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Polychlorinated Biphenyl Exposure and Effects in Transformer Repair Workers

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Fifty-five present and past transformer repair workers exposed to polychlorinated biphenyls (PCBs) and 56 unexposed comparison workers were evaluated in a clinical-epidemiologic study. The groups were similar in most demographic variables. Adipose tissue lipid and serum PCBs concentrations were higher in current exposed workers (geometric means adipose 2.1 ppm, serum 12.2 ppb). Concentrations in comparison (0.6 ppm and 4.6 ppb) and previously exposed (0.83 ppm and 5.9 ppb) workers were lower. Statistically significant differences in serum albumin and lactic dehydrogenase, but not in other liver function tests, were seen between the exposed and comparison groups; however, after adjustment for confounding variables, no correlations were observed between liver function tests and either adipose or serum PCBs concentrations. Statistically significant correlation both before and after adjustment for confounding variables were seen with adipose PCBs and 24-hr urinary 17-hydroxycorticosteroid excretion and with serum PCBs and serum γ-glutamyl transpeptidase. Both associations could reflect microsomal enzyme induction among other possibilities. No differences were seen in fasting serum triglycerides, total cholesterol, LDL, HDL or VLDL cholesterol between the two exposure groups. A statistically significant correlation between serum PCBs and serum triglycerides, total cholesterol, and VLDL cholesterol was removed by adjusting for confounding variables. No correlation was seen between adipose PCBs concentrations and any serum lipid component. Partition phenomena could account for these findings.

Capillary column GC/ECD was used to quantitate individual PCB congeners in adipose tissues. Quantifiable levels of many congeners were found in subjects from all exposure groups, including microsomal enzyme inducers 2, 3′,4,4′,5-pentachlorobiphenyl (CBP); 2,3,3′,4,4′-penta-CBP; 2,2′,3,4,4′,5-hexa-CBP; 2,3,3′,4,4′,6-hexa-CBP; 2,3′,4,4′,5,5′-hexa-CBP; 2,2′,3,3′,4,4′,5-hepta-CBP; and 2,3,3′,4,4′,5,6-hepta-CBP.

We have recently conducted a detailed clinical-epidemiological study of current and past transformer repair workers exposed to PCBs and a comparison group of nonexposed workers. Our results for liver function tests, measures reflecting possible enzyme induction-related effects, and serum lipid levels are presented. Particular attention is given to the relationship between serum lipid concentrations and concentrations of total PCBs congeners in adipose tissue lipid in workers in the three exposure groups (current exposed, previously exposed and comparison) is compared. The full results of this study are being reported elsewhere (*1*,*2*).

Methods

Transformer Maintenance Workers

The exposed workers were switchgear shop employees involved in transformer maintenance functions which included (a) sampling and testing transformer fluids for dielectric properties; (b) "adding and topping off" transformers when the level of oil was low within the transformer itself; (c) cleanup of any spills or leaks in the transformer vaults using absorbent material and sometimes a solvent such as 1,1,1-trichloroethane; (d) repair of transformers, a process which might require drainage of up to 200 gallons of the transformer oil and the replacement of bushings within the unit; and (e) filtering of the transformer oil to upgrade its dielectric properties. According to employees, occupational exposure to leaking transformers was quite common.

An initial industrial hygiene survey was performed to evaluate the extent of employee PCB exposure (*3*). Table 1 displays the results of PCB air concentrations, obtained from personal breathing zone sampling, by job task. The predominant PCB exposure was from Aroclor 1260; Aroclors 1254 and 1242 were used less frequently. Analysis of bulk oils from transformers failed to detect TCDD and showed tetrachlorinated dibenzofuran (TCDF) concentrations ranging from 13 to 116 ppb by weight. In one of these samples, 2,3,7,8-TCDF was quantitated at 31 ppb. No TCDF could be detected in any air sample.

