE, which was present at background levels.

Reference values were obtained on 25 office workers in a Connecticut office in 1979. Their geometric mean analytical values were for serum Aroclor 1242, 6.6 ppb; for Aroclor 1254, 14.4 ppb; for Aroclor 1260, 8.3 ppb; for p,p'-DDE, 11.3 ppb. Thus, taking the correction factor x for the 1976 data as 10, the mean xenobiotic levels in the study population in 1976 and 1979 were, for Aroclor 1242, about 220 and 40 times the background levels, respectively; for Aroclor 1254 and 1260, about 4–6 times the background; and for DDE, about the same as background.

Also for $x = 10$, Table 3 indicates that in the 44 to 45 months between the 1976 and 1979 examinations, the geometric mean level of serum Aroclor 1242 fell from 1470 to 277 ppb, or 81%, and that of serum Aroclor 1254 from 84 to 55 ppb, or 35%. Both calculations must be taken with caution, given the imprecision of the analysis, since they are uncorrected for changes in the composition of the study population and highly depen-

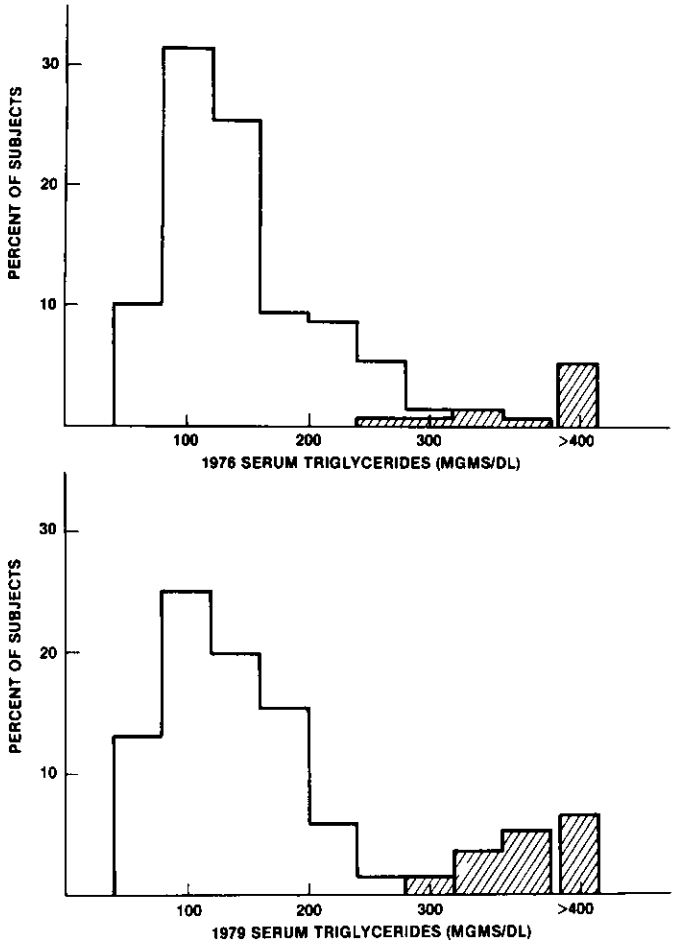

FIGURE 1. Serum triglyceride levels (mg/dL) in the study population. Cross-hatched area indicates values falling above the 95th percentile for age from the Lipid Research Clinics Prevalence Study (*31*).

dent upon the estimated value of the correction factor, x. The implied extent of clearance of retained LPCB is less sensitive to the estimated value of x, but more difficult to interpret, since some direct exposure to Aroclor 1016 continued during the first third of the interval between the examinations. Investigation of the rates of clearance of individual PCB isomers in this population is continuing.

Because of the analytical uncertainties in the 1976 serum PCB data, we also examined two other measures of PCB exposure, namely, the estimates of relative exposure based on analysis of the individual job activities, and the measurements of PCB air levels in the various working areas, made at the time of the 1976 examination. The correlations of these measures with the 1976 and 1979 serum LPCB and HPCB values are shown in Table 4.

The measurements of area air levels proved to be a poor estimate of exposure, and were dropped from further consideration in the regressions against clinical variables. The relative exposure estimate showed a high correlation with serum LPCB in 1976 (r = 0.73, declining to 0.51 in 1979), indicating that it reflected estimated current exposure to Aroclor 1016, which was

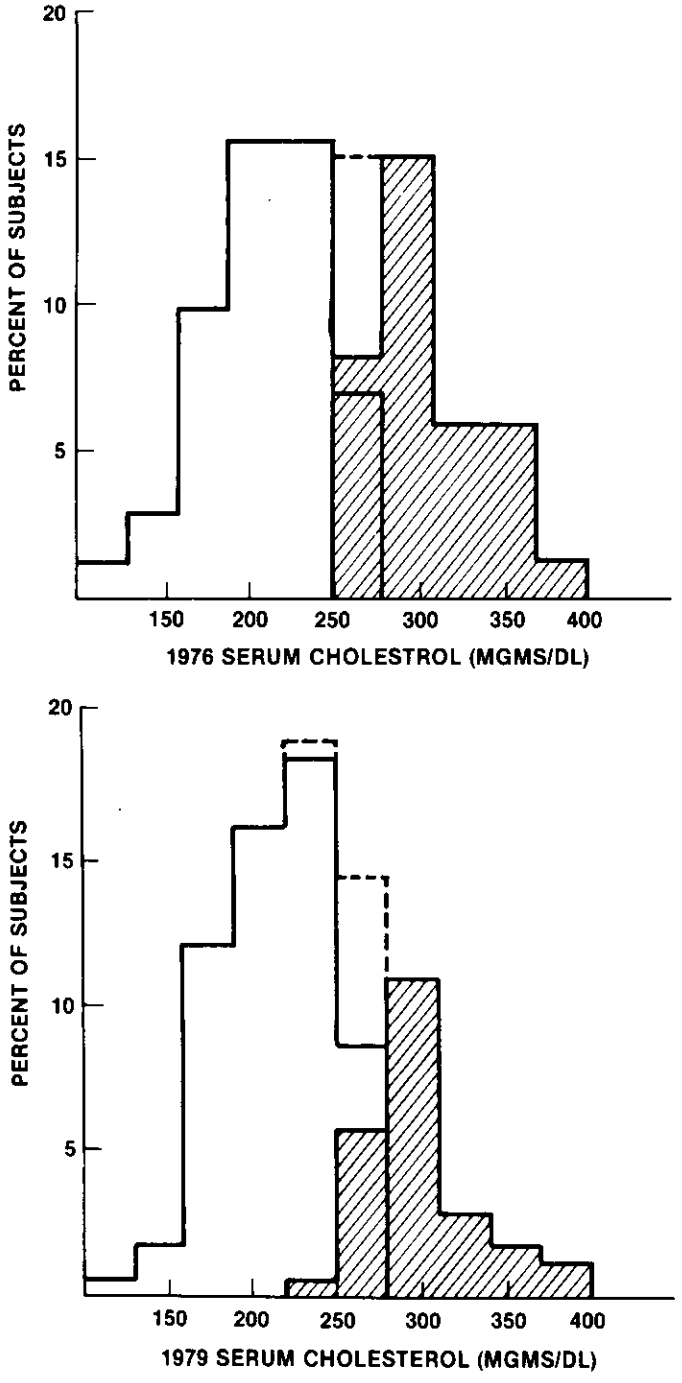

FIGURE 2. Serum total cholesterol levels (mg/dL) in the study population. Cross-hatched areas indicate values falling above the 95th percentile for age from the Lipid Research Clinics Prevalence Study (*31*).

in use at the time. The correlations between the exposure estimate and the serum HPCBs were lower but equal in 1976 and 1979 (r = 0.36).

Relationships of Independent Variables to PCB Exposure

The correlation coefficients for the association of the individual independent variables selected for the re

Table 3. Distributions of serum PCB and DDE in study population of PCB-exposed capacitor workers.

Descriptor of serum parameter	1976 log mean − log x[a]	± SD	GM[b]	Percentiles 5	Percentiles 95	MV[a]	1979 log mean	± SD	GM[a]	Percentiles 5	Percentiles 95	MV[a]
Measures of lower PCBs												
Aroclor 1242, ppb	2.167	0.486	147.1x	23.4x	926.2x	9	2.443	0.463	277.1	48.1	1598.1	1
LPCB, ppb	1.560	0.481	36.3x	5.7x	226.9x	9	1.832	0.463	67.9	11.8	391.6	1
Lipid LPCB, ppm	0.968	0.474	9.3x	1.5x	56.3x	9	1.245	0.432	17.6	3.4	90.3	1
Measures of higher PCBs												
Aroclor 1254, ppb	0.924	0.414	8.4x	1.8x	40.3x	9	1.740	0.442	54.9	10.3	292.4	1
Aroclor 1260, ppb							1.543	0.447	34.9	6.4	190.0	30
HPCB (1254), ppb	0.472	0.411	3.0x	0.6x	14.2x	9	1.285	0.442	19.3	3.6	107.7	1
HPCB (1260), ppb							1.375	0.447	23.7	4.4	129.2	30
Lipid HPCB (1254), ppm	− 0.120	0.396	0.8x	0.2x	3.4x	9	0.695	0.400	5.0	1.1	22.7	1
Lipid HPCB (1260), ppm							0.785	0.406	6.1	1.3	28.6	30
Measures of total PCBs												
TPCB (1242, 1260), ppb							1.979	0.437	95.2	18.2	499.0	30
Lipid TPCB, ppm							1.392	0.405	24.6	5.3	114.4	30
Measures of p,p'-DDE												
DDE, ppb	0.033		1.08x			27	1.005	0.318	10.1	3.0	33.7	1
Lipid DDE, ppm							0.305	0.284	2.0	0.7	6.0	1

[a] GM = geometric mean; MV = missing values.
[b] Most likely value of log x = 1.0; x = 10.

Table 4. Correlation coefficients for associations between serum PCB levels, area air levels, and the job analysis exposure estimate in 1976 and 1979.

	1976 Exposure estimate (N = 181)	1976 Area air level (N = 180)	1979 Exposure estimate (N = 172)	1979 Area air level (N = 100)
LPCBs (1242)				
Gross serum concn.	0.731	0.144	0.506	− 0.014
Serum lipid concn.	0.727	0.167	0.516	0.029
HPCBs (1254)				
Gross serum concn.	0.368	0.080	0.360	− 0.029
Serum lipid concn.	0.360	0.102	0.369	0.010
HPCBs (1260)				
Gross serum concn.			0.359	− 0.025
Serum lipid concn.			0.363	0.014
Exposure estimate	1.0	− 0.084	1.0	− 0.164

gression study with the various measures of PCB exposure, as obtained by simple regression, are shown in Table 5.

The tabulated data indicated strong associations of age and/or service time with HPCBs in both 1976 and 1979, and with LPCBs in 1979, probably reflecting a time-dependent accumulation of the more slowly me tabolized PCB isomers. There were significant negative correlations between the body mass index and the serum lipid LPCB in 1976 and significant positive correlations with the gross serum LPCBs and HPCBs in 1979. In 1979, LPCB values were significantly higher in females than males (positive sign of coefficient) but lower in smokers (negative sign), probably reflecting oxidase induction (*32*). 1979 PCB levels in retirees were not significantly different from those in workers who continued in employment. Urinary specific gravity (SPG) and the presence of diabetes or alcoholism showed no association with serum PCB levels, but SPG was the one independent variable showing association with the exposure estimate in 1976. Higher levels of LPCBs were found in nonfasting individuals in 1976.

Relationships of Clinical Laboratory Findings to PCB Exposure

Tables 6, 7, 8 and 9 show the results of applying the three regression procedures to the clinical laboratory findings using as independent variables the 1976 and 1979 levels of LPCB, HPCB, and DDE (each expressed as both the log gross serum and log serum lipid value except for DDE in 1976), and the PCB exposure estimate (EXE), respectively. In each case, we have tabulated the regression coefficients for the associations with PCB or DDE, $\hat{\beta}_1$, and their confidence intervals for those clinical parameters that showed a significant

Table 5. Correlation coefficients relating measures of PCB exposure and the selected independent variables.

Dependent variable	Independent variables								
	Age	Ser	Sex	SPG	BMI	DS	SC	FNF	JS
Gross serum PCBs									
LPCBs, 1976	0.107	0.073	0.011	- 0.121	- 0.090	- 0.045	- 0.132	- 0.188*	
LPCBs, 1979	0.259*	0.191*	0.160*	0.084	0.208*	0.096	- 0.173*		- 0.015
HPCBs, 1976	0.421*	0.394*	- 0.091	- 0.111	- 0.013	- 0.086	0.009	- 0.021	
HPCBs, 1979	0.516*	0.549*	- 0.026	0.037	0.189*	0.141	- 0.050		0.005
Serum lipid PCBs									
LPCBs, 1976	0.028	- 0.007	0.030	- 0.111	- 0.172*	- 0.121	- 0.172*	- 0.211*	
LPCBs, 1979	0.209*	0.140	0.185*	0.077	0.136	0.061	- 0.199*		- 0.008
HPCBs, 1976	0.340*	0.314*	- 0.014	- 0.099	- 0.109	- 0.001	- 0.037	- 0.045	
HPCBs, 1979	0.493*	0.535*	0.014	0.026	0.114	0.109	- 0.069		0.014
Exposure estimate									
1976	0.004	- 0.009	- 0.040	- 0.158*	- 0.106	- 0.115	- 0.109	- 0.138	
1979	0.004	- 0.009	- 0.040	- 0.062	- 0.036	- 0.115	- 0.109		0.084

*Statistical significance ≤ 5%.

Table 6A. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum LPCB, as determined by three regression procedures: log gross serum LPCBs.

		Log gross serum LPCBs[b]								
		Simple regression			Multiple regression			Step regression		
			Confid. limits			Confid. limits			Confid. limits	
Dependent variable[a]	$\bar{x}$	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95
1976										
Log triglycerides	2.14	0.07	0.01	0.14	0.10*	0.03	0.17	0.10*	0.03	0.16
Cholesterol	252	24.9*	8.48	41.4	24.3*	7.15	41.5	25.7*	9.49	42.0
Log SGPT	1.46	0.03	–0.01	0.09	0.07*	0.02	0.13	0.08*	0.02	0.13
Log GGTP	1.10	0.07	–0.01	0.15	0.12*	0.04	0.21	0.13*	0.05	0.21
Log total bilirubin	–0.34	–0.09*	–0.14	–0.03	–0.08*	–0.15	–0.02	–0.09*	–0.15	–0.03
Direct bilirubin	0.15	–0.03*	–0.06	–0.01	–0.04*	–0.06	–0.01	–0.04*	–0.06	–0.01
Uric acid	5.73	0.08	–0.31	0.46	0.31	–0.01	0.64	0.35*	0.04	0.66
Log blood glucose	2.01	–0.01	–0.03	0.01	–0.001	–0.02	0.02	–0.001	–0.02	0.01
Phosphorus	3.01	0.14*	0.01	0.27	0.20*	0.04	0.35	0.16*	0.01	0.30
RBC	4.94	–0.07	–0.20	0.06	–0.07	–0.18	0.05	–0.08	–0.19	0.02
Lymphocytes	2.33	0.03*	0.04	0.55	0.42*	0.12	0.71	0.35*	0.07	0.63
1979										
Log triglycerides	2.16	0.18*	0.11	0.25	0.15*	0.08	0.22	0.14*	0.07	0.21
Cholesterol	238	34.3*	18.8	49.8	25.6*	8.81	42.4	24.0*	7.90	40.1
Log GGTP	1.20	0.11*	0.03	0.20	0.10*	0.02	0.19	0.12*	0.04	0.20
Log total protein	0.86	0.01*	0.002	0.02	0.01	–0.001	0.02	0.01	–0.001	0.02
Globulin	2.92	0.19*	0.05	0.33	0.10	–0.05	0.24	0.13	–0.005	0.26
Hemoglobin	15.4	–0.04*	–0.78	–0.02	–0.20	–0.56	0.16	–0.20	–0.54	0.13
% Lymphocytes	30.9	–0.49	–3.02	2.04	–1.92	–4.69	0.85	–1.44	–4.31	1.00
Monocytes	0.48	0.07*	0.01	0.14	0.09*	0.02	0.17	0.08*	0.01	0.15
% Monocytes	6.96	1.18*	0.38	1.99	1.41*	0.54	2.27	1.41*	0.58	2.23

[a]See Table 1 for abbreviations. Asterisk (*) indicates 95% confidence limits did not include zero.
[b]N (1976) for simple regression = 189–194. N for multiple regresion and step regression = 159–166 except hematology where there are 41 missing values (Table 1).

association in one of the six regressions performed. The test of significance was that the 95% confidence interval for $\hat{\beta}_1$ not include zero; statistically significant associa tions are indicated by asterisks. In addition, in Tables 6–8 we have listed the partial r values for the backward step regressions against the log serum lipid xenobiotic (e.g., LPCB, HPCB or DDE) and the other independent variables. The partial r values listed are generally those where the regression coefficient was found to be of statistical significance, which, depending on the number of degrees of freedom, generally corresponded to a partial $r > 0.15$; in addition, we have listed some borderline associations, as indicated by partial r values of 0.14–0.15. A comparison of the $\hat{\beta}_1$ values across these various regressions indicates the sensitivity of the relation to confounding by the other independent variables, and

Table 6B. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum LPCB, as determined by three regression procedures log serum lipid LPCBs.

