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Human Exposure to Polychlorinated Biphenyls and Polybrominated Biphenyls

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Polychlorinated Biphenyls

Introduction

Although the polychlorinated biphenyls (PCBs) have been used in a wide variety of industrial applications in the U. S. from 1930 until 1970, when their distribution was voluntarily restricted to closed systems, there is scant information on human exposure to adverse human health effects in the U. S. In the U. S., minimal human exposure of the population to PCBs is limited to food, air, and water, while significant human exposure appears to be limited to sports fishermen consuming fresh water fish from contaminated streams and lakes; and to occupational exposure in industrial workers.

Dietary Exposure to PCBs

The May 1972 Report of the Interdepartmental Task Force on PCBs (*1*) summarized the findings in food sampling programs conducted by the Food and Drug Administration and the Department of Agriculture. Jelinek et al. (*2*) have provided an update to that summary and evaluated trends which is presented below.

The 1972 Task Force report (*1*) outlined three broad sources of food contamination. These are restated here in order to show which sources have been effectively controlled and which sources apparently persist, as reflected by results obtained in continued food sampling: (1) environmental contamination (background levels of PCBs in fish from lakes and streams); (2) industrial accidents (isolated incidents involving direct leakage and spillage or contact of PCB fluids and other PCB containing materials on animal feeds, feed ingredients, or food); (3) food packaging materials (PCB migration to food packaged in PCB-contaminated paper products).

As discussed in the 1972 Task Force report (*1*), there were a number of other positive findings in foods which could not be traced to one of these broad sources prior to 1972 and the source of such occasional findings remain speculative. However, in more recent years, essentially all positive findings of PCBs in the food supply have been attributable to one or more of these three sources.

Jelinek and Corneliussen (*2*) reported that for the 1969-1975 period, there has been a significant decrease in PCB levels in all foods with the exception of fish, where no particular trend has been noted. From that observation they concluded that procedures instituted to exclude the use of PCBs in "open" applications have been effective, but that more needs to be done to prevent their entry into the aquatic environment.

Jelinek and Corneliussen (*2*) presented data on

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FDA's sampling program showing a very conclusive decline in FY 1973–1975 period in terms of occurrence rate of PCBs and maximum levels found in milk, eggs, cheese, animal feeds and components, processed fruits, and baby foods. Except for fish, occurrence rates in FY 1975 had dropped to zero or less than 1% for all categories, and there were no findings in excess of the existing temporary tolerances. Similar data were presented covering USDA's sampling of meat and poultry which also showed a decline, to 0.3% positive and only 0.6% above the temporary tolerance.

Jelinek and Corneliussen (2) also reviewed FDA Total Diet Study findings (FY '71-75), which showed that all food classes of the total diet have declined to no PCB occurrence and no calculable daily intake of PCBs, except in the meat-fish-poultry composites. About 40% of these composites continue to contain detectable PCBs, although only traces have been detected in the latter years. The limit of quantitative detection in the Total Diet Study is about 0.05 ppm: positive findings below that level are generally reported as traces since they are not reliably quantitated.

Occurrence of PCBs ended in 1973 in all other categories, notably in dairy product composites and the composites of grain and cereal products. This probably reflects the control measures effected on animal feeds and on the control of ingredients in recycled paper used for food packaging. What remains, based on the Total Diet Study, is a continued low level occurrence (about 40% positive and only at trace levels) in the meat-fish-poultry composites. The fact that levels in these composites have declined to only traces further supports the inference that the meat and poultry and eggs no longer contain detectable PCBs and that the low level findings are primarily due to the fish in those composites. This would imply that the PCB levels in the diet may have "bottomed out" and may remain static until such time as there is a change in the levels for fish.

Estimates of dietary intake of PCBs based on the Total Diet Study must be taken as gross estimates because only traces are currently found and some type of estimated value must be assigned to those traces to calculate microgram per day intakes of PCBs. Jelinek and Corneliussen (2) used a set of consistent assumptions for those traces in computing the daily intakes for the FY '71–75 period. Their calculations showed a steady decline from 15 μg/day down to 8.7 μg/day, with all of this coming from the meat-fish-poultry group in FY '74-75 (minor and declining portions attributable to other food classes in earlier years).

Review of this information implies that, although the various assumptions for trace residue reportings and varying food consumