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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The third category is studies that were done because the populations in question were known or suspected to be exposed to PCBs, rather than because some untoward health outcome had been observed first.

Many published reports combine some or all of these types of investigations. In the sections that follow, we consider first the studies of accidental over-exposure; second, the studies of PCB exposure versus body burden; and third, the epidemiologic studies of exposed populations. In the latter section, the discussion will be organized with respect to the health effects that were investigated. These are:

(1) dermatologic symptoms,
(2) biochemical alterations,
(3) other symptoms and illnesses,
(4) carcinogenicity.

ACCIDENTAL HEAVY EXPOSURE

Two epidemiologic studies of accidental exposure have been reported. The first (Heiga et al., 1954) described an outbreak of chloracne in a plant in which a process change had introduced an unspecified PCB compound into the work environment. Breathing zone levels of PCB were stated to be 0.1 mg/m^3. Seven of 14 exposed workers developed chloracne, but liver function tests were normal in six of these, with some borderline abnormalities in the seventh. The chloracne disappeared after treatment, and the single borderline liver function abnormality improved, but did not disappear after 13 months. Improved process control prevented any recurrence.

Although the estimated PCB level must be accepted with reservation because of the state of the art at that time, it is clear that the chloracne resulted from the PCB exposure. Given the lack of controls and the small rate of abnormal liver function, it is unlikely that the PCB exposure had any connection with the liver function findings.

The second incident is the now famous Yusho incident in 1968 which has been documented in many reports (Kuratsune et al., 1972; Urabe et al., 1979) in which some thousand Japanese became ill after eating cooking oil which had been contaminated with Kanechlor 400, a PCB compound of Japanese manufacture.

The most common acute symptoms observed were hyperpigmentation and acne-like lesions, discharge from the eyes, central nervous system symptoms, and vomiting and diarrhea. There was a dose-response relationship between the amount of oil ingested

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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 unusually 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 (Funatau 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 generelization can be made from this incident to lower level environmental or occupational exposures to PCBs.

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ENVIRONMENTAL LEVELS AND BODY BURDENS

Two studies of the relationship between ingestion of PCBs and blood levels of PCBs have been reported (MDPH, 1975; Kreiss et al., 1981). In each case the study was concerned with ingestion of fish known to contain relatively high levels of PCBs. In the first, an association was found between blood PCBs and exposure level as estimated by the amount of Lake Michigan sport fish consumed. In the second, the relationship between blood PCBs and a complex of factors was examined in a population in an area with high levels of environmental contamination. Age, sex, and fish consumption, in that order of importance, were associated with blood levels of PCBs. To the extent that fish consumption measures ingestion of PCBs, these studies confirm that blood PCBs are a function of ingestion of PCBs as well as of age and sex. Other associated variables were examined in Kreiss et al. (1981) but will be discussed in the following section.

A number of studies of blood PCBs and exposure to PCBs have been made, most of them in conjunction with studies of health effects. The portions of the studies relevant to this section are reviewed here.

There are three types of studies. The first compares groups which have had different exposure levels as estimated from process considerations or environmental measurements. For convenience, such a study design will be called Type A. The second, which we will designate Type B, measures the change over time in a single group after PCBs have been removed from the environment (or after the group has left the environment). The third, Type C, compares groups that have had different durations of exposure. Often the same report will contain more than one type of study. For example, an exposed group may be compared with an unexposed group (Type A) and within the exposed group long-term exposed workers may be compared with short-term workers (Type C).

The measure of body burden has in most cases been a single number representing, depending on the study, blood PCBs, plasma PCBs, serum PCBs (all of which are called "blood" PCBs in this review), or level of PCBs in adipose tissue. Analytic methods have varied over time and among investigators. More recently, measures of body burden have sought to determine seperately the levels of higher chlorinated biphenyls (5 or more chlorine atoms per molecule) and lower chlorinated biphenyls.

Table 1 lists the studies considered in this section, with the type of design and whether or not separate determinations of higher and lower chlorinated biphenyls were made. All of the studies except Baker et al. (1980) are occupational.

