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# Metabolic and health consequences of occupational exposure to polychlorinated biphenyls

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a maintenance facility. Data
employees of the private util-
o worked in transformer
sformer overhaul, and 21 in
pational exposure to PCBs.

EVALUATIONS
strial hygiene evaluations at
ble from ABS on request.
me PCB and levels of skin
were measured during sur-
iene conducted at times
the medical surveys. Per-
ollected on florosil, a mag-
nt, by using a Sipin SP1
rate of about 200 cc/min
The PCBs were desorbed
zene and analysed by using
an electron capture detec-
on was 0·01 μg per tube.
on Whatman smear tabs
ead, nose, and cheek area
wipe samples were ana-
ed to determine the
ntamination with

undertaken to determine
ed clinical and biochemi-
PCB concentration as an
xposure to PCB. A ques-
to each participant by a
n demographic data, and
d tobacco consumption,
es (a copy is available
sent and previous occu-
tained from plant em-
hysical examination was
physicians. Neither the
ere blinded with respect
icipants.
ations were performed
blood drawn after a
ology (haemoglobin,
d differential count),
inorganic phosphorous,
acid, cholesterol, total
bin, alkaline phospha-
nd glutamic-oxalacetic
um glutamic-pyruvic
um gamma-glutamyl
um creatinine, serum
serum protein elec-
Ur y creatinine and
phyrin, and

porphobilinogen were measured on spot urine specimens. Urinary glucose and protein determinations were performed at the study site by dipstick method.

Plasma total cholesterol, triglycerides (TG), and high density lipoprotein cholesterol (HDL-C) determinations were performed by the Lipid Research Centre, University of Cincinnati, following standardised Lipid Research Centre methods,[7] slightly modified for HDL-cholesterol determinations.[8] Low density lipoprotein cholesterol (LDL-C) levels were calculated[9] in all subjects except three with triglyceride levels greater than 400 mg/dl.

The clinical evaluations at the public and private utilities were identical with those described above, except that, in addition, urinary 17-ketosteroid and 17-hydroxysteroid concentrations were measured and standardised for urinary creatinine excretion on spot urines.

Serum PCB determinations were performed by Environmental Science and Engineering, Inc. in Gainesville, Florida, using a slightly modified version of an electron capture gas chromatographic procedure developed for the Office of Toxic Substances, United States Environmental Protection Agency.[10,11] PCB components were quantitated as lower chlorinated biphenyls (L-PCBs) and higher chlorinated biphenyls (H-PCBs) by comparing retention times on the gas chromatogram with those of standard samples of Aroclor 1242 and Aroclor 1254. Peaks eluting before DDE (injected in the column in a pesticide mixture control) were included in the serum L-PCB determination, and those after DDE in the serum H-PCB determination. The L-PCBs so quantitated were predominantly biphenyl molecules with four or fewer chlorine atoms per molecule, and the H-PCBs were predominantly biphenyl molecules with five or more chlorine atoms per molecule.[12] Major peaks that appeared in both Aroclor 1242 and 1254 standards with equivalent retention times were quantitated only once, as either serum L-PCB or serum H-PCB. Because of the similarity in composition of Aroclor 1016 and Aroclor 1242, no specific quantitation was attempted for Aroclor 1016, and instead the serum L-PCB quantitation was taken to be representative of the distribution of PCB isomers found in both these products. Because of the low concentrations of PCB, mass spectral confirmation of individual peak identity was not attempted. Quality control procedures included the analysis of two in-vitro spiked pool specimens and of one blind split duplicate in each analytical run.

STATISTICAL METHODS

Inspection of histograms and normal probability plots of the various blood tests showed that logarithmic transformation (base 10) was required to "normalise" the following data: serum L-PCB and H-PCB concentrations, SGOT, SGPT, GGTP, AK, total and direct bilirubin, glucose, BUN, creatinine, T-4, TG, HDL-C, and LDL-C. Parametric statistical analyses were performed with the log-transformed data, using standard packaged statistical programs.[13–15] Deficits in tabulations from specified total numbers of participants are attributable to missing values for data, which required elimination of the individuals with the missing values from the particular analysis.