	Log serum lipid LPCBs[a]								
	Simple regression			Multiple regression			Step regression		
		Confid. limits			Confid. limits			Confid. limits	
Dependent variable[a]	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95
1976									
Log triglycerides	–0.04	–0.11	0.03	0.01	–0.07	0.08	0.01	–0.07	0.08
Cholesterol	–1.65	–18.8	15.5	1.82	–16.4	20.1	1.82	–16.4	20.1
Log SGPT	–0.002	–0.06	0.06	0.05	–0.01	0.11	0.05	–0.01	0.10
Log GGTP	0.02	–0.06	0.10	0.10*	0.01	0.19	0.11*	0.02	0.19
Log total bilirubin	–0.08*	–0.04	–0.02	–0.09*	–0.15	–0.02	–0.09*	–0.15	–0.03
Direct bilirubin	–0.03*	–0.05	–0.01	–0.04*	–0.06	–0.01	–0.04*	–0.06	–0.01
Uric acid	–0.09	–0.48	0.30	0.25	–0.09	0.59	0.31	–0.02	0.63
Log blood glucose	–0.02*	–0.04	–0.003	–0.003	–0.02	0.01	–0.003	–0.02	0.01
Phosphorus	0.16*	0.02	0.29	0.22*	0.06	0.38	0.19*	0.04	0.34
RBC	–0.01	–0.23	0.03	–0.11	–0.23	0.01	–0.12*	–0.23	–0.01
Lymphocytes	0.23*	0.01	0.54	0.38*	0.08	0.69	0.39*	0.09	0.69
1979									
Log triglycerides	0.08	–0.01	0.16	0.05	–0.03	0.13	0.04	–0.03	0.12
Cholesterol	12.2	–5.20	29.6	2.64	–15.5	20.8	2.88	–14.7	20.4
Log GGTP	0.07	–0.02	0.16	0.07	–0.02	0.16	0.07	–0.02	0.16
Log total protein	0.007	–0.003	0.02	0.003	–0.01	0.01	0.003	–0.01	0.01
Globulin	0.12	–0.26	0.27	0.02	–0.13	0.17	0.02	–0.13	0.17
Hemoglobin	–0.59*	–1.00	–0.19	–0.31	–0.69	0.06	–0.32	–0.68	0.03
% Lymphocytes	–1.67	–4.38	1.03	–3.26*	–6.14	–0.39	–1.95	–4.65	0.75
Monocytes	0.08*	0.01	0.16	0.11*	0.03	0.19	0.10*	0.02	0.17
% Monocytes	1.36*	0.50	2.21	1.61*	0.71	2.52	1.58*	0.71	2.46

[a] N (1979) for simple regression = 172–174. N for multiple regression and step regression = 165–166.

Table 6C. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum LPCB, as determined by three regression procedures independent variables.

	Independent variables[a]											
	Step regression			Partial r								
		Confid. limits										
Dependent variable[a]	$\hat{\beta}_1$	5	95	Age	Sex	SPG	BMI	DS	SC	JS	FNF	Log $(LPCB)_{SL}$
1976												
Log triglycerides	0.01	–0.07	0.08	0.20	–0.22	–0.15	0.28	0.26		X		
Cholesterol	1.82	–16.4	20.1	0.35			0.20			X		
Log SGPT	0.05	–0.01	0.10		–0.29		0.35			X		
Log GGTP	0.11*	0.02	0.19		–0.19		0.15	0.15		X	0.29	0.20
Log total bilirubin	–0.09*	–0.15	–0.03			0.20		–0.19		X		–0.22
Direct bilirubin	–0.04*	–0.06	–0.01		–0.17			–0.16	–0.20	X	0.17	–0.21
Uric acid	0.31	–0.02	0.63	–0.47			0.45			X	0.16	
Log blood glucose	–0.003	–0.02	0.01	0.14			0.32	0.39		X		0.19
Phosphorus	0.19*	0.04	0.34						0.16	X		0.19
RBC	–0.12*	–0.23	–0.01		–0.58					X		–0.17
Lymphocytes	0.39*	0.09	0.69							X	0.16	0.23
1979												
Log triglycerides	0.04	–0.03	0.12	0.19			0.40				X	
Cholesterol	2.88	–14.7	20.4	0.34			0.18				X	
Log GGTP	0.07	–0.02	0.16	0.16	–0.26	0.18	0.21				X	
Log total protein	0.003	–0.01	0.01	–0.14			0.23		0.19		X	
Globulin	0.02	–0.13	0.17				0.27			–0.15	X	
Hemoglobin	–0.32	–0.68	0.03		–0.54						X	
% Lymphocytes	–1.95	–4.65	0.75							0.19		
Monocytes	0.10*	0.02	0.17						0.21	–0.21	X	0.20
% Monocytes	1.58*	0.71	2.46		–0.16		–0.15			–0.23	X	0.27

[a] See text for abbreviations.

Table 7A. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum HPCB (1254), as determined by three regression procedures: log gross serum HPCBs[a]c

		Log gross serum HPCBs								
		Simple regression			Multiple regression			Step regression		
			Confid. limits			Confid. limits			Confid. limits	
Dependent variable[a]	$\bar{x}$	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95
1976										
Log triglycerides	2.14	0.13*	0.06	0.21	0.11*	0.01	0.20	0.12*	0.04	0.21
Cholesterol	251.9	38.7*	19.8	57.6	31.1*	7.63	54.6	35.1*	13.1	57.1
Log SGPT	1.46	0.04	-0.03	0.11	0.08*	0.002	0.15	0.06	-0.003	0.13
Log GGTP	1.10	0.12*	0.03	0.21	0.15*	0.03	0.26	0.15*	0.05	0.25
Log alk. phos.	1.42	0.07*	0.02	0.11	0.06	-0.004	0.13	0.07*	0.01	0.12
Log total bilirubin	-0.34	-0.08*	-0.15	-0.02	-0.12*	-0.21	-0.03	-0.10*	-0.18	-0.03
Direct bilirubin	0.15	-0.03	-0.05	0.001	-0.04*	-0.08	-0.006	-0.04*	-0.07	-0.008
Log total protein	0.86	-0.002	-0.01	0.01	-0.01	-0.02	0.01	-0.006	-0.02	0.01
Log albumin	0.65	-0.01	-0.02	0.003	-0.008	-0.02	0.007	-0.007	-0.02	0.008
Log BUN	1.19	0.04*	0.001	0.09	0.02	-0.04	0.06	0.02	-0.03	0.06
Creatinine	1.30	-0.01	-0.09	0.06	-0.06	-0.15	0.03	-0.05	-0.13	0.04
Log B/C ratio	1.08	0.05*	0.002	0.09	0.04	-0.02	0.09	0.04	-0.01	0.08
Iron	110.7	-13.6*	-26.1	-1.16	-10.5	-27.3	6.33	-10.1	-24.1	4.14
RBC	4.94	-0.08	-0.23	0.07	-0.06	-0.21	0.10	-0.09	-0.22	0.04
WBC	7.0	1.00*	0.40	1.59	1.34*	0.55	2.14	0.95*	0.28	1.63
Lymphocytes	2.33	0.33*	0.02	0.63	0.72*	0.29	1.15	0.70*	0.27	1.13
% Monocytes	4.37	-1.07*	-1.91	-0.23	-1.08*	-2.98	-0.63	-1.67	-2.61	-0.73
1979										
Log triglycerides	2.16	0.22*	0.15	0.29	0.19*	0.10	0.27	0.19*	0.12	0.26
Cholesterol	238.2	47.3*	31.6	63.0	36.1*	15.9	56.3	39.4*	20.7	58.2
Log GGTP	1.20	0.14*	0.05	0.22	0.07	-0.03	0.17	0.10*	0.02	0.19
Log alk. phos.	1.47	0.06*	0.02	0.10	0.04	-0.01	0.10	0.05*	0.01	0.10
Direct bilirubin	0.14	-0.02	-0.05	0.004	-0.02	-0.05	0.01	-0.02	-0.05	0.001
Log blood glucose	2.00	0.04	-0.02	0.06	0.02	-0.003	0.04	0.02*	0.003	0.04
Globulin	2.92	0.21*	0.07	0.36	0.11	-0.07	0.29	0.12	-0.02	0.27
Log A/G ratio	0.18	-0.04*	-0.06	-0.01	-0.01	-0.04	0.02	-0.01	-0.04	0.02
Log BUN	1.23	0.08*	0.04	0.12	0.04	-0.001	0.09	0.05*	0.005	0.09
Log B/C ratio	1.11	0.06*	0.02	0.11	0.03	-0.02	0.09	0.04	-0.01	0.09
Monocytes	0.48	0.08*	0.01	0.16	0.10*	0.01	0.19	0.08*	0.01	0.16
% Monocytes	6.96	1.23*	0.38	2.07	1.32*	0.25	2.38	1.13*	0.27	1.99

[a]See Table 6 footnotes.

the effects of conversion from gross serum to serum lipid concentration of the xenobiotic.

The most consistent finding in Tables 6–9 was the strong, positive associations of log serum triglycerides and cholesterol with the log gross serum level of PCBs and DDE which has been found by others (*13,15,21,22*). The association disappeared when the xenobiotic level was expressed as the concentration in serum lipids, or as the PCB exposure estimate. This disappearance was associated with a 70 to 130% decline in the value of $\hat{\beta}_1$. This finding was exhibited in all regressions whether against log LPCB, HPCB, or DDE, and whether for 1976 or 1979. A similar, but less dramatic change was exhibited by regressions against measures of the hepatic enzymes (log GGTP, log SGPT and log alkaline phos phatase). These parameters frequently showed signifi cant associations with the log gross serum levels of PCB or DDE, but the $\hat{\beta}_1$ values dropped 20 to 50% upon conversion to serum lipid levels. The only associations then remaining significant in the final backward step regressions were those of 1976 log GGTP with log LPCB, log HPCB, and EXE. None of the other clinical parameters showed consistent declines of this magnitude in $\hat{\beta}_1$.

A second consistent finding was strong negative associations of PCBs, but not DDE, with the two measures of bilirubin, direct bilirubin and log total bilirubin, in 1976. These associations were seen for all measures of log PCB (LPCB, HPCB and EXE) in almost all of the regressions. Only two associations remained in 1979 (HPCB, EXE), when the PCB levels were lower.

A third set of findings consisted of associations between the hematological variables and the serum lipid PCBs. In 1976 significant negative associations were found between RBCs and both log serum lipid LPCB and HPCB, and between the monocytes and both log serum lipid HPCB and the exposure estimate. There were positive associations between lymphocytes and log serum lipid LPCB, and between WBCs and log serum lipid HPCB. Similar associations with the log gross serum DDE were found for the lymphocytes, monocytes, and WBCs. In separate step regression studies log total bilirubin was selected in place of log serum lipid PCB values in the cases of RBCs and the lympho-

Table 7B. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum HPCB (1254), as determined by three regression procedures: log serum lipid HPCBs.

	Log serum lipid HPCBs								
	Simple regression			Multiple regression			Step regression		
		Confid. limits			Confid. limits			Confid. limits	
Dependent variable[a]	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95
1976									
Log triglycerides	−0.02	−0.10	0.06	−0.07	−0.17	0.03	−0.08	−0.17	0.02
Cholesterol	2.68	−17.8	23.2	−11.1	−35.3	13.1	−11.5	−35.6	12.6
Log SGPT	−0.01	−0.08	0.06	0.03	−0.04	0.11	0.03	−0.04	0.10
Log GGTP	0.06	−0.04	0.16	0.09	−0.02	0.21	0.11*	0.002	0.21
Log alk. phos.	0.04	−0.02	0.09	0.02	−0.04	0.09	0.03	−0.03	0.09
Log total bilirubin	−0.08*	−0.15	−0.01	−0.12*	−0.21	−0.03	−0.11*	−0.19	−0.02
Direct bilirubin	−0.02	−0.05	0.005	−0.04*	−0.07	−0.001	−0.03*	−0.07	−0.002
Log total protein	−0.005	−0.02	0.01	−0.01	−0.03	0.01	−0.015*	−0.03	−0.003
Log albumin	−0.01	−0.02	0.002	−0.01	−0.03	0.002	−0.014*	−0.028	−0.001
Log BUN	0.03	−0.01	0.07	0.003	−0.05	0.05	0.003	−0.05	0.05
Creatinine	−0.05	−0.1	0.03	−0.10*	−0.18	−0.01	−0.09*	−0.18	−0.01
Log B/C ratio	0.05*	0.002	0.09	0.04	−0.02	0.09	0.04	−0.01	0.09
Iron	−15.2*	−28.1	−2.21	−13.1	−29.9	3.77	−13.2	−28.2	1.74
RBC	−0.13	−0.28	0.03	−0.12	−0.28	0.03	−0.15*	−0.29	−0.02
WBC	0.97*	0.35	1.59	1.20*	0.39	2.01	0.98*	0.26	1.69
Lymphocytes	0.30	−0.02	0.62	0.58*	0.14	1.02	0.36	−0.02	0.74
% Monocytes	−0.87	−1.77	0.02	−1.45*	−2.64	−0.60	−1.61*	−2.63	−0.59
1979									
Log triglycerides	0.11*	0.03	0.20	0.04	−0.06	0.13	0.04	−0.06	0.13
Cholesterol	25.3*	6.72	43.9	2.06	−20.1	24.2	2.19	−19.6	24.0
Log GGTP	0.09	−0.01	0.19	0.02	−0.09	0.13	0.02	−0.09	0.13
Log alk. phos.	0.05*	0.003	0.10	0.03	−0.03	0.08	0.03	−0.01	0.08
Direct bilirubin	−0.02	−0.05	0.004	−0.02	−0.06	0.01	−0.03*	−0.06	−0.002
Log blood glucose	0.04*	0.02	0.06	0.02	−0.01	0.04	0.02	−0.005	0.04
Globulin	0.14	−0.02	0.31	−0.004	−0.19	0.18	−0.004	−0.19	0.18
Log A/G ratio	−0.02	−0.04	0.01	0.001	−0.03	0.04	0.001	−0.03	0.04
Log BUN	0.08*	0.03	0.12	0.04	−0.01	0.08	0.04	−0.003	0.09
Log B/C ratio	0.05*	0.01	0.10	0.02	−0.03	0.08	0.02	−0.03	0.08
Monocytes	0.10*	0.03	0.18	0.12*	0.03	0.22	0.11*	0.03	0.19
% Monocytes	1.48*	0.55	2.41	1.56*	0.44	2.69	1.42*	0.48	2.36

[a]See Table 6 footnotes.

cytes. Similar selections, reflecting similar co linearities, occurred in the cases of phosphate (with LPCB) and creatinine (with HPCB). Smoking was a significant confounding variable in the cases of direct bilirubin, WBCs, and phosphate.

In 1979 strong positive associations were found between all measures of exposure to PCB (but not DDE) and the absolute and relative monocyte levels. The bilirubins did not replace PCBs in the step regressions, but smoking was a significant confounder. The positive associations of cholesterol and serum sodium with the relative exposure estimate in 1976 and the negative association of log serum lipid DDE with serum iron in 1979 appeared to be singular findings.

The 1530 regressions used to generate the data shown in Tables 6–9 showed at least one significant association (5% level) with one measure of exposure in one of the regressions for 26 of the 42 clinical variables. The incidence of significant associations with the clinical variables was positively influenced by the number of independent variables included in the regressions. The independent variables used in Tables 6–9 regressions all showed multiple associations with the clinical laboratory parameters. This group of independent variables did not, however, include measures of alcohol consumption or socioeconomic status, both of which have been used in other studies (*21,22*). The data available indicates that there can be important colinearities among the dependent variables. Because of the uncertainties presented by chance associations, unused or unidentified confounders, and colinearities among variables we have focussed our interpretations upon those associations that were seen consistently in the step regressions against log serum lipid PCBs, but not in the corres ponding regressions against log DDE.

The mean $\hat{\beta}_1$ coefficients of Tables 6–9 express the best estimates of the dependence of the clinical laboratory variables on log PCB, and their 95% confidence limits indicate the uncertainties of these estimates. For associations observed to be statistically significant we have multiplied the lower and upper $\hat{\beta}_1$ confidence limit values by the observed range of log PCBs in order to determine whether the product resulted in values for the laboratory variables outside the normal expected

Table 7C. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum HPCB (1254), as determined by three regression procedures: independent variables.

	Independent variables[a]								
	Partial r								
Dependent variable	Age	Sex	SPG	BMI	DS	SC	JS	FNF	Log $(HPCB)_{SL}$
1976									
Log triglycerides	0.20	–0.22	–0.15	0.28	0.26		X		
Cholesterol	0.35			0.20			X		
Log SGPT		–0.29		0.37			X		
Log GGTP		–0.18		0.19			X	0.28	0.16
Log alk. phos.					0.14		X		
Log total bilirubin			0.21		–0.17		X	0.15	–0.20
Direct bilirubin		–0.17				–0.17	X	0.19	–0.17
Log total protein		–0.16				–0.17	X		–0.19
Log albumin		–0.27			–0.16		X		–0.17
Log BUN	0.16		0.34	0.19			X		
Creatinine	0.19	–0.40	0.23				X		–0.17
Log B/C ratio			0.17				X		
Iron			0.20	–0.15			X		
RBC		–0.59					X		0.18
WBC						0.29	X		0.21
Lymphocytes							X		0.16
% Monocytes							X	–0.27	–0.27
1979									
Log triglycerides	0.21			0.40				X	
Cholesterol	0.35			0.19				X	
Log GGTP	0.18	–0.28	0.19	0.23				X	
Log alk. phos.				0.14				X	
Direct bilirubin		–0.16				–0.15		X	–0.14
Log blood glucose	0.29		0.16		0.38			X	
Globulin				0.27			0.15	X	
Log A/G ratio	–0.21			–0.24			–0.16	X	
Log BUN	0.20		0.34	0.23				X	
Log B/C ratio	0.26		0.30					X	
Monocytes						0.19	–0.21	X	0.21
% Monocytes							–0.24	X	0.23

ranges. For these criteria, the only variables having statistical significance outside the normal ranges were the 1976 percent lymphocytes and the 1979 percent monocytes. For all other parameters the observed associations with log PCB levels reflected variations within the normal laboratory ranges.

Figures 3 and 4 show partial residual plots for two laboratory variables, log total bilirubin in 1976 and the percent monocytes in 1979, as calculated at the end of the stepwise regression, plotted against log serum lipid LPCB. They represent plots of a predictor variable against the dependent variable with the "effects" of all other predictor variables statistically removed (*33*). For the log total bilirubin data of Figure 3, the partial r was –0.22 (p = 0.01) and β_1 about –0.09 log units/decade of LPCB (Table 6). For 2.2 decades of LPCB, the range of the $\hat{\beta}_1$ product was –0.07 to –0.33 (mean = -10.2). When controlled for confounders, all study data (Fig. 3) fell between 0.1 and 1.0 mg/dL (mean = 0.3 mg/dL), which is within the normal range (Table 1).

As shown in Figure 4 the 1979 percent monocyte data were more tightly grouped (partial r = 0.28), and the $\hat{\beta}_1$ estimate was 1.38%/LPCB decade. For the 2.5 decade range of LPCB, the range of $\hat{\beta}_1$ products corresponded to an increment in percent monocytes of 1.8 to 6.2% (mean = 3.5%). Inspection of the histogram along the monocyte axis indicates a range of percent monocytes from 5.5 to 15.5% (mean = 10.5%) rather than the normal range of 0 to 8% (Table 1).

Discussion

PCB Levels in the Study Population

This investigation has shown that certain former operations in capacitor manufacturing presented high exposures to PCBs, particularly during the 1954–1977 period when the more volatile lower PCBs (Aroclor 1242 and 1016) were in extensive use. During this period PCB air levels in the affected working areas were probably at least the 690 μg/m observed in 1975, accompanied by extensive dermal contact as well.