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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
Meroni 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 2

Studies of Blood PCB Levels Before and After Exposure Levels Changed, and Interval From Exposure Change to Remeasurement

Study	Exposure Change	Interval to Remeasurement (months)	Decrease in Blood PCB Level (percent)
Hara et al., 1974, 1975	Ceased	12	ca75
Hasegawa et al., 1972	Ceased	1	None
Kitamura et al., 1973	Ceased	3	>50
Ouw et al., 1976	Decreased	2	None

decrease after three months gives rise to some uneasiness. However, in the former study exposure was decreased but still present, while in the latter study PCB use had ceased. Ouw et al. (1976) also suggest that after exposures in their study plant had decreased, workers did not wear gloves as recommended, so that the blood PCB levels may have resulted from skin contact.

Table 3 shows the findings for the Type C studies other than Maroni et al. (1981a) and Smith et al. (1982) that is, for those that compared duration of exposure with a single measurement of blood PCB level. The results are not consistent. The study of Bumgerner et al. (1973) found very low levels (average 4 ug/kg) in exposed workers, which may have accounted for their failure to find a relationship with duration. On the other hand, the exposed workers in Hasegawa et al. (1977) had an average level of 370 ug/kg and still showed no relationship with duration.

The studies of Maroni et al. (1981a) and Smith et al. (1982) suggest a possible explanation. Maroni et al. (1981a) made separate comparisons of high chlorinated PCBs and low chlorinated PCBs between workers with present and past exposures. They found differences in the low chlorinated PCBs but not in the high chlorinated compounds. Even though their analysis did not adjust for age, it suggests that the relationship between blood PCB levels and duration and recency of exposure may be a function of the level of chlorination of the PCBs. Smith et al. (1982), however, in an elaborate analysis

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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	--
Hare 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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differ in design from many of the studies that were not motivated by accident reports.

These studies are listed in Table 4 with a summary of the findings by major category. Five of the reports are in Japanese (Hara et al., 1974, 1975; Hasegawa et al., 1972; Inoue et al., 1975; Kitamura et al., 1973). The details of those studies are taken from the NIOSH criteria document for PCBs (NIOSH, 1977).

Two of the studies (Kaappanen and Kolho, 1973; SCDH, 1978) are not specific as to health effects. The first of these is a comparison of groups with different work exposures and different blood PCB levels (74-1900 ug/kg in the 12 persons with the greatest exposure) in which the authors simply state that all persons studied were in good health. The second is a study of 32 workers in a capacitor plant, 10 of whom were exposed regularly to PCBs. The authors state that there is "no evidence of physical harm resulting from working with PCBs".

The remaining 16 studies in Table 4 are reviewed below with respect to their findings in each major category of health effects. The studies are considered in the order of their population.

Dermatologic Effects

There are 12 studies of dermatologic effects associated with PCB exposure. The first is Meigs et al. (1954) described in the above section on accidental heavy exposure, who found that 7 of 14 exposed workers got chloracne where the PCB concentration in their breathing zones averaged 0.1 mg/m^3. Hasegawa et al. (1972) reported an unstated number of cases of hyperpigmentation of the hands, and acne-like lesions of the jaw, back, and thighs in exposed workers. The average blood PCBs in the workers was 370 ug/kg. However, the authors state that skin complaints were unrelated to blood PCB levels and appeared to be due to skin contact. Kitamura et al. (1973) reported a range of skin disorders in 10 of 13 exposed workers with an average blood level of 820 ug/kg. The disorders occurred on parts of the body not normally in direct contact with PCBs. Hara et al. (1974, 1975) reported that about 45 percent of 118 capacitor workers complained of blackheads and other acne-like symptoms while working with PCBs. The complaints were not related to blood levels of PCBs, and virtually disappeared within a year after exposure had ceased.

Inoue et al. (1975) reported one case of chloracne in an exposed worked whose blood PCBs were in the 190 to 210 ug/kg range, but no symptoms in the rest of a small work force whose

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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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blood PCBs ranged from 130 to 520 ug/kg. The Michigan Department of Public Health (1975) reported no relationship of any Yusho symptoms to consumption of fish with high levels of PCBs. Ouw et al. (1976) reported 14 cases of dermatitis, eye irritation, or burning sensations on the skin out of 34 exposed workers, where air levels of PCBs ranged from 0.32 to 2.22 mg/m^3. The complaints appeared to occur more often in those with higher blood PCB levels. Fischbein et al. (1979) reported that about 50 percent of 326 capacitor manufacturing workers reported a history of dermatological symptoms, the most common symptom being a rash. Those with symptoms had higher blood levels of high chlorinated PCBs. Baker et al. (1980) reported no chloracne in 18 exposed workers (average blood PCBs 75.1 ug/kg) or 19 members of their families (average blood PCBs 33.6 ug/kg). Maroni et al. (1981b) reported 10 cases of dermatitis (5 diagnosed as active or past chloracne) out of 80 exposed workers. The average blood PCB level in the study was 342 ug/kg. Chase et al. (1982) observed chloracne and an increase in other dermatological findings in 86 exposed male railroad workers, but the findings were not significantly associated with blood or fat PCB levels. Smith et al. (1982) found no chloracne in a study population of 324 exposed workers in capacitor manufacturing and transformer repair, whose average blood PCBs ranged from 38 to 546 ug/kg. However, there was a significant association of skin rash or dermatitis with blood levels of high chlorinated PCBs.

Interpretation of this mass of data is complicated by the difficulty of diagnosing chloracne, the uncertainties of blood PCB determinations, and the changing technology for making such determinations. Nevertheless, the data suggest strongly that when PCB blood levels exceed about 150 to 200 ug/kg, chloracne can occur. However, most studies have shown that the occurrence of chloracne is not further associated with blood PCB levels. This suggests that (a) personal idiosynoratic factors may be involved and/or (b) that the high blood levels are an indicator of the existence of environmental contamination which actually produces chloracne by skin contact.

The reports of dermatitis other than chloracne suffer from an additional complication. According to the National Health Survey, about one-third of all Americans of working age have at least one current skin condition serious enough to warrant evaluation by a physician (NCHS, 1979). Clearly, substantially more than one-third must have either a current condition or a history of such a condition in the past. The prevalance figures reported by Maroni et al. (1981b) and Fischbein et al. (1979) are, therefore, not in themselves remarkable, but the agreement of Fischbein et al. (1979) and Smith et al. (1982) on the relationship between dermatitis and

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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 cholinesterase) 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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phospholipide, and beta-lipoprotein in exposed workers. Three of the other four studies found no relationship of cholesterol to blood PCBs (Baker et al., 1980; Chase et al., 1982; Smith et al., 1982) while one found increased cholesterol at higher blood levels of PCBs (Kreiss et al., 1981). Kreiss et al.)1981) and Smith et al. (1982) also present contradictory findings with respect to HDL cholesterol levels; the former found no relationship to blood PCBs, but the latter found an inverse relationship.

Five studies examined triglyceride levels. Four found an increase with increased blood PCBs (Hara et al., 1974, 1975; Baker et al., 1980; Chase et al., 1982; Smith et al., 1982) while one found no relationship when cholesterol level was taken into account (Kreiss et al., 1981).

In summary, most studies, including one non-occupational study, have associated increased triglycerides with PCB exposure. The data on cholesterol show no relationship in three studies, and an increase and decrease in one study each. HDL cholesterol either decreased or was unchanged (one study each). Even if PCB exposure has some effect on fat metabolism, it appears to be without any apparent clinical significance.

Blood and Blood Pressure

There are five studies of blood chemistry: Bumgarner et al. (1973), Kitamura et al. (1973), Fischbein et al. (1979), Baker et al. (1980), and Maroni et al. (1981b). None of them report any relationship of blood chemistry to PCB levels.

Bumgarner et al. (1973) and Kreiss et al. (1981) measured blood pressure in exposed persons. Bumgarner et al. (1973) found no association with PCBs, but Kreiss et al. (1981) found a statistically significant association between diastolic blood pressure and blood PCBs. Since there was no control group and since Kreiss et al. (1981) are the only investigators to report this finding, its significance is not clear at this time.