## Results

ENVIRONMENTAL PCB LEVELS

*Electrical equipment manufacturing plant*—The time-weighted average (TWA) personal air sample concentrations of PCBs, all obtained for workers in F-30, G-44, or an area ("miscellaneous assembly") adjacent to the impregnation ovens (located in F-30), ranged from non-detectable to 264 μg/m³, with a median of 81 μg/m³. The current OSHA standard and ACGIH threshold limit value for 42% chlorinated biphenyls are both 1000 μg/m³. Skin smear wipes of selected workers, all from F-30 or the area adjacent to F-30, ranged from 10 μg/100 cm² to 668 μg/100 cm² of PCB accumulated over the course of a shift. These findings indicated work-related skin contamination by PCBs that would not be quantified under present sampling methods, which are limited to air sampling for PCBs.

*Public utility company*—Two industrial hygiene surveys were conducted, one in November 1976 and the other in August 1977. During the November survey, all personal air samples for PCBs (analysed as Aroclor 1254) were under the limit of detection, —that is, under 1 μg/tube, corresponding to a concentration of under 19 μg/m³. During the August 1977 survey, personal air samples for PCBs (analysed as Aroclor 1260) ranged from 37 to 215 μg/m³. The current OSHA standard and ACGIH threshold limit value for 54% chlorinated biphenyl are both 500 μg/m³.

*Private utility company*—Samples obtained during yearly inspection of transformers in underground vaults showed personal air exposures varying from 0·4 to 8·8 μg/m³. Wipe samples from the hands and face of two employees varied from 5 μg/100 cm² to 487 μg/100 cm². A wipe of the table top containing test equipment and the floor of the test area showed about 800 μg/100 cm² for PCBs, showing localised or general smearable contamination. Personal air samples obtained during overhaul of transformers varied from 3·1 to 82·3 μg/m³. Wipe samples from

ted, without occupational or
e to PCBs, were 11·6 ng/ml
ively.
concentrations among work-
pment manufacturing plant
to 50 times the community
ean serum H-PCB concen-
out two to four times the
level. Mean serum L-PCB
ny times greater among
equipment manufacturing
nsformer maintenance and

nge

| | Range (ng/ml) |
|---|---|
| | 210-3330 |
| | 34-2400 |
| | 8-1500 |
| | 1-370 |
| | 5-52 |
| | 1-59 |
| | 9-48 |
| | 12-52 |

e

| | Range (ng/ml) |
|---|---|
| | 20-250 |
| | 10-250 |
| | 7-130 |
| | 1-110 |
| | 7-24 |
| | 1-19 |
| | 7-250 |
| | 3-25 |

repair workers, while mean serum H-PCB concentrations among workers at the electrical equipment manufacturing plant more closely resembled concentrations among the transformer maintenance and repair workers.

The relation of serum log(L-PCB) and log(H-PCB) concentrations, and personal air levels of PCBs, was examined among workers at the electrical equipment manufacturing plant. Time-weighted average personal air level exposure measurements were available for 10 job descriptions, to which 20 participants in the survey were assigned. The correlation of personal PCB air levels with serum log(L-PCB) concentration was significant ($r = 0·66$, $p = 0·0013$); but the correlation of personal PCB air levels with serum log(H-PCB) concentration was not ($r = 0·37$, $p = 0·11$). The lack of statistical significance of the latter correlation may well have been a function of the size of the data set available for the analysis. Data were not available to permit similar analyses for the transformer maintenance and repair workers.

The use of protective equipment (protective clothes, gloves, and respirators) increased with personal air level exposure. Thus, while a significant positive correlation between the use of protective equipment and serum log(L-PCB) and log(H-PCB) concentrations could be shown (data not given), the primary association was likely between personal air level exposure and the use of protective equipment rather than the use of protective equipment and serum log(PCB) concentration.

### QUESTIONNAIRE DATA

The relationships between serum PCB concentration and response to questions concerning symptoms and past illnesses were examined. Age and study site were potential confounding variables that had to be taken into account in the analysis, so that it might reasonably be inferred that any observed associations had not resulted from the effect of the confounding variables alone. The questionnaire response data were analysed by a logistic regression in which the logarithm of the odds for a positive ("Yes") response for the dichotomous variable (questionnaire response) was modelled as a linear function of independent predictor variables, such as serum log(L-PCB) and log(H-PCB) concentrations, as well as the confounders' age and study site. The following histories of symptom were significantly associated with either serum log(L-PCB) or log(H-PCB) concentration, or both, in the presence of the confounders (see table below).

### PHYSICAL EXAMINATIONS

No consistent patterns of abnormalities were noted on physical examination at any study site. None of the participants was found to have acneform lesions suggestive of chloracne. Although a correlation was noted between serum log(H-PCB) concentration and diastolic blood pressure at the electrical equipment manufacturing plant ($r = 0·1395$, $F_{1,219} = 4·61$), multiple linear regression including the additional confounding variables age and sex showed the apparent association of diastolic blood pressure with increasing serum log(H-PCB) concentration to have been attributable to an association primarily with age (partial $r = 0·2742$, $F_{1,217} = 17·64$) as well as with sex (partial $r = 0·1381$, $F_{1,217} = 4·27$).

### LABORATORY DATA—BLOOD TESTS

Simple correlations between serum log(L-PCB) and log(H-PCB) concentrations and the results of clinical biochemistry and haematological tests were computed for participants at each study site separately. Statistically significant correlations are summarised in table 3. To control for confounding by age (and sex, at the electrical equipment manufacturing plant), multiple linear regression equations were computed for each statistically significant correlation, with serum log(PCB) concentration, age, and (at the electrical equipment manufacturing plant only) sex as independent variables. Because of the collinearity of serum log(L-PCB) and log(H-PCB) concentrations, separate regressions were computed, with serum log(L-PCB) and the confounder(s) as predictors, and serum log(H-PCB) and the confounder(s) as predictors. The squared partial correlations, "partial $R^2$," were computed. This is a measure of the variance of the outcome variable still to be accounted for by serum log(PCB) concentration, relative to the variance already

| *Symptom* | *Associated with log(L-PCB) level in presence of confounders ~ $\chi^2(1)$** | *Associated with log(H-PCB) level in presence of confounders ~ $\chi^2(1)$** |
|---|---|---|
| Coughing on the job or soon after work | 5·05 | 3·87 |
| Irritated or burning eyes | 7·66 | 11·29 |
| Unexplained loss of appetite | 5·70 | 3·40 |
| Unexplained tingling in the hands | 5·16 | 3·51 |
| Rash or dermatitis | 0·04 | 4·51 |

*$Pr(\chi^2(1) \geq 3·84) = 0·05$.

Table 3 *Product-moment correlations between selected clinical biochemistries and haematologies and serum log(L-PCB) and log(H-PCB) concentrations, by study site*