Subsequent industrial hygiene surveys by our group

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Table 1. PCB air concentrations from personal breathings zone samples by job task.[a]

Job Task	Sample duration, hr	Concentration, μg/m³	8 hr TWO concentration, μg/m³
Oil drain plug repair and cleanup	3.2	60.0	24.0
	3.2	55.7	22.3
	3.1	43.1	16.7
Sight gauge and oil drain plug repair and cleanup	3.2	17.4	7.0
	3.2	14.7	5.9
	3.2	7.9	3.2
Cleanup of PCB leak	1.0	3.1	0.4
	1.0	3.1	0.4
	1.0	0.1	0.01
Secondary oil leak repair and cleanup (2 vaults)	5.8	17.1	12.4
	5.9	12.3	9.1
	5.4	10.6	7.2
	6.5	8.7	7.1
	5.9	8.0	5.9
	4.5	7.4	4.2
	3.8	8.3	3.9
	5.2	4.7	3.1
	5.0	4.7	2.9
	3.7	5.5	2.5
	5.5	3.3	2.3
	5.2	4.8	2.1
	3.5	3.2	2.1
	2.7	2.1	0.7
	1.5	3.6	0.7

[a]From Moseley et al. (*3*).

have drawn attention to important role of skin contact and percutaneous absorption of PCBs in this group (*4*). Other studies currently in progress in our laboratory indicate that PCBs are well absorbed through the skin.

Study Design

A nonprospective study was performed utilizing current and past switchgear shop employees and a comparison group of presently employed operating engineers who had never been occupationally exposed to PCBs.

A total of 72 exposed men (43 currently exposed and 29 previously exposed) were invited to participate in the study. This number represented all persons employed at the switchgear shop since its opening in 1971. The 55 participants (38 currently exposed and 17 previously exposed) represented 76.4% of the total eligible work force; 2.8% of the eligible men accepted appointments but failed to keep them, 12.5% refused to participate because they had left the area, and the remaining six nonparticipants (8.3%) live in the area, but refused to participate. The final participants represented 87% of the currently exposed and 55% of the previously exposed workers.

Operating engineers were selected for the comparison group because of similar required skill and education levels. A preliminary questionnaire to gather demographic data, including age, race, smoking habits, alcohol intake and to exclude previous occupational exposure to PCBs, was given to this group. The final comparison group was selected for balance of age and race with the exposed group.

Examination Methods

Each participant was hospitalized for 24 hr. A detailed questionnaire was administered by a trained interviewer. A detailed physical examination was performed. Skinfold thickness was measured to the nearest millimeter with a Holtain skinfold caliper at three sites, triceps, suprailiac and subscapular, to enable body fat content to be measured.

Patients were instructed to take nothing by mouth other than water after 10:00 PM on the night before admission to the hospital. On admission, early morning fasting blood samples were obtained. Using standard laboratory procedures, blood was analyzed for total protein, albumin, bilirubin, alkaline phosphatase (APH), lactic dehydrogenase (LDH), serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), γ-Glutamyl transpeptidase (GGT), T-3 and T-4. A lipid profile was obtained. Plasma samples were extracted with zeolite and isopropanol and analyzed by Lipid Research Clinic Program continuous flow (Auto Analyzer II) procedures (*5*). Cholesterol was determined by a colorimetric reaction using the Lieberman-Burchard reagent, and triglycerides were measured fluorometrically. Calculation of cholesterol content of high-density lipoproteins (HDL), low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) was determined after ultracentrifugal fractions were obtained, separation of HDL cholesterol fraction by addition of manganese chloride and heparin solutions was completed before analysis (*6*). The LDL cholesterol was obtained by subtracting HDL cholesterol from the cholesterol contained in the entire

ultracentrifugal bottom fraction (d 71.006). The VLDL cholesterol was calculated as the difference between total plasma cholesterol concentration and that of the ultracentrifugal bottom fraction.

A 24-hr urine collection was obtained with the sample kept on ice in the dark and refrigerated for the collection period. The urine was then fractionated with preservative added to the aliquot for porphyrin analysis. Analysis for 24-hr excretion levels of creatinine δ-aminolevulinic acid, 17-ketosteroids and 17-hydroxycorticosteroids was performed according to standard laboratory procedures. Uroporphyrins and coporphyrins were quantitated by thin-layer chromotography (*7,8*).

In the absence of a specific contraindication, the half-life of antipyrine was measured. Prior to oral antipyrine administration of 18 mg/kg, a fasting blood sample was drawn for baseline determination. Blood was drawn 4, 8 and 12 hr after administration. Meals were spaced in such a way as to occur after venesection in order to avoid lipemic serum. Plasma antipyrine levels were determined for each subject by the method of Brodie et al. (*9*).

Serum and adipose tissue were obtained for PCB analysis. After local anesthesia, adipose tissue was aspirated through a 15-gauge needle from the upper outer quadrant of subcutaneous buttock tissue. The adipose sample was washed with normal saline into a pesticide free glass vial and frozen prior to analysis.

Samples were analyzed by packed-column gas chromatography with electron capture detection (GC/ECD) according to a protocol adapted from EPA Pesticide Monitoring Methods (*10*) to accomodate the very small adipose sample weights (3–900 mg). The GC/ECD chromatograms were quantitated using the method of Webb and McCall (*11*) and reported as total PCBs.

PCBs were confirmed in 18 selected samples by gas chromatography/mass spectroscopy. With the exception of phthalate and adipate plasticizers, the only potential interferents observed were DDE and DDT. These components had also been detected in the GC/ECD analysis so that they were not included in the PCB values reported.

The serum PCB concentration was computed for peaks eluting after DDE, the adipose PCB concentration was determined for all peaks. The total PCB level was expressed as a concentration in serum and in adipose tissue lipid, respectively.

To measure the concentration of individual PCB congeners, capillary-column GC/ECD was used (*12*).

Data Handling and Analysis

Demographic and employment characteristics of the exposed and comparison group were compared using the chi-square test and t-test for discrete and continuous characteristics, respectively.

In the case of serum PCBs, adipose PCBs and continuous variables on which PCBs could have an impact, univariate statistics (mean, variance, skewness, kurtosis, extremes, etc.) box plots and stem and leaf displays were generated to examine the distribution of each variable and its natural logarithm transformation in all study subjects, and for the exposed and non-exposed groups. Either the original data or the transformed data, whichever yielded the distribution more closely resembling that of a normal random variable, were used for further analyses. If neither the original data nor the transformed data yielded a reasonably normal distribution, nonparametric methods were used.

All PCB concentrations were log transformed after adding 0.01 ppm to adipose concentrations and 0.1 ppb to serum concentrations to eliminate zero values. These transformed data were used for further analyses.

Serum and adipose tissue lipid PCB concentrations in current exposed, past exposed and comparison groups were analyzed using analysis of variance with Duncan's multiple range test. A T-test was used to compare serum and adipose PCB concentrations in all exposed and the comparison group.

Preliminary analysis of continuous variables on which PCBs could have an impact was done by performing T-tests for differences in the means of these variables between the exposed and comparison groups. The nonparametric Wilcoxon rank-sum test was used when necessary. Variables that were statistically significant at the 0.10 level as well as variables of particular interest from the PCB literature were selected for further analysis.

Pearson product-moment correlations were calculated for serum and adipose tissue lipid PCBs and each of the selected continuous variables. For each Pearson correlation, a linear regression model was fit with the continuous factor as the dependent variable and the PCB variable, either serum or adipose tissue lipid, and potential confounding factors as the independent variables. The partial correlation coefficient adjusted for potential confounding factors was then calculated from the regression sums of squares. The significance of the partial correlation is the significance of the PCB variable in the regression model after inclusion of potential confounding factors.

Results and Discussion

Demographic and Employment Characteristics of the Two Groups

The exposed and comparison groups were almost identical in terms of mean age, racial composition and marital status. There was a slightly higher proportion of current smokers and alcohol drinkers in the switchgear employees. The only statistically significant difference was in the number of employees who currently both drink alcohol and smoke. All of the exposed group and none of the comparison group gave a history of occupational exposure to PCBs. The average duration of work in the switchgear shop for exposed workers was 3.75 years.

Table 2. Serum and adipose total PCB concentrations for current exposed, previously exposed groups, all exposed and comparison groups.[a]

	Serum PCBs			Adipose PCBs		
	N	Range, ppb	Geometric mean, ppb	N	Range, ppm	Geometric mean, ppm
Current exposed	37	1–300	12.2	36	0.233	2.1
Previously exposed	17	1–30	5.9	16	0.35.1	0.83
Total exposed	54	1–300	9.7	52	0.2–33	1.6
Comparison	54	1–15	4.6	53	0.2–3	0.6

[a]Group comparisons using log transformed data and F-test and two-tailed t-test show statistically significant differences among the current exposed, past exposed and comparison groups and the total exposed and comparison groups, respectively, at the 0.01 level.

Table 3. Results of tests of liver function in exposed and comparison groups.[a]

Test	Exposed group	Comparison group	p value
Serum total protein, g/dL	7.17	7.32	Borderline $p = 0.058$
Serum albumin, g/dL	4.55	4.66	0.015
Serum bilirubin, mg/dL	0.58	0.62	NS
Serum alkaline phosphatase, mU/mL	76.7	66.7	Borderline $p = 0.054$
Serum LDH, mU/mL	202.3	186.8	0.042
Serum SGOT, mU/mL	26.3	25.0	NS
Serum SGPT, mU/mL	23.3	26.0	NS

[a]Geometric means.
[b]Pooled variance estimate t-test 2-tail probability comparing log transformed means. NS = not significant at the 0.05 level. Borderline values are noted.

Table 4. Pearson correlation coefficients for PCB concentrations and laboratory results, without adjustment for confounding variables.

	Log adipose PCBs		Log serum PCBs	
Variable	Correlation coefficient	p value[a]	Correlation coefficient	p value[a]
Log total protein	0.163	NS	- 0.028	NS
Log albumin	- 0.086	NS	- 0.022	NS
Log bilirubin	- 0.108	NS	- 0.138	NS
Log APH	0.140	NS	0.177	NS
Log SGOT	- 0.106	NS	0.096	NS
Log SGPT	-0.195	NS	- 0.053	NS

[a]NS = not significant at the 0.05 level.

PCBs Concentrations

Table 2 shows the geometric mean serum and adipose tissue lipid total PCB concentrations in the current exposed, past exposed, total exposed and comparison groups. The concentrations in both serum and adipose tissue lipid were significantly different among the three exposed groups and between the total exposed and comparison groups. It was of interest that mean values for the previously exposed group, though somewhat higher, were not significantly different from those of the comparison group, despite reportedly high occupational exposures sustained in the past. These findings are compatible with considerable excretion of PCBs over time.

Liver Function Indicators

Table 3 shows the results of liver function tests in the exposed and comparison groups. Significant differences were seen for serum albumin and for serum LDH with the more abnormal value seen in the exposed group in each case. Differences of borderline significance were observed for serum total protein and serum alkaline phosphatase.

Table 4 shows the Pearson correlation coefficients between log serum and adipose PCBs and the various liver function tests. It is seen that the only significant correlation was a negative correlation with SGPT and adipose PCBs. Table 5 demonstrates that after linear adjustment for potential confounding variables, no significant associations are observed between adipose or serum PCBs and any of the studied variables.

PCBs, Enzyme Induction and Related Effects

A variety of measurements were made which to a greater or lesser extent measure microsomal enzyme induction, among other factors. These included the antipyrine half-life; urinary excretion of aminolevulinic acid

Table 5. Partial correlation coefficients for log PCB concentrations and liver function tests after adjustment for confounding variables.[a]

Variable[a]	Log adipose PCBs		Log serum PCBs	
	Correlation coefficient	p value[b]	Correlation coefficient	p value[b]
Log total protein	- 0.102	NS	0.027	NS
Log albumin	- 0.056	NS	0.096	NS
Log bilirubin	-0.104	NS	- 0.078	NS
Log APH	0.019	NS	0.084	NS
Log LDH	0.048	NS	0.103	NS
Log SGOT	0.007	NS	0.187	NS
Log SGPT	-0.134	NS	0.016	NS

[a]Linearly adjusted for age, smoking, alcohol, history of liver disease.
[b]NS = not significant at the 0.05 level.

Table 6. Measures possibly reflecting microsomal enzyme induction in exposed and comparison groups.

Test	Exposed group[a]	Comparison group[a]	p value[b]
Serum GGT, U/L	26.8	22.9	NS
Serum T_4, (IU)	8.24	8.8	0.016
Urinary ALA, mg/24 hr	2.81	2.48	NS
Urinary 17OH steroids, mg/24 hr	6.43	7.41	Borderline $p = 0.055$
Urinary uroporyphyrins, mg/24 hr	10.5	10.7	NS
Urinary corproporphyrins, mg/24 hr	76.6	91.1	NS
Antipyrine half-life, T/2 hr	10.7	12.43	Borderline $p = 0.069$

[a]Geometric means, except for ALA, 17OH and coproporphyrins, which are arithmetic means.
[b]t-Test using log-transformed values, except for ALA, 17OH and coproporphyrins. NS = not significant at the 0.05 level. Borderline values are noted.

Table 7. Pearson correlation coefficients for PCB concentrations and laboratory results, without adjustment for confounding variables.

Variable	Log adipose PCBs		Log serum PCBs	
	Correlation coefficient	p value[a]	Correlation coefficient	p value[a]
Log serum GGT	0.086	NS	0.194	0.045
Log serum T_4	- 0.109	NS	- 0.009	NS
Urinary ALA	- 0.108	NS	- 0.028	NS
Urinary 17OH Steroids	- 0.315	0.002	- 0.146	NS
Log urinary uroporphyrins	0.002	NS	- 0.169	NS
Urinary coproporphyrins	- 0.099	NS	-0.080	NS
Log antipyrine half-life	- 0.131	NS	0.023	NS

[a] NS = not significant at the 0.05 level.

(ALA), 17-hydroxysteroids, uroporphyrin and coproporphyrin; serum T4 and serum GGT. The latter might also be considered as a liver function test. Only the antipyrine half-life is a direct measure of microsomal enzyme function. Nevertheless, to some extent these tests may be considered together as reflecting a group of functions that could be altered as a result of changes in cellular metabolism which might be induced by PCBs. It has been shown that different PCB congeners produce different patterns of induction and differ markedly in their potency for induction (*13,14*). As shown in Table 6, the level of serum tetraiodothyronine (T4) was significantly lower in the exposed group than the comparison group and borderline differences were seen for 24-hr urinary 17-hydroxycortocosteroid excretion and antipyrine half-life. Table 7 shows the Pearson correlation coefficients for log adipose serum PCBs and selected variables before adjustment for confounding variables, and Table 8 shows the partial correlation coefficients after adjustment. It is seen that in both instances there is a statistically significant positive correlation between the log serum GGT and log serum PCBs and a statistically significant negative correlation between the urinary 17-hydroxycorticosteroid excretion and log adipose PCBs.

A correlation between serum GGT and serum PCBs (*15*) or elevations of GGT in PCBs-exposed workers (*16*) has been observed previously. An elevated GGT may have a number of causes which include, but are not confined to, enzyme induction. Of particular interest was the strong negative correlation between adipose PCBs and urinary 17-hydroxysteroid excretion. It should be noted that no similar correlation was seen in the case of 17-ketosteroid excretion. The reason for this association is not entirely clear; it could represent the induction of metabolizing enzymes, although other possible

Table 8. Partial correlation coefficients for log PCB concentrations and selected laboratory measures reflecting microsomal enzyme induction after adjustment for confounding variables.

Variable	Linearly adjusted for	Log adipose PCBs		Log serum PCBs	
		Correlation coefficient	p value[a]	Correlation Coefficient	p value[a]
Log serum GGT	Age, smoking, alcohol history of liver disease	0.106	NS	0.231	0.029
Log serum T_4	Age	- 0.113	NS	- 0.016	NS
Urinary 170H steroids	Age, smoking, alcohol	- 0.338	0.001	- 0.120	NS
Urinary ALA	Age, alcohol, SGOT	- 0.013	NS	0.048	NS
Log urinary uroporphyrin	Age, alcohol, SGOT	0.011	NS	- 0.176	NS
Urinary coproporphyrin	Age, alcohol, SGOT	- 0.092	NS	- 0.080	NS
Log antipyrine half-life	age, smoking, alcohol calculated body fat content,[b] SGOT	- 0.104	NS	- 0.011	NS

[a]NS = not significant at the 0.05 level.
[b]Calculated from skin fold thickness and weight.

explanations such as interference with a servo mechanism regulating hormone synthesis or metabolism cannot be excluded. We did not observe any significant correlation between PCB levels and antipyrine half-life and thus could not confirm the previous observation of Alvares (*17*) who reported reduced antipyrine half-life in exposed workers. Maroni and colleagues (*18*) have also described increased urinary excretion of D-glucaric acid in exposed workers, which is also felt to reflect microsomal enzyme induction.

It is important to recognize that enzyme induction by PCBs is isomer-specific. The isomer mixture that constitutes the total PCBs differs in different Aroclors and within the tissues of different individuals. The most appropriate investigation of possible enzyme induction will involve the exploration of the correlation between the appropriate tissue concentration of those isomers capable of induction and measures of specific types of enzyme induction in humans. As I will discuss sub sequently, we now have the technology and initial data to allow us to proceed to perform these studies.

Serum Lipid Concentrations and PCBs

A number of previous studies have reported statistically significant correlations between serum PCBs concentrations and serum lipid levels (*15,19,20*). These results have been interpreted as indicating that PCBs may alter lipid metabolism at levels of exposure and bioaccumulation insufficient to produce overt symp toms. This contention has received some support from experimental studies (*21*). The serum lipid concentration associated with serum PCBs include triglycerides (*15,19,20*), and total cholesterol (*15*). An inverse correlation with plasma high-density lipoprotein (HDL) cholesterol has been observed (*15*).