In our study population, selected so as to include those working in or near the plant PCB exposure zone, the mean serum lipid LPCB level in 1976 (Table 3) was estimated to be 93 ppm (5–95% range, 15–560 ppm), adjusted for a factor of 10 analytical error. This serum lipid value corresponded to a mean body burden of 2.0 g (0.3–12.3 g) for the population mean body weight of 77 kg (22 kg of fat). These retained LPCBs were com-

Table 8A. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum *p, p'*-DDE, as determined by three regression procedures: log gross serum DDE.[a]

	Log gross serum DDE									
		Simple regression			Multiple regression			Step regression		
			Confid. limits			Confid. limits			Confid. limits	
Dependent variable[a]	$\bar{x}$	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95
1976										
Log triglycerides	2.13	0.08*	0.05	0.11	0.07*	0.03	0.10	0.08*	0.05	0.11
Cholesterol	251.3	12.7*	5.05	20.4	8.37	–0.13	16.9	10.1*	2.00	18.2
Log GGTP	1.09	0.04*	0.002	0.08	0.02	–0.02	0.06	0.03	–0.01	0.07
Log alk. phos.	1.42	0.04*	0.02	0.06	0.04*	0.02	0.07	0.04*	0.02	0.07
Log total protein	0.86	0.002	–0.002	0.006	0.009	–0.001	0.009	0.005*	0.001	0.009
WBC	7.02	0.33*	0.08	0.57	0.41*	0.12	0.70	0.35*	0.08	0.62
Lymphocytes	2.33	0.23*	0.11	0.34	0.30*	0.16	0.44	0.26*	0.13	0.40
% Lymphocytes	33.8	1.42	–0.11	2.95	2.04*	0.17	3.91	1.37	–0.38	3.11
% Monocytes	4.38	–0.36*	–0.70	–0.02	–0.40	–0.80	0.004	–0.46*	–0.83	–0.08
1979										
Log triglycerides	2.16	0.31*	0.21	0.41	0.28*	0.18	0.38	0.30*	0.21	0.39
Cholesterol	238.2	48.6*	25.8	71.5	32.6*	7.56	57.6	30.4*	6.07	54.7
Log alk. phos.	1.47	0.09*	0.04	0.15	0.09*	0.03	0.15	0.10*	0.04	0.16
Log total protein	0.86	0.01	–0.004	0.02	0.01*	0.001	0.03	0.01	–0.001	0.03
Log albumin	0.64	–0.02*	–0.03	–0.01	–0.006	–0.02	0.01	–0.006	–0.02	0.01
Globulin	2.92	0.30*	0.10	0.50	0.23*	0.02	0.44	0.24*	0.04	0.43
Log A/G ratio	0.18	–0.06*	–0.09	–0.02	–0.03	–0.07	0.01	–0.03	–0.07	0.01
Serum Ca	9.67	–0.02	–0.22	0.18	–0.10	–0.33	0.13	–0.08	–0.29	0.13
Serum Iron	108.6	–10.3	–24.3	3.68	–10.0	–25.5	5.50	–8.81	–22.9	5.30

[a]See Table 6 footnotes.

Table 8B. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum *p, p'*-DDE, as determined by three regression procedures: log serum lipid DDE.[a]

	Simple regression			Multiple regression			Step regression		
		Confid. limits			Confid. limits			Confid. limits	
Dependent variable[a]	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95
1976									
Log triglycerides									
Cholesterol									
Log GGTP									
Log alk. phos.									
Log total protein									
WBC									
Lymphocytes									
% Lymphocytes									
% Monocytes									
1979									
Log triglycerides	0.08	–0.04	0.20	0.06	–0.06	0.18	0.07	–0.04	0.19
Cholesterol	–3.10	–29.7	23.5	–20.8	–47.9	6.34	–21.6	–47.9	4.76
Log alk. phos.	0.07*	0.002	0.13	0.07	–0.002	0.13	0.08*	0.01	0.14
Log total protein	–0.003	–0.02	0.01	0.001	–0.01	0.02	0.001	–0.01	0.02
Log albumin	–0.02*	–0.04	–0.004	–0.01	–0.03	0.008	–0.01	–0.03	0.007
Globulin	0.15	–0.08	0.38	0.07	–0.16	0.30	0.08	–0.15	0.30
Log A/G ratio	–0.04	–0.08	0.002	–0.01	–0.06	0.03	–0.02	–0.06	0.03
Serum Ca	–0.17	–0.39	0.06	–0.24*	–0.48	–0.001	–0.22	–0.45	0.008
Serum Iron	–19.7*	–35.0	–4.43	–19.6*	–36.0	–3.20	–17.5*	–33.1	–2.00

[a]See Table 6 footnotes.

posed almost entirely of PCB isomers with gas chromatographic peaks having retention times (relative to DDE = 100) of 37, 71 and 84 (*27,34*), the other LPCB components of Aroclors 1016 and 1242 being much more readily metabolized in the human. Regression studies of serum lipid LPCB values with length of service indicated no significant statistical association, so that steady state levels appeared to have been reached within the first few years of employment. Thus, the levels of retained LPCBs observed in 1976 could have been rep-

Table 8C. Regression and correlation coefficients for 1976 and 1979 clinical variables showing at least one significant association with a measure of serum *p, p'*-DDE, as determined by three regression procedures: independent variables.

	Independent variables								
	Partial *r*								
Dependent variable	Age	Sex	SPG	BMI	DS	SC	JS	FNF	Log (DDE)
1976									
Log triglycerides				0.29	0.27				0.38
Cholesterol	0.31			0.20					0.19
Log GGTP		–0.19		0.17				0.26	
Log alk. phos.									0.31
Log total protein	–0.23					–0.17			0.16
WBC						0.25			0.20
Lymphocytes					–0.16				0.33
% Lymphocytes									
% Monocytes						0.16		–0.25	–0.21
1979									
Log triglycerides	0.21			0.40					
Cholesterol	0.35			0.19					
Log alk. phos.				0.14					0.18
Log total protein	–0.14			0.23		–0.19			
Log albumin	–0.21						–0.15		
Globulin				0.27			0.15		
Log A/G ratio	–0.21			–0.24			–0.16		
Serum Ca					0.15				
Serum Iron		–0.20							–0.17

[a]See Table 6 footnotes.

Table 9. Regression coefficients for 1976 and 1979 clinical variables showing at least one significant association with a estimate of relative exposure to PCB in 1976 (EXE), as determined by three regression procedures.[a]

			Simple regression			Multiple regression			Step regression			
				Confid. limits			Confid. limits			Confid. limits		Partial
Dependent variable[a]	*N*	$\bar{x}$	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	$\hat{\beta}_1$	5	95	(EXE)
1976												
Cholesterol	193	251.3	7.86	–1.33	17.0	9.62	–0.16	19.4	10.5*	1.26	19.7	0.18
Log GGTP	192	1.09	0.03	–0.01	0.10	0.06*	0.01	0.10	0.06*	0.01	0.10	0.20
Log total bilirubin	194	–0.34	–0.04*	–0.08	–0.01	–0.05*	–0.09	–0.02	–0.05*	–0.08	–0.01	–0.20
Direct bilirubin	193	0.15	–0.01	–0.02	0.002	–0.02*	–0.03	–0.001	–0.02*	–0.03	–0.001	–0.17
Log blood glucose	193	2.01	–0.01*	–0.02	–0.004	–0.01	–0.02	0.003	–0.01	–0.02	0.001	
Log A/G ratio	191	0.21	0.02*	0.001	0.03	0.01	–0.005	0.03	0.01	–0.004	0.03	
Serum Na	192	139.5	–0.10	–0.55	0.34	–0.54*	–1.02	–0.06	–0.53*	–0.98	–0.08	–0.18
Serum iron	192	112.1	–6.35*	–12.3	–0.36	–3.89	–10.8	3.00	–4.23	–10.8	2.30	
Lymphocytes	153	2.33	0.14	–0.01	0.28	0.19*	0.02	0.36	0.15	–0.01	0.31	
Monocytes	153	0.31	–0.01	–0.05	0.02	–0.01	–0.04	0.03	–0.01	–0.04	0.03	
% Monocytes	153	4.38	–0.34	–0.74	0.06	–0.35	–0.82	0.11	–0.46*	–0.90	–0.02	
1979												
Cholesterol	174	238.5	4.72	–4.09	13.5	4.83	–3.91	13.6	4.94	–3.43	13.3	
Log GGTP	174	1.20	0.01	–0.03	0.06	0.02	–0.02	0.07	0.02	–0.02	0.07	
Log total bilirubin	174	–0.22	–0.02	–0.05	0.01	–0.03*	–0.06	–0.001	–0.03*	–0.06	–0.004	–0.18
Direct bilirubin	174	0.14	–0.01	–0.02	0.01	–0.01	–0.03	0.003	–0.01	–0.03	0.001	
Log blood glucose	174	2.00	–0.004	–0.01	0.01	–0.001	–0.01	0.01	–0.002	–0.01	0.01	
Log A/G ratio	174	0.18	–0.003	–0.02	0.01	–0.006	–0.02	0.07	–0.005	–0.02	0.01	
Na	174	139.4	–0.05	–0.46	0.37	–0.02	–0.43	0.40	–0.02	–0.43	0.39	
Iron	172	108.5	–0.96	–6.17	4.25	–0.78	–6.17	4.62	–0.78	–6.17	4.62	
Lymphocytes	175	2.09	–0.03	–0.14	0.08	–0.03	–0.16	0.09	–0.03	–0.14	0.09	
Monocytes	175	0.48	0.04*	0.001	0.08	0.04*	0.004	0.08	0.05*	0.01	0.08	0.18
% Monocytes	175	6.9	0.58	0.14	1.03	0.61*	0.17	1.05	0.64*	0.20	1.07	0.22

[a]See footnotes to Table 6.

resentative of those present throughout the Aroclor 1242 and 1016 periods of use.