| *Clinical biochemistry* | *No of observations* | *Correlation with serum log(L-PCB)* | *Correlation with serum log(H-PCB)* |
|---|---|---|---|
| *Electrical equipment manufacturing plant* | | | |
| Log(SGOT) | 220 | 0·1308* | 0·1894* |
| Log(GGTP) | 217 | 0·1936* | 0·2651* |
| Uric acid | 220 | 0·1151 | 0·1955* |
| Cholesterol | 221 | 0·1308 | 0·2615* |
| Log(triglyceride) | 221 | 0·1621* | 0·3212* |
| Log(HDL-cholesterol) | 221 | −0·0837 | −0·1473* |
| Log(LDL-cholesterol) | 218 | 0·0575 | 0·1473* |
| Beta-globulin | 217 | 0·1163 | 0·1526* |
| Haemoglobin | 221 | 0·0617 | 0·1492* |
| *Public utility company* | | | |
| Log(triglyceride) | 46 | 0·0222 | 0·4292* |
| Log(HDL-cholesterol) | 46 | 0·0528 | −0·4148* |
| *Private utility company* | | | |
| Log(SGOT) | 46 | 0·3173* | −0·0927 |
| Cholesterol | 46 | 0·2872* | 0·0471 |

* Statistically significant ($p < 0·05$) correlation.

accounted for by the regression on the confounders alone.[16] The results are summarised in table 4.

Neither serum log(L-PCB) nor log(H-PCB) concentrations were significant predictors of serum uric acid, beta-globulin, LDL-cholesterol, or haemoglobin when confounding variables age and sex were taken into consideration. Significant partial correlations, however, in the presence of the confounding variables, between log(SGOT), log(GGTP), cholesterol, log(triglyceride), and log(HDL-cholesterol); and either serum log(L-PCB) or log(H-PCB) concentrations, were still shown at at least one site.

Given the same data available at three sites, it would be reasonable to expect meaningful correlations/associations to be found at more than one site. Accordingly, homogeneity of trend was investigated across all three sites by an analysis of covariance. The results are summarised in table 5. It is apparent that log(SGOT), log(GGTP), log(triglyceride), and log(HDL-cholesterol) were

Table 4 *Partial correlations between clinical biochemistries and serum log(L-PCB) and log(H-PCB) concentrations, by study site*

| *Clinical biochemistry* | *Correlation with serum log(L-PCB)* | *Correlation with serum log(H-PCB)* |
|---|---|---|
| *Electrical equipment manufacturing plant* | | |
| Log(SGOT) | 0·1085 | 0·1579* |
| Log(GGTP) | 0·1618* | 0·2017* |
| Uric acid | 0·0037 | 0·0101 |
| Cholesterol | 0·0899 | 0·1822* |
| Log(triglyceride) | 0·1234 | 0·2526* |
| Log(HDL-cholesterol) | −0·0449 | −0·0887 |
| Log(LDL-cholesterol) | 0·0001 | 0·0027 |
| Beta-globulin | 0·0086 | 0·0128 |
| Haemoglobin | 0·0000 | 0·0028 |
| *Public utility company* | | |
| Log(SGOT) | 0·1436 | −0·1753 |
| Log(GGTP) | 0·0724 | −0·0777 |
| Cholesterol | −0·0827 | −0·2020 |
| Log(triglyceride) | 0·0819 | 0·5182* |
| Log(HDL-cholesterol) | 0·0242 | −0·4403* |
| Log(LDL-cholesterol) | −0·0111 | 0·0474 |
| *Private utility company* | | |
| Log(SGOT) | 0·3182* | −0·1242 |
| Log(GGTP) | 0·0859 | −0·2115 |
| Cholesterol | 0·3227* | −0·0357 |
| Log(triglyceride) | 0·2661 | −0·0494 |
| Log(HDL-cholesterol) | 0·0929 | −0·1425 |
| Log(LDL-cholesterol) | 0·0421 | 0·0007 |

* Statistically significant ($p < 0·05$) correlation.