Our study provides an opportunity to examine these effects in more detail since we measured serum PCBs, adipose tissue lipid PCBs and several serum lipid fractions in both exposed individuals and an unexposed comparison group.

Table 9 shows the mean concentrations of serum triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol and VLDL cholesterol in the exposed and comparison groups. It is seen that the values are not statistically significant; interestingly, the triglyceride concentration, is slightly higher in the comparison group.

Table 9. Serum lipid concentrations, exposed and comparison groups.

	Mean or geometric mean[a]	
	Exposed group	Comparison group
Triglycerides, mg/dL	116[a]	128[a]
Total cholesterol, mg/dL	191	197
HDL cholesterol, mg/dL	43[a]	40[a]
LDL cholesterol, mg/dL	120	126
VLDL cholesterol, mg/dL	23[a]	25[a]

[a]Geometric mean used for variables with log normal distribution. None of these differences are statistically significant at the 0.05 level.

Table 10. Pearson correlation coefficients for serum lipid concentrations and log PCB levels before adjustment for confounding variables.

	Log serum PCB		Log adipose PCB	
	Correlation coefficient	p[a]	Correlation coefficient	p[a]
Log triglycerides	0.259	0.007	- 0.019	NS
Total cholesterol	0.202	0.036	0.031	NS
Log HDL cholesterol	0.053	NS	0.063	NS
LDL cholesterol	0.143	NS	0.021	NS
Log VLDL cholesterol	0.270	0.005	- 0.010	NS

[a]NS = not significant at the 0.05 level.

Table 10 shows the serum lipid concentrations and log PCB levels before adjustment for compounding variables analyzed with the SAS program using Pearson correlation coefficients. It is seen that the log triglyceride, total cholesterol and log VLDL cholesterol are all positively correlated with log serum PCB levels at a statistically significant level. However, no statistically significant correlations—indeed, rather low correlation coefficients—were observed between log adipose PCBs and all measured serum lipid values.

Table 11 shows the partial correlation coefficients for serum lipid concentrations and log PCB levels after linear adjustments for potentially confounding variables.

Table 11. Partial correlation coefficients for serum lipid concentrations and log PCB levels after adjustment for confounding variables.[a]

	Log serum PCB		Log adipose PCB	
	Correlation coefficient	p value[b]	Correlation coefficient	p value[b]
Log triglycerides	0.200	NS	− 0.080	NS
Total cholesterol	0.012	NS	0.018	NS
Log HDL cholesterol	0.077	NS	0.049	NS
LDL cholesterol	0.066	NS	0.028	NS
Log VLDL cholesterol	0.211	NS	0.082	NS

[a]Linearly adjusted for age, race, smoking, alcohol intake, history of liver disease, T7, glucose, family history of diabetes, high lipids and heart attacks.
[b]NS = not significant at the 0.05 level.

It is seen that the correlation coefficients between the log serum PCB concentration and log triglycerides, total cholesterol and log VLDL cholesterol are reduced and no longer achieve statistical significance; correlation coefficients between the adipose tissue lipid PCBs remain low and are not statistically significant.

This interesting group of observations—little difference in serum lipid concentrations between the exposed and comparison groups; statistically significant positive correlations between log serum PCBs, and log triglycerides, total cholesterol and VLDL cholesterol; no significant correlations between log adipose PCB tissue lipid and serum lipid concentrations; and the reduction of the correlation with serum PCBs below the level of statistical significance when the influence of potential confounders are removed—are all consistent with an explanation that the observed phenomena may result, at least in part, from a partitioning effect of PCBs in serum lipids. If PCBs were carried preferentially in the triglyceride and VLDL fractions of serum, we might expect to see this constellation of findings. If this explanation is correct, for a given concentration of PCBs in adipose tissue lipid, the serum PCB concentration would alter with the triglyceride concentration, other factors remaining equal. It is not, therefore, necessary to invoke a PCB-dependent alteration in lipid metabolism to explain these findings. Partitioning phenomena also seem consistent with reported observations of quite strong correlations with serum lipid levels over a relatively large range of PCBs concentrations. These findings do not, of course, rule out an added effect of PCBs on lipid metabolism, particularly with higher PCB body burdens.

