PCBS: HUMAN AND ENVIRONMENTAL HAZARDS

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Chapter 20 "The epidemiology of PCBs"

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CHAPTER 20

THE EPIDEMIOLOGY OF PCBs

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INTRODUCTION

This is a review and evaluation of the epidemiologic evidence concerning the health effects of exposure to polychlorinated biphenyls (PCBs), particularly at levels that do not cause acute toxic effects. A study is considered "epidemiologic evidence" if it measures, directly or indirectly, the differences in the risk of ill health among populations with different exposures to PCBs.

In the past several decades there have been many clinical studies of the effects of heavy exposures to PCBs (e.g., Von Wedel et al., 1943; Schwartz, 1936). Such studies are extremely useful in identifying the kinds of effects that should be investigated. However, they do not address the question of the risk of incurring such effects and are, therefore, not included in this review.

The studies reviewed here fall into three categories. First, there are studies of accidental heavy exposures and the resulting acute and chronic effects. In each case the study was prompted by an outbreak of illness or the occurrence of a death in an exposed population, after which the population was studied.

Second, there are studies of the relationship between exposure to PCBs and the resulting body burden of PCBs in serum or adipose tissue. Strictly speaking, these are not epidemiologic studies since they do not deal with health effects. However, if a relationship between level of exposure and body burden cannot be verified, the interpretation of epidemiologic studies becomes difficult if not impossible.

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and the proportion of persons reporting symptoms. Three years later about half the patients had improved, but still had symptoms. Six years later many patients still reported such symptoms as headache, stomach pain, numbness of the extremities, joint pain, and respiratory symptoms.

Out of ten live births to women affected by Yusho, nine showed hyperpigmentation and most had increased eye discharges. These symptoms later disappeared. Although there have been reports of premature eruption of teeth (2 children out of a series of 13) and unusally wide fontanelles and sagittal sutures (3 out of 13), it is not at all clear that these findings represent any more than the normal variation to be expected, since no control observations were made (Funatsu et al., 1972).

In general, laboratory tests of the Yusho victims showed elevated serum triglyceride levels, low serum cholesterol in serious cases, and elevated serum glutamic-oxaloacetic transaminase (SGOT) and serum glatamic-pyruvic transaminase (SGPT) levels in serious cases (Higuchi, 1976).

As of the end of 1977, fifty-one deaths among Yusho patients had been identified. The percentage of cancer deaths (35.4) exceeded that of the prefecture in which the deaths occurred (21.1). However, the figures do not appear to be very useful for several reasons. First, after the original incident, the criteria for diagnosis of Yusho had been changed, so that it is impossible to determine the denominator which produced this number. The completeness of ascertainment of the deaths is unknown. In addition, no adjustment for age appeared to have been made in the above comparison. Finally, the average elapsed time from exposure to death was less than ten years, and cannot be calculated precisely because the dates of death are not provided. This may well be too short a period for cancers resulting from the exposure to show up.

Although the Yusho incident represented a massive ingestion of PCBs, recent reanalysis of the cooking oil and of the estimated intake by the patients shows that the exposure to polychlorinated dibenzofurans (PCDFs) and polychlorinated quaterphenyls (PCQs) was about equal to the exposure to PCBs, and current determinations of PCQs in blood and other tissues of Yusho patients have shown levels similar to that of PCBs (Kimbrough, 1980). It is, therefore, doubtful whether any generalization can be made from this incident to lower level environmental or occupational exposures to PCBs.

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TABLE 1

Studies of Environmental Levels and Body Burden of PCBs by Type of Body Burden Measure

Study	Study Type[a]	High and Low Chlorinated PCBs	Adipose PCBs
Baker et al., 1980	A	No	No
Bumgarner et al., 1973	C	No	No
Chase et al., 1982	A,C	No	Yes
Hara et al., 1974, 1975	B,C	No	No
Hasegawa et al., 1972	A,B,C	No	No
Inoue et al., 1975	A,C	No	No
Karppanen and Kolho, 1973	A	No	Yes
Kitamura et al., 1973	B	No	No
Maroni et al., 1981a	A,C	Yes	No
Ouw et al., 1976	A,B	Yes	No
Smith et al., 1982	A,C	Yes	No

[a]A = Comparisons of groups with different exposure levels
B = Evaluation of results of decreasing or removing exposure
C = Comparisons of groups with different durations of exposure

All of the Type A studies agree in showing a higher body burden of PCBs in populations with higher environmental exposure, except for one anomaly in Baker et al. (1980). There, persons exposed to sludge containing PCBs had slightly lower blood levels than the controls, on the average. However, the sludge-exposed persons and the controls were not matched for age, which Kreiss et al. (1981) showed to be the most important factor associated with blood PCB level. It, therefore, appears unequivocal that higher exposure to PCBs means a higher body burden, all other things being equal.

The Type B studies appear at first glance to be more equivocal (Table 2). Two studies show a decrease when exposure ceased or decreased and two do not. However, the studies showing no decrease remeasured their study groups within a month or two after exposure changed. The ones showing a decrease remeasured after three months and one year.

The fact that Ouw et al. (1976) found no decrease after two months while Kitamura et al. (1973) found over a 50 percent

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TABLE 3

Studies of PCB Levels by Duration of Exposure

Study	Relationship of Blood PCB to		
	Duration of Exposure	Age	Race
Bumgarner et al., 1973	No	No	No
Chase et al., 1982	Yes	Yes	--
Hara et al., 1974, 1975	Yes	--	--
Hasegawa et al., 1972	No	--	--
Inoue et al., 1975	Yes	--	--

of high and low chlorinated blood PCBs versus present and past exposure, found no "evidence either to support or refute different accumulation kinetics in humans for the lower and higher chlorinated biphenyls". Nevertheless, they found a significant correlation between current personal air PCB levels and low chlorinated blood PCBs, but no significant correlation with high chlorinated blood PCBs.

In summary, body burdens of PCBs are clearly related to the level of exposure to environmental PCBs. Observations of a decrease in the burden of PCBs after exposure is eliminated or decreased are not consistent. The lack of consistency may be due to the short periods of observation of some of the studies, or possibly to differences in the average chlorination of the PCBs involved. Studies of the relationship of PCB burden to duration of exposure again are not consistent. There is a suggestion that this may be due to the confounding effects of age and sex, or to differences in the metabolism of high and low chlorinated PCBs, with the higher PCBs being more likely to accumulate in adipose tissue.

EPIDEMIOLOGIC STUDIES OF PCBs AND HEALTH

Excluding mortality studies, there are 18 epidemiologic studies of health effects related to PCB exposure. The accident report of Meigs et al. (1954) is included since it did not

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TABLE 4

PCB Epidemiology Studies (Other Than Mortality) and Summary of Findings[a]

Study	Dermatologic Findings	Physiological Parameters	Symptoms and Illness	Other
Alvares et al., 1977	--	Y	--	--
Baker et al., 1980	N	Y	N	--
Bumgarner et al., 1973	--	N	--	--
Chase et al., 1982	Y	Y	Y	--
Fischbein et al., 1979	Y	N	Y	--
Hara et al., 1974, 1975	Y	Y	--	--
Hasegawa et al., 1972	Y	Y	--	--
Inoue et al., 1975	Y	--	--	--
Kaappanen and Kolho, 1973	--	--	--	N
Kitamura et al., 1973	Y	N	--	--
Kreiss et al., 1981	--	Y	N	N
Maroni et al., 1981b	Y	Y	Y	--
Meigs et al., 1954	Y	Y	Y	--
MDPH, 1975	N	--	N	--
Ouw et al., 1976	Y	N	--	--
Smith et al., 1982	Y	Y	Y	--
SCDH, 1978	--	--	--	N
Warshaw et al., 1979	--	Y	Y	Y

[a]Y = Findings associated with exposure
N = No findings associated with exposure
No entry = No data presented

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high chlorinated blood PCBs suggests that this association may be real.

Liver Function

Ten studies examined liver function. Meigs et al. (1954) found one borderline abnormal liver function in 14 exposed workers. Hasegawa et al. (1972) found mild disturbances in exposed workers (increased SGOT, SGPT, SAP, decreased serum cholninesterase) which they did not consider to be clinically significant. Kitamura et al. (1973), Ouw et al. (1976), Fischbein et al. (1979), and Baker et al. (1980)(a non-occupational study) found no abnormalities associated with exposure, except that Ouw et al. (1976) found a high BSP retention in four out of seven workers with blood levels above 500 ug/kg.

Maroni et al. (1981b) found 16 out of 80 workers with abnormalities in GGT, OCT, and transaminases. Their blood PCB levels were higher than those in the workers with normal liver function. Kreiss et al. (1981)(non-occupational study) found no relation between liver function and blood PCBs when age and alcohol consumption were taken into account. Chase et al. (1982) found among exposed railroad workers a statistically significant correlation between blood PCBs and SGOT after adjusting for age. Smith et al. (1982) found elevated SGOT and GGT levels in persons with higher blood PCB levels.

In summary, six studies of the ten found some mild liver function abnormalities, none of which were associated with any measurable adverse health effects. The two non-occupational studies, Baker et al. (1980) and Kreiss et al. (1981), found no abnormalities associated with blood PCB leve. Fischbein et al. (1979) in their study of capacitor manufacturing workers, noted that "there was a paucity of abnormal results in the biochemical studies."

Finally, Alvares et al. (1977) reported that in five workers occupationally exposed to PCBs, the rate of drug metabolism was significantly higher than in a group of controls matched for age, sex, and smoking and drinking habits.

Fat Metabolism

Six studies considered cholesterol levels. One (Bumgarner et al., 1973) found no relationship between cholesterol level and blood PCB level. One of the remaining five (Hasegawa et al., 1972) found a decrease in cholesterol, glycerides,

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weight loss, anorexia, fatigue, headache, eye irritation, cough, shortness of breath, nausea, vomiting, diarrhea, abdominal pain, arthralgia, and persistent rash. The third study (Kreiss et al., 1981) reported the same thing for prevalence of illness or weight loss in the preceding year, use of medication, use of medical care, history of heart disease, and percentage of pregnancies ending in miscarriage, stillbirth, or infant death.

Of the occupational studies, Chase et al. (1982) reported no evidence of organ toxicity from the medical histories or physical examinations of 86 exposed railroad workers. Three studies reported various symptoms. Fischbein et al. (1979) reported a history of gastrointestinal symptoms in 18 percent of 326 capacitor manufacturing workers, a prevalence of from 3.0 to 15.2 percent of various musculoskeletal symptoms, and a prevalence of from 4.8 to 27.8 of various neurological symptoms. These were, however, unrelated to duration of employment or to level of blood PCBs. Maroni et al. (1981b) reported eight cases of gastrointestinal complaints in 80 exposed workers, with no indication of whether there was a relationship to duration of employment. They also reported two bleeding haemangiomas and one case of chronic myelocytic leukemia. These findings do not appear to have any significance, since they apparently are unrelated to the circumstances of exposure.

Smith et al. (1982) reported an increased prevalence of general malaise and possibly altered peripheral sensation with increased blood PCB levels among occupationally exposed workers, but found no clinical abnormalities on physical examination.

Finally, one study of pulmonary function (Warshaw et al., 1979) reported decreased vital capacity in 243 capacitor workers. However, the pulmonary function values in the study population, most of whom were current or ex-smokers, were compared with a standard population of non-smokers, so that the effect of smoking was not taken into account.

The weight of evidence, as Smith et al. (1982) conclude, is that no studies to date "have shown that occupational exposure to PCBs is associated with any adverse health outcome, to be distinguished from demonstrable subclinical biochemical alterations."

There appear to be no significant clinical effects associated with the occupational or environmental exposures studied in these reports.

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TABLE 5

Inconsistencies in Studies of Cancer in PCB Exposed Populations With Findings

Study	Number Studied	Findings
Bahn et al., 1976; 1977	92	Melanoma[a]
Zack and Musch, 1982	89	Lung
Brown and Jones, 1981	2,567	Liver Rectum
Bertazzi et al., 1981	1,310	Digestive[b], Lymphatic, and hematopoietic

[a]Significant at 1 percent level
[b]Significant at 5 percent level

Brown and Jones (1981) studies 2,567 workers in a capacitor plant. About half the cohort had a latency period of 20 yrs or more. Although there was an excess of liver cancer deaths, it was inversely related to duration and latency of exposure, which does not support an occupational explanation. There was also an excess of rectal cancer. However, the two plants studied are located in an area whose mortality from rectal cancer is greater than the U.S. average (Mason et al., 1975). Since U.S. population rates were used as a basis for comparison, the rectal cancer excess is at least partly an artifact.

Bertazzi et al. (1981) studied 1,310 workers with at least six months employment in capacitor manufacturing between 1946 and 1970. Although excess digestive cancer was observed, there were no liver cancer deaths. The total number of deaths was small (27) and the excess cancer observed was based on two or three deaths for each of the two major sites involved. There is no indication of the duration or latency of exposure for the cancer deaths. The authors state that there were no other major exposures at the plant, and propose to continue the study with a larger cohort. In spite of the statistical significance of the excesses from all cancers, this study must be considered a preliminary report, particularly since it shares with the other studies a failure to agree on any particular pattern of mortality.

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exposures. However, they do exhibit a pattern, which is that none of the studies agree on the cancer sites at which an excess mortality was found, and the excesses that were found are in general not statistically significant. One must conclude that the findings of the mortality studies reflect a sporadic pattern of excess mortality at different sites which is not consistent with a carcinogenic effect of PCBs. In addition, where an examination of duration and latency of exposure was possible, no association with these variables was found (Brown et al., 1981).

Taken as a whole, the epidemiologic studies find that high occupational exposures to PCBs may cause dermatitis of various kinds, but that there are no other clinically observable effects, including the occurrence of cancer.

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