Symptoms, Illness, and Other Conditions

Eight studies investigated symptoms, illness, and other conditions in persons exposed to PCBs. None of the three non-occupational studies reported any abnormalities. The first of these (MDPH, 1975) compared the incidence of 18 conditions, most of which were reported in Yusho disease, in consumers of sports fish containing PCBs and in controls. The second (Baker et al., 1980) found none of the following conditions were associated with blood PCB levels in a community study; fever,

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weight loss, anorexia, fatigue, headache, eye irritation, cough, shortness of breath, nausea, vomiting, diarrhea, abdominal pain, arthralgia, and persistant 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 prevalance 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 apperently 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 (Wareham 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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Carcinogenicity

It is generally agreed that epidemiologic evidence for carcinogenicity should fulfill certain requirements in order to be acceptable. These requirements, presented below, deal with the study design, the logic of the observed pattern, and the repeatability of the results (Doll, 1981).

(1) Positive associations in groups of individuals with known exposure (case-control or cohort studies).

(2) That are not explained by bias in recording or detection.

(3) That are not explained by confounding.

(4) That are not explained by chance.

(5) That vary appropriately with dose.

(6) That vary appropriately with period of exposure.

(7) That are observed repeatedly in different circumstances.

There are four studies directed solely or primarily to the question of the carcinogenicity of PCBs. Table 5 lists the studies and their findings. They are reviewed here keeping in mind Doll's requirements.

The most obvious feature in Table 5 is that no study agrees with any other. That is, the requirement of repeatability is not met.

The first study by Bahn et al. (1976, 1977) observed three melanomas in a group of 92 research and development and refinery workers. These workers had an unknown exposure to other possible carcinogens, so that there could have been confounding. In any case, the study was withdrawn for revision in the definition of the exposed population, and has not yet been released (NIOSH, 1977).

Zack and Musch (1982) studied 89 Monsanto workers exposed for at least six months between 1945 and 1965 inclusive. There were no deaths from cancer of the liver or cirrhosis. The excess in respiratory cancer was based on four deaths and was not statistically significant. As with Bahn et al. (1976, 1977), there was confounding because of other chemical exposure at the plant and, in this case, possibly cigarette smoking.

TABLE 5

Inconsistencies in Studies of Cancer in PCB Exposed Populations With Findings

Study	Number Studied	Findings
Bahn et al., 1976; 1977	92	Malanoma[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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The existing mortality studies of occupational exposure do not show the agreement that would lead one to infer an excess risk of cancer. Much of the conflicting findings can be attributed to the possible effect of confounding exposures, and to the "noise level" of sporadic excesses which would be expected in the absence of any occupational hazard.

SUMMARY AND CONCLUSIONS

The epidemiologic studies of exposure to PCBs show that the body burden in exposed persons, whether the exposure is by ingestion, inhalation, or skin contact, is related to the environmental levels and distribution of PCB. The relation of body burden to duration of exposure is less clear, and appears to differ depending on the degree of chlorination of the PCBs. Nevertheless, the evidence is clear that higher exposures mean higher blood PCB levels, and that persons with occupational exposures have blood PCB levels that may be an order of magnitude greater than that of environmentally (that is, non-occupationally) exposed persons.

Occupational exposure to PCBs at high levels has been associated with the occurrence of chloracne, but the relationship is not straightforward, suggesting that the actual risk of chloracne is also a function of individual susceptibility and personal work habits, as well as possible exposure to other contaminants.

Dermatologic problems other than chloracne are associated with occupational exposure, and may be related to exposure to high chlorinated PCBs.

Alterations of liver function and fat metabolism associated with PCB exposure have been observed in several studies, but are characterized by investigators as mild and of no clinical significance.

The one fact on which all occupational studies of health effects agree is that there has been no clinical illness associated with PCB exposure other than dermatitis. Studies of non-occupationally exposed populations have found neither dermatitis nor other clinical evidence of exposure-related effects, with the exception of a single study which suggests that diastolic blood pressure may be related to blood level of PCBs.

Mortality studies concerned primarily with cancer present problems of interpretation due to the small sample size of some of the studies, and to the confounding effect of other

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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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