Table 5 *Inter-site comparisons of correlations: homogeneity of trend of selected clinical biochemistries with serum log(L-PCB) and log(H-PCB) plus confounders*

| Clinical biochemistry | Regression on serum log(L-PCB) plus confounders | | Regression on serum log(H-PCB) plus confounders | |
|---|---|---|---|---|
| | Homogenous trend? | Significant trend? | Homogenous trend? | Significant trend? |
| Log(SGOT) | Yes | Yes | Yes | No |
| Log(GGTP) | Yes | Yes | No | No |
| Cholesterol | Yes | No | No | No |
| Log(triglyceride) | Yes | Yes | No | Yes |
| Log(HDL-cholesterol) | Yes | No | Yes | Yes |

significantly associated with either serum log(L-PCB) or log(H-PCB) concentrations, or both across all three sites. The trend was homogeneous for log(SGOT) regressed on log(L-PCB), log(GGTP) regressed on log(L-PCB), log(triglyceride) regressed on log(L-PCB), and log(HDL-cholesterol) regressed on log(H-PCB). The trend was not homogeneous for log(triglyceride) regressed on log(H-PCB). Biochemistries for which non-homogeneity of trend was noted in the absence of significant trend were of no practical interest.

### LABORATORY DATA—URINE TESTS

Urinary glucose, protein, porphyrin, and steroid excretion were not correlated with either serum L-PCB or H-PCB concentrations.

## Discussion

Serum log(PCB) correlated significantly with symptoms suggestive of mucous membrane and skin irritation, of systemic malaise, and of altered peripheral sensation; and with serum log(SGOT), log(GGTP), plasma log(triglyceride), and log(HDL-cholesterol). These correlations occur in the absence of overt clinical dysfunction identifiable on physical examinations. The simultaneous changes in SGOT, GGTP, plasma triglyceride, and HDL-cholesterol are evidence of an effect on the liver of exposure to PCB, the biological significance of which is not clear. A positive correlation between serum GGTP and triglyceride has been described,[17] as has the rise of serum GGTP in the presence of drugs known to induce liver microsomal enzymes.[18] It has been suggested that the positive association of GGTP and triglyceride may reflect hepatic microsomal enzyme induction, with an increase in the hepatic content of enzymes related to triglyceride synthesis.[19] In support of this conjecture, PCBs are well known to induce hepatic microsomal (mixed function oxidase) enzymes both in laboratory animals[20] and in man.[21] Therefore, alterations in liver enzyme tests in association with increasing serum PCB concentration may not themselves be predictive of future chronic liver disease but may reflect liver microsomal enzyme induction. It should be emphasised, however, that the consistent inverse associations of log(H-PCB) with log(HDL-cholesterol) at all three worksites may have long-term cardiovascular significance, given the significant inverse, independent associations of HDL-cholesterol with coronary artery disease.[22]

In general, a lack of clinically apparent illness among workers with high levels of exposure to PCB and high serum PCB concentrations seems to have been the rule.[23–27] None the less, correlations of exposure to PCB or serum PCB concentrations have been reported with various clinical biochemical tests in the absence of clinically detectable disease, including positive correlations with SGOT[24 26] and GGTP[28] (Avitto V N. 15th annual meeting of US Public Health Service Professional Association, Houston, 26–29 May 1980), negative correlation with serum bilirubin,[29] and positive correlations with plasma cholesterol[28] and triglyceride.[5 30 31] More recently, however, findings of "dermatotoxicity" in association with increasing plasma PCB concentrations, and of increasing serum triglyceride concentrations in association with increasing plasma PCB concentrations, have been reported.[32] Two reports[33 34] from Italy have documented, among workers exposed to 54% chlorinated biphenyl in the manufacture of electrical capacitors, signs of "hepatotoxicity" (primarily hepatomegaly) along with rises of liver enzyme tests and four cases of chloracne (among 80 workers). No "definite association" was found between chloracne and blood PCB concentration. By contrast, abnormal liver enzyme tests and blood PCB concentrations, particularly trichlorobiphenyl blood concentrations, were positively associated.

One would expect that adverse human health effects from exposure to PCB, if they exist, would most readily be identified in groups with the greatest exposures (excluding poisoning attributable to accidental contamination of food). None of the published occupational or epidemiological studies (including ours), however, have shown that occupational exposure to PCBs is associated with any adverse health outcome, to be distinguished from

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