It is interesting to review the findings of Chase et al. (*20*) in light of our results, since their study also incorporated measures of serum and adipose PCB concentrations, serum triglycerides, total cholesterol and HDL cholesterol, although the comparison group used in that study was small and not particularly well matched. The PCB concentration levels in the exposed and nonexposed groups were broadly similar to those we observed; some apparent differences may be due to differences in analytic technique. Table 12 shows the mean values Chase obtained for triglycerides, total cholesterol and HDL cholesterol in the exposed, nominally exposed and nonexposed groups. It is seen that no statistically significant differences were observed between the groups and interestingly the triglyceride level was actually higher in the nonexposed group, despite the younger mean age.

Table 12. Selected variables in 120 workers by PCB exposure category.[a]

	Exposed group	Nominally exposed group	Nonexposed group
Triglycerides, mg/dL	136	129	146
Total cholesterol, mg/dL	232	238	238
HDL cholesterol, mg/dL	59	57	62
Number in group	89	15	19
Mean age, yr		37	31
Mean plasma PCB, ppb	33	14	12
Mean adipose PCB, ppm	5.6	1.4	1.3

[a]Data from Chase et al. (*20*).

Table 13. Partial correlation coefficients in 86 PCB-exposed workers.[a]

	Plasma PCBs		Adipose PCBs	
	Correlation coefficient	p value	Correlation coefficient	p value[b]
Serum triglyceride (adjusting for age)	0.54	0.001	0.20	NS
Serum triglyceride (adjusting for length of employment)	0.55	0.001	0.23	NS

[a]Data from Chase et al. (*20*).
[b]NS = not statistically significant at $p = 0.05$.

As shown in Table 13, Chase et al. (*20*) found a statistically significant correlation between plasma PCBs and plasma triglycerides, which remained after limited adjustment (for age and length of employment); however, no significant correlation was seen with fat PCBs and plasma triglycerides. These findings show a similar pattern to those that we observed and also appear capable of being explained as a possible result of partitioning phenomena.

Adipose Tissue Concentrations of PCB Congeners

The use of capillary column GC/ECD resulted in over 91 separate quantifiable PCB peaks in one or more serum or adipose tissue lipid samples. Of these, 75 peaks have been structurally identified. Certain of these peaks contain more than one congener (generally two congeners), so that the 75 peaks represent 95 possible congeners. A further 16 peaks still have not been assigned specific structures.

Table 14 shows the results for certain congeners which are of interest and which were quantifiable in more than 65% of the adipose tissue samples in each exposure group.

Table 14. Percentage of adipose tissue lipid samples showing quantifiable levels of certain PCB congeners and mean concentration in samples with quantifiable levels, by exposure groups.

Congener[a]	Currently exposed group (N = 38)		Previously exposed group (N = 17)		Comparison group (N = 56)	
	% above quantifiable level	Mean of quantifiable levels, ppb	% above quantifiable level	Mean of quantifiable levels, ppb	% above quantifiable level	Mean of quantifiable levels, ppb
2,3,3',4,4',6-Hexa-CBP	94	25.1	73	3.0	81	3.6
2,4',4,4',5,5'-Hexa CBP	79	25.9	87	6.8	75	7.5
2,2',3,3',4,4',5-Hepta-CBP	91	387.1	100	107.2	94	73.2
2,3,3',4,4',5,6-Hepta-CBP	85	57.1	87	15.2	90	12.4
2,2',3,3',4,4',5,5'-Octa-CBP	82	79.9	80	31.9	92	26.3

[a]CBP = chlorobiphenyl.

The percentage of samples in which the congener was above the quantifiable limit and the mean concentration in samples in which the congener was above the quantifiable limit are displayed. These isomers are all microsomal enzyme inducers (*22*). For example, whereas 2,2',3,3',4,4',5,5'-octachlorobiphenyl exhibits phenobarbitone-type induction, 2,3',4,4',5,5'-hexachlorbiphenyl is also capable of inducing hepatic microsomal cytochrome P-450 but appears to resemble isosafrole in its inducting pattern (*23*).

The ability to find measurable tissue levels of these congeners will enable us to compare the actual tissue levels of PCBs of specific biological interest with appropriate biochemical and physiologic indices. We are currently pursuing this approach which has promise of generating dose–effect data of maximum utility for the purposes of understanding the possible consequences of environmental hazards and for human risk assessment.