The mean serum HPCB level in 1976 was estimated to be 8 ppm (2–34 ppm), corresponding to a mean body burden of 0.2 g (0.04–0.7 g). These HPCBs were composed primarily of penta- and hexachlorobiphenyl isomers (*27,34,35*) resulting either from exposures to Aroclor 1242 (which contained a few percent of the lower

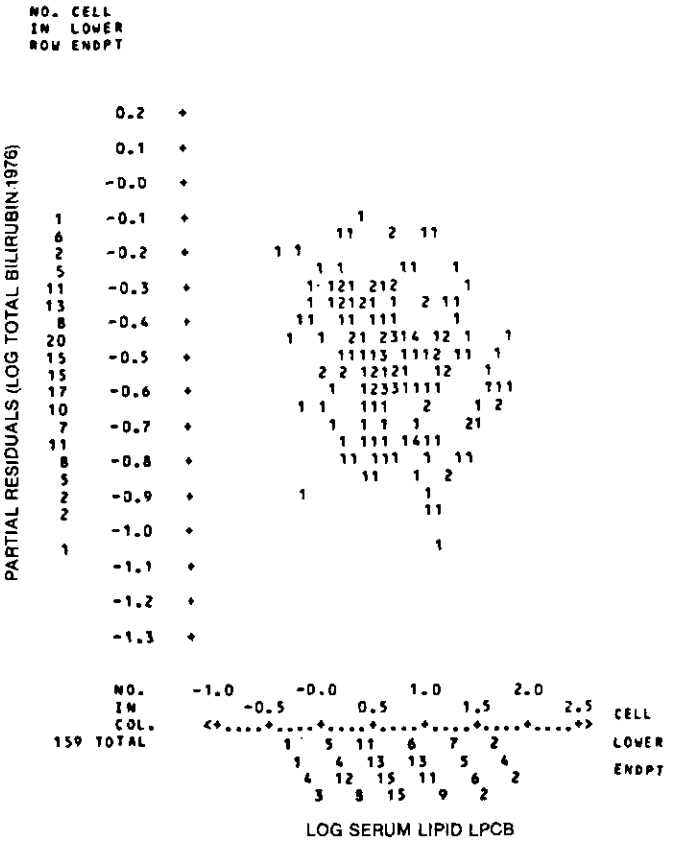

FIGURE 3. Partial residuals for log total bilirubin in 1976 following final step regression (Table 6) vs. log serum lipid LPCBs. Histograms are shown along each axis. The number of values in the cells are given by the numerals.

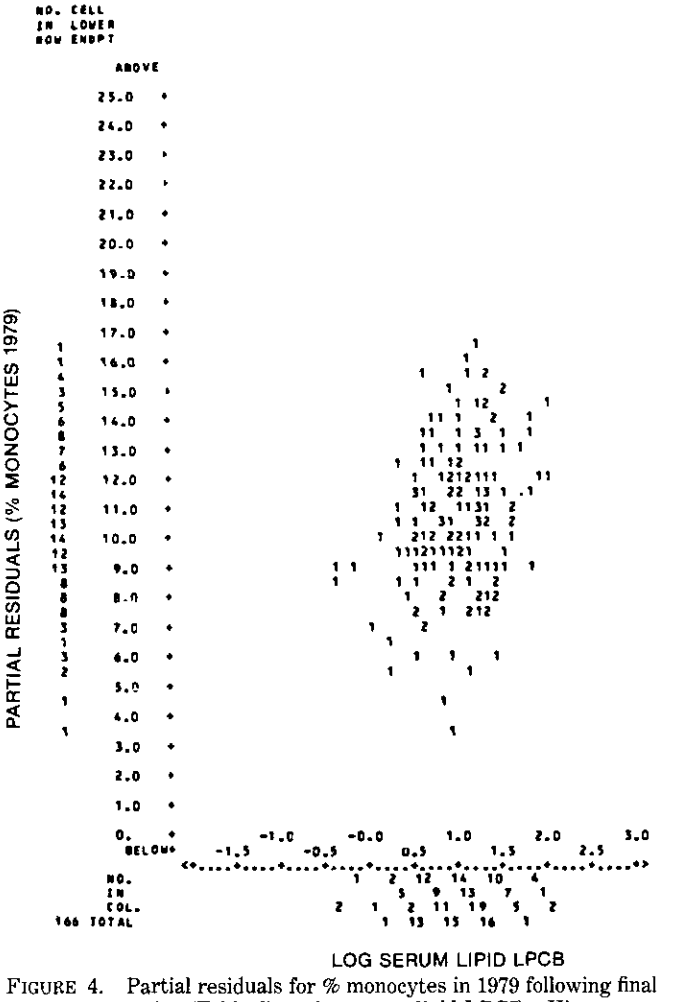

FIGURE 4. Partial residuals for % monocytes in 1979 following final step regression (Table 6) vs. log serum lipid LPCBs. Histograms are shown along each axis. The number of values in the cells are given by the numerals.

HPCBs), or from earlier exposures to Aroclor 1254. Their levels were significantly associated with length of service, so that the upper 5% of HPCB levels observed in 1976 (long service, directly exposed workers) may be representative of the exposed population in 1954, at the end of the period when Aroclor 1254 was the major dielectric fluid used.

The Aroclor 1242 values reported to us by the analyst were approximately 4 times the calculated LPCB values (Table 3). We have shown elsewhere that the minimum initial concentrations of Aroclors 1016 plus 1242 required to account for the most persistent LPCB peaks were about 7.5 times the residual LPCB levels (*27*). Thus, the minimal LPCB uptake by the study population may be estimated as 15 g (2.5–92 g). This estimated uptake is a minimum since even the most persistent LPCB peaks have a finite clearance rate (unpublished observations). The longer service employees could have absorbed several times this minimal PCB uptake, but until better data on PCB clearance becomes available, actual cumulative LPCB uptakes cannot be estimated more precisely.

The mean LPCB body burden in 1979 (29 months after discontinuance of major exposure) was estimated as 0.4 g (0.7–2.0 g), indicating a clearance of 80%. The serum lipid HPCB means in 1976 and 1979 were within the error band of the analytical technique (*27*) and a conclusion of significant clearance is probably unwarranted. Chen (*35*) has reported clearance rates for various pentachlorobiphenyl isomers in Taiwanese Yusho patients that appear to be at least 10-fold greater than we observed in capacitor workers (*27*); however, such clearance might be related to P-448 oxidase induction by PCDFs in the Yusho patients. Although these estimates of PCB fat levels and uptakes are only approximate, they serve to define the dose ranges within which the observed responses can be ascribed.

PCB Effects on Serum Lipids and Serum Enzymes

Previous investigators have reported statistical associations between log gross serum levels of PCBs and the serum levels of triglycerides, total cholesterol and certain serum enzymes. Our findings were in general agreement with such reports. We found significant associations of log serum triglycerides and total choles-

terol with every measure of log gross serum PCBs and DDE in the final step regressions. Similar associations were found for log GGTP, and in some cases for log SGPT, with log gross serum PCBs, and for log alkaline phosphatase with log gross serum DDE.

It is now evident, however, that such associations arise because the level of PCBs in the serum is itself determined by that of the serum lipids (*23,24*). When the PCB concentrations were expressed as levels in serum lipids, which would be expected to correlate with the pharmacological activities (*24,25*), all the associations between serum lipids or enzymes and log gross serum LPCB, HPCB or DDE disappeared except for those between log GGTP and log PCBs, and between log alkaline phosphatase and log DDE. Similarly, Chase et al. (*13*), who reported associations with gross serum PCBs, found no significant correlation between either serum triglycerides or SGOT and the adipose tissue fat biopsy PCB levels. Although elevated levels of serum triglycerides, total cholesterol and SGPT were found in our study population (Table 3), serum GGTP levels were generally in the normal range, and the regression studies indicated stronger associations with obesity (body mass index).

PCB Effects on Microsomal Enzymes

Elevated serum GGTP levels have been prominently mentioned in the literature as an index of microsomal enzyme induction in the human (*36–40*). Recent studies (*41*), however, have in part disputed this conclusion. In their review of environmental hepatic injury, Popper et al. (*42*) found only meager evidence of substantiated chronic hepatic effects. They concluded that conventional liver function tests were of limited value in detecting hepatic abnormalities and that the evidence so far indicates that too many other processes influence GGTP activity in man to make it a useful index of induction. The clinical implications of elevated GGTP levels in man are reviewed by Guzelian elsewhere in this symposium.

However, the interpretation of the relationship between serum GGTP and serum lipid PCBs as evidence of microsomal enzyme induction is strengthened by the finding of strong inverse statistical associations between both direct and total bilirubin levels and serum lipid PCBs in 1976 during the period of active PCB exposure. A weak residual association between serum lipid HPCB and direct bilirubin (partial $r = 0.14$) was found in 1979 when the mean total bilirubin (mostly unconjugated) had risen from 0.46 to 0.61 mg/dL without change in the mean direct bilirubin (conjugated form) (Table 1).

Since the original observations of Yaffe et al. (*43*) on the therapeutic use of phenobarbital to enhance glucuronide-conjugating capacity in infant hyperbilirubinemia, a substantial literature has developed linking drugs (*36,44*) and other xenobiotics (*45,46*) to induction of microsomal enzymes, including enhanced glucuronyl transferase, resulting in increased conjugation and accelerated hepatic elimination of bilirubin. D-Glucaric acid is the main excretory product of the glucuronic acid conjugation pathway and its urinary level also has been advocated as a measure of enzyme induction (*47–50*). Drugs and chemicals inducing microsomal enzymes are often metabolized by the induced oxidases (*32*), and it appears likely that such induction would accelerate clearance of PCBs as well as bilirubin (*49,51*).

Hirayama et al. (*52*) reported serum total bilirubin levels of 0.87 ± 0.33 mg/dL in 257 normal controls and 0.48 ± 0.26 mg/dL in 121 Yusho patients, indicating a 46% decrease in the latter. However, the observations were made at a time when the PCB levels had declined to background values, so that the pharmacologically active agents present were probably the PCDFs. Induction of glucuronyl transferase by Aroclor 1242 and 1016 has been reported in rats (*16,53*), as has also that of demethylases (*16,53*), aniline hydroxylase, (*53*) and cytochrome P-450 (*16,53*), but not that of the P-448 cytochrome (*16*).

Burse et al. (*54*) have shown that rats fed 100 ppm of Aroclor 1242 or 1016 (3.9–6.6 and 3.5–6.9 mg/kg/day) reach equilibrium adipose tissue fat concentrations of 35 to 143 or 69 to 236 ppm, respectively, at 6 months, levels in the range of those observed in this study (Table 3). Similar levels in rats were also reported by Goldstein et al. (*53*), who found a 3-and 12-fold increase in liver glucuronyl transferase activity with Aroclors 1016 and 1242, respectively.

The most compelling evidence for microsomal enzyme induction in man is a response to drug administration (*42*). In 1977, Alvares et al. (*16*) reported antipyrene half-times reduced 31% over matched controls in five capacitor workers with PCB exposures of 4 to 16 years drawn from the same plant population as the present study. The effect was statistically significant ($p<0.005$) and the half-times were significantly less than the average values of much larger groups of normal healthy subjects. The statistical associations of the present study, taken together with the findings of Alvares et al., appear to indicate induction of the microsomal enzymes GGTP, glucuronyl transferase, and P-450 oxidase in the study population during active exposure in 1976. The enzyme inductions appeared to be smaller than those in rats carrying similar levels of lipid LPCBs and to have become virtually undetectable by 1979.

PCB Effects on Hematological Parameters

The findings of significant associations between log serum lipid PCBs and some hematolotical variables was unexpected because Maroni et al. (*14*) reported normal hematology including WBCs and differentials and no abnormal reports in occupationally exposed PCB workers have been mentioned by others (*11–13,15,17*). In 1976 the clinical reports (Table 2) suggested a slight decline in PMNs with some increases in lymphocytes, monocytes and eosinophils, and normal values for RBCs, hemoglobins and hematocrits.

Interpretations of these data are difficult because of the shared associations with DDE and the colinearities with either total or direct bilirubin or both. For the associations with log total bilirubin, the partial r values were: RBC, +0.19; lymphocytes −0.22; and creatinine, 0.24; for direct bilirubin, they were: phosphate, −0.18; and creatinine, 0.23. We tend to the interpretation that these variables are correlated with the enzyme induction process.

In 1979, although both the monocytes and eosinophils were only marginally elevated in the study population based on clinical reports (Tables 1 and 2), the statistical association of serum PCB levels and the monocyte counts was strong.

Because of the absence of a monocytosis in 1976, its lack of association with either DDE or total or direct bilirubin in 1979, and its absence among retirees in 1979, we hypothesized that the effect might be related to a new exposure in the workplace, perhaps to the PCB-substitute dielectric. However, we recently studied 54 workers with no prior PCB exposure who were currently exposed to the substitute and found no monocyte elevations. Although a number of solvents were in use in the environment in 1979, the monocytosis was mild compared to that observed by Minot and Smith (*55*) in the case of tetrachlorethane exposure, where the monocyte levels were elevated 20 to 40%. The effect of the change from the manual (1976) to automated differential analysis (1979) is unknown. We have also hypothesized that the monocytosis observed in 1979 might be related to the increased incidence of chronic obstructive lung disease, heavy smoking or concurrent respiratory infections. We are currently studying the associations between the spirometric variables (FVC, FEV, FEV/FVC) and the hematological parameters in the study population and are restudying the entire population, which should cast further light on any such relationships.

Clinical Consequences of PCB Exposure

These findings differ from those of most other recent studies of environmentally or occupationally exposed populations in offering evidence of microsomal enzyme induction, which is consistent with the extensive LPCB clearance also observed in these highly exposed workers. The evidence is statistical in nature and the associated parameters remained within their normal clinical ranges, except possibly for the lymphocytes in 1976 and the monocytes in 1979. The effects were therefore physiological rather than pathological and appeared to subside following the cessation of PCB use. The long-term consequences of such enzyme induction are obscure (*42*).

The present clinical health of the study population appears to meet community medical standards. Despite the prevalence of cardiovascular risk factors (obesity, elevated cholesterol levels, smoking, etc.) the mortality experience has been normal. The paucity of clinical abnormalities is consistent with laboratory studies in rats involving chronic administration of Aroclor 1242 and 1016, producing tissue fat levels comparable to the serum lipid PCB levels observed here. Such studies (*54*) have shown no overt symptoms of clinical poisoning and no pathological evidence of liver damage. The production of serious liver damage in rats (*56*) requires the use of a largely nonmetabolizable PCB, such as Aroclor 1260, at a cumulative dose of 2.5 g/kg, which would result in tissue lipid HPCB levels above 10,000 ppm, as compared to those in our study population of 8 ppm in 1976 and 5 to 6 ppm in 1979. It is evident, therefore, why the serious hepatic effects in the test rat could not be observed in man.

The authors are grateful for the technical assistance of Sheila Grady in data collation, Barbara Sack, Ronald Chapman and Barbara Moreen in statistical analysis support, and Helen Walton in manuscript preparation. We particularly appreciate the advice and counsel of Gerald Hahn, Carolyn Morgan and John Bergeron in statistics.

REFERENCES

1. Versar, Inc. PCBs in the United States: Industrial Use and Environmental Distribution. Report under EPA Contract No. 68013259. U.S. Dept. of Commerce, NTIS PB 252012, Feb. 25, 1976.
2. Drinker, C. K., Warren, M. F., and Bennett, G. A. The problems of possible systemic effects from certain chlorinated hydrocarbons. J. Ind. Hyg. Toxicol. 19: 283–299 (1937).
3. Treon, J. F., Cleveland, F. P., Cappel, J. W., and Atchley, R. W. The toxicity of the vapors of Aroclor 1242 and 1254. Am. Ind. Hyg. Assoc. Quart. 17: 204–213 (1956).
4. Elkins, H. E. Chemistry of Industrial Toxicology. Wiley, New York, 1950, p. 149.
5. Clark, F. M. Insulating Materials for Design and Engineering Practice. Wiley, New York, 1962, p. 194.
6. Masuda, Y., Kuroki, H., Yamaryo, T., Haraguchi, K., Kuratsune, M., and Hsu, S. T. Comparison of causal agents in Taiwan and Fukuoka PCB poisoning. Chemosphere 11: 199–206 (1982).
7. Buser, H. R., Bosshardt, H. P., and Rappe, C. Formation of polychlorinated dibenzofurans (PCDFs) from the pyrolysis of PCBs. Chemosphere 1: 109–119 (1978).
8. Hasegawa, H., Sato, M., and Tsurata, H. PCB concentration in the blood of workers handling PCB. Occup. Health 10: 50–55 (1972).
9. Kitamura, M., Tsukamoto, T., Sumino, K., Hayakawa, K., Shibita, T., and Hirano, I. The PCB levels in the blood of workers employed in a condenser factory. Japan. J. Ind. Health 47: 354–355 (1973).
10. Hara, I., Herada, H., Kimura, S., Endo, T., and Kawomo, K. Follow-up health examination in an electrical condenser factory after cessation of PCB usage (1st Report). Japan. J. Ind. Health 16: 365–366 (1974).
11. Karppanen, E., and Kolho, L. The concentration of PCB in human blood and adipose tissue in three different research groups. In: PCB Conference II. National Swedish Environmental Protection Board Publications, Stockholm, 1973, pp. 124–128.
12. Ouw, K. H., Simpson, G. R., and Siyali, D. S. The use and health effects of Aroclor 1242, a polychlorinated biphenyl, in an electrical industry. Arch. Environ. Health 31: 189–194 (1976).
13. Chase, K. H., Wong, O., Thomas, D., Berney, B. W., and Simon, R. K. Clinical and metabolic abnormalities associated with occupational exposure to polychlorinated biphenyls (PCBs). J. Occup. Med. 24: 109–114 (1982).
14. Maroni, M., Columbi, A., Arbosti, G., Cantoni, S., and Foa, V. Occupational exposure to polychlorinated biphenyls in electrical workers. II. Health Effects. Brit. J. Ind. Med. 38: 55–60 (1981).
15. Smith, A. B., Schloemer, J., Lowry, L. K., Smallwood, A. W., Ligo, R. N., Tanaka, S., Stringer, W., Jones, M., Hervin, R.,

and Glueck, C. J. Metabolic and health consequences of occupational exposure to polychlorinated biphenyls (PCBs). Brit. J. Ind. Med. 39: 361–369 (1982).
16. Alvares, A. P., Fischbein, A., Anderson, K. E., and Kappas, A. Alterations in drug metabolism in workers exposed to poly chlorinated biphenyls. Clin. Pharmacol. Therap. 22: 140–146 (1977).
17. Fischbein, A., Wolff, M. S., Lilis, R., Thornton, J., and Selikoff, I. J. Clinical findings among PCB-exposed capacitor manufactur ing workers. Ann. N.Y. Acad. Sci. 320: 703–715 (1979).
18. Warshaw, R., Fischbein, A., Thornton, J., Miller, A., and Selikoff, I. J. Decrease in vital capacity in PCB-exposed workers in a capacitor manufacturing facility. Ann. N.Y. Acad. Sci. 320: 277–283 (1979).
19. Brown, D. P., and Jones, M. Mortality and industrial hygiene study of workers exposed to polychlorinated biphenyls. Arch. Environ. Health 36: 120–128 (1981).
20. Humphrey, H. E. B. Evaluation of humans exposed to halogenated biphenyls. Am. Chem. Soc. Div. Environ. Chem. Preprints 20 (No. 2): 272 (1980).
21. Baker, E. L., Jr., Landrigan, P. J., Gluck, C. J., Zack, M. M. Jr., Liddle, J. A., Burse, V. W., Houseworth, W. J., and Needham, L. L. Metabolic consequences of exposure to polychlorinated biphenyls in sewage sludge. Am. J. Epidemiol. 112: 553–563 (1980).
22. Kreiss, K., Zack, M. M., Kimbrough, R. D., Needham, L. L., Smrek, A. L., and Jones, B. T. Association of blood pressure and polychlorinated biphenyl levels. J. Am. Med. Assoc. 245: 2505–2509 (1981).
23. Morgan, D. P., and Roan, C. C. Chlorinated hydrocarbon pesticide residue in human tissues. Arch. Environ. Health 20: 452–457, 1970.
24. Brown, J. F., Jr. Polychlorinated biphenyl (PCB) partitioning between adipose tissue and serum. Bull. Environ. Contam. Toxicol., 33: 277–280.
25. Ferguson, J. The use of chemical potentials as indices of toxicity. Proc. Roy. Soc. (London) B127: 387–403 (1939).
26. Henry, R. J. Clinical Chemistry Principles and Technics. Harper and Row, New York, 1968, pp. 836–844.
27. Lawton, R. W., Brown, J. F., Jr., Ross, M. R., and Feingold, J. Comparability and precision of serum PCB measurements. Arch. Environ. Health, in press.
28. Newson, W. B., Morgan, C. B., and Caporal, P. 1983 STATPAC simplified—a short introduction to how to run STATPAC, a general statistical package for data analysis. General Electric Corporate R&D Report No. 83CRD146, Schenectady, NY, 1983.
29. Dixon, W. J., and Brown, M. G. Biomedical Computing Programs, P. Series. University of California Press, Berkeley, 1977.
30. Metropolitan Life Insurance Company. New weight standards for men and women. Statistical Bull. 40: 1–4 (Nov.-Dec. 1959).
31. Anonymous. Plasma lipid distributions in selected North Ameri can populations: The Lipid Research Clinics Program Prevalence Study. Circulation 60: 427–439 (1979).
32. Conney, A. H. Pharmacological implications of microsomal enzyme induction. Pharmacol. Rev. 19: 317–366 (1967).
33. Larsen, W. A., and McCleary, S. J. The use of partial residual plots in regression analysis. Technometrics 14: 781–790 (1972).
34. Wolff, M. S., Thornton, J., Fischbein, A., Lilis, R., and Selikoff, I. J. Disposition of polychlorinated biphenyl congeners in occupationally exposed persons. Toxicol. Appl. Pharmacol. 62: 294–306 (1982).
35. Chen, P. H., Luo, M. L., Wong, C. K., and Chen, C. J. Comparative rates of elimination of some individual polychlo rinated biphenyls from the blood of PCB-poisoned patients in Taiwan. Food Chem. Toxicol. 20: 417–425 (1982).
36. Whitfield, J. B., Moss, D. W., Neale, G., Orme, M., and Breckenridge, A. Changes in plasma gamma-glutamyl transpeptidase activity associated with alterations in drug metabolism in man. Brit. Med. J. 1: 316–318 (1973).
37. Martin, P. J., Martin, J. V., and Goldberg, D. M. Gamma-glutamyl transpeptidase, triglycerides, and enzyme induction. Brit. Med. J. 1: 17–18 (1975).
38. Martin, J. V., and Martin, P. J. Enzyme induction as a possible cause of increased serum-triglycerides after oral contraceptives. Lancet i: 1107–1108 (1976).
39. Bartels, H., Hauck, W., and Vogel, I. Aminopyrine—an effective modifier of liver and serum gamma glutamyl transpeptidase. J. Pediatr. 86: 298–301 (1975).
40. Teschke, R., Brand, A., and Strohmeyer, G. Induction of hepatic microsomal gamma-glutamyltransferase activity following chronic alcohol consumption. Biochem. Biophys. Res. Commun. 75: 718–724 (1977).
41. Goldberg, D. M. The expanding role of microsomal enzyme induction, and its implications for clinical chemistry. Clin. Chem. 26: 691–699 (1980).
42. Popper, H., Gerber, M. A., Schaffner, F., and Selikoff, I. J. Environmental hepatic injury in man. In: Progress in Liver Disease, Vol. 7 (H. Popper and F. Schaffner, Eds.), Grune and Stratton, New York, 1982, pp. 605–638.
43. Yaffe, S. J., Levy, G., Matsuzawa, T., and Baliah, T. Enhancement of glucuronide-conjugating capacity in a hyperbilirubinemic infant due to apparent enzyme induction by phenobarbital. N.Engl. J. Med. 275: 1461–1466 (1966).
44. Kuntzman, R. Drugs and enzyme induction. In: Annual Review of Pharmacology, Vol. 9 (H. W. Elliott, W. C. Cutting and R. H. Dreisbach, Eds.), Annual Reviews Inc., Palo Alto, CA, 1969, pp. 21–36.
45. Juchu, M. R., Gram, T. E., and Fouts, J. R. Stimulation of hepatic microsomal drug-metabolizing enzyme systems in pri mates by DDT. Gastroenterology 51: 213–218 (1966).
46. Hunter, J., Maxwell, J. D., Stewart, D. A., Williams, R., Robinson, J., and Richardson, A. Increased hepatic microsomal enzyme activity from occupational exposure to certain organo chlorine pesticides. Nature 237: 399–401 (1972).
47. Marsh, C. A. Metabolism of D-glucuronolactone in mammalian systems. Identification of D-glucaric acid as a normal constituent of urine. Biochem. J. 86: 77–86 (1963).
48. Hunter, J., Maxwell, J. D., Stewart, D. A., and Williams, R. Urinary D-glucaric acid excretion and total liver content of cytochrome P-450 in guinea pigs: relationship during enzyme induction and following inhibition of protein synthesis. Biochem. Pharmacol. 22: 743–747 (1973).
49. Notten, W. R. F., and Henderson, P. T. The interaction of chemical compounds with the functional state of the liver. I. Alterations in the metabolism of xenobiotic compounds and D-glucuronic acid pathway. Int. Arch. Environ. Health 38: 197–207 (1977).
50. Notten, W. R. F., and Henderson, P. T. The interaction of chemical compounds with the functional state at the liver. II. Estimation of changes in D-glucaric acid synthesis as a method for diagnosing exposure to xenobiotics. Int. Arch. Environ. Health 38: 209–220 (1977).
51. Calabrese, E. J. Insufficient conjugate glucuronidation activity: a possible factor in polychlorinated biphenyl (PCB) toxicity. Med. Hypothesis 3: 162–165 (1977).
52. Hirayama, C., Okumura, M., Nagai, J., and Masuda, Y. Hypobilirubinemia in patients with polychlorinated biphenyls poisoning. Clin. Chim. Acta 55: 97–100 (1974).
53. Goldstein, J. A., Hickman, P., Burse, V. W., and Bergman, H. A comparative study of two polychlorinated biphenyl mixtures (Aroclors 1242 and 1016) containing 42% chlorine on the induction of hepatic porphyria and drug metabolizing enzymes. Toxicol. Appl. Pharmacol. 32: 461–473 (1975).
54. Burse, V. W., Kimbrough, R. D., Villanueva, E. C., Jennings, R. W., Linder, R. E., and Sovocool, G. W. Polychlorinated biphenyls. Storage, distribution, excretion, and recovery: liver morphology after prolonged dietary ingestion. Arch. Environ. Health 29: 301–307 (1974).
55. Minot, G. R., and Smith, L. W. The blood in tetrachlorethane poisoning. Arch. Int. Med. 28: 687–702 (1921).
56. Kimbrough, R. D., Squire, R. A., Linder, R. E., Strandberg, J. D., Montali, R. J., and Burse, V. W. Induction of liver tumors in Sherman strain female rats by polychlorinated biphenyl Aroclor 1260. J. Natl. Cancer Inst. 55: 1453–1459 (1975).