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REFERENCES

1. Emmett, E. A., et al. In preparation.
2. Agnew, J., Bleecker, M. L., and Emmett, E. A. In preparation.
3. Moseley, C. L., Geraci, C. L., and Burg, J. Polychlorinated biphenyl exposure in transformer maintenance operations. Am. Ind. Hyg. Assoc. J. 43: 170–174 (1982).
4. Lees, P. S. J., Corn, M., and Breysse, P. N. Evidence for dermal absorption as the major route of body entry during exposure of transformer maintenance and repairmen to PCBs. Submitted.
5. Lipid Research Clinics Program. Manual of Laboratory Opera tions, Vol. I. U. S. Department of Health Education and Welfare, Washington DC, 1974.
6. Technicon Instruments Corporation. Total cholesterol procedure N-24, Technicon Auto Analyzer Methodology. Technicon Instruments Corp., Tarrytown, NY, 1970.
7. Scott, C. R., Labbe, R. F., and Nutter, J. A rapid assay for urinary porphyrins by thin layer chromatography. Clin. Chem. 18: 493–500 (1976).
8. Nutter, J., and Labbe, R. F. Improved screening tests for porphyrins (Letter to the editor). Clin. Chem. 18: 739 (1976).
9. Brodie, B. B., Axelrod, J., Soberman, R., and Levy, B. B. The estimation of antipyrine in biological materials. J. Biol. Chem. 179: 25–29 (1949).
10. Watts, R. R. Analysis of pesticide residues in human and environmental samples. A compilation of methods selected for use in pesticide monitoring programs. Document number EPA-600/8-80-038, Health Effects Research Laboratory, U. S. Environ mental Protection Agency, Research Triangle Park, NC, 1980.
11. Webb, R. G., and McCall, A. C. Quantitative PCB standards for electron capture gas chromatography. J. Chromatogr. Sci. 11: 366–373 (1973).
12. Pellizzari, E., Moseley, M. A., and Cooper, S. D. Recent advances in the analysis of polychlorinated biphenyls in environmental and biological media. Submitted.
13. Alvares, A., and Kappas, A. The inducing properties of polychlorinated biphenyls on hepatic monooxygenases. Clin. Pharmacol. Therap. 22: 809–816 (1977).
14. Safe, S. Polybrominated biphenyls, polychlorinated naphthalenes and polychlorinated terphenyls as microsomal enzyme inducers. In: Toxicology of Halogenated Hydrocarbons: Health and Ecological Effects (M. A. G. Khan and R. H. Stanton, Eds.), Pergamon Press, New York, 1981, pp. 97–120.
15. Smith, A. B. Metabolic and health consequences of occupational exposure to polychlorinated biphenyls. Brit. J. Ind. Med. 39: 361–369 (1982).
16. Maroni, M., Colombi, A., Arbosti, G., Cantoni, S., and Foa, V. Occupational exposure to polychlorinated biphenyls in electrical workers. I Environmental and blood polychlorinated biphenyls concentrations. Brit. J. Ind. Med. 38: 49–54 (1981).
17. Alvares, A., Fischbein, A., Anderson, K. E., and Kappas, A. Alterations in drug metabolism in workers exposed to polychlorinated biphenyls. Clin. Pharmacol. Therap. 22: 140–146 (1978).
18. Maroni, M., Colombi, A., Antonini, C., Cassina, T., and Foa, V. D-Glucaric acid excretion as a tool for biological monitoring in occupational medicine. In: Organ-Directed Toxicity, Chemical Indices and Mechanisms (IUPAC) (S. S. Brown and D. S. Davies, Eds.), Pergamon Press, New York, 1981.
19. Baker, E. L., Landrigan, P. J., Glueck, C. J., Zack, M. M., Liddle, J. A., Burse, V. W., Housworth, W. J., and Needham, L. L. Metabolic consequences of exposure to PCBs in sewage sludge. Am. J. Epidem. 112: 553–563 (1980).
20. 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).
21. Kohli, K. K., Gupta, B. N., Albro, P. W., and McKinney, J. D. Effects of inducers of drug metabolism enzymes on triglyceride and phospholipid synthesis. Chem. Biol. Interact. 36: 117–121 (1981).
22. Safe, S., Parkinson, A., Robertson, L., Cockerline, R., Safe, L., Bandiera, S., Okey, A. PCBs as AHH inducers. In: Chlorinated Dioxins and Related Compounds: Impact on the Environment (O. Hutzinger, Ed.), Pergamon Press, New York, 1982.
23. Parkinson, A., Robertson, L. W., and Safe, S. H. Induction of rat hepatic microsomal cytochrome P-450 by 2,3',4,4',5,5'-hexa chlorobiphenyl. Biochem. Pharmacol. 32: 2269–2279 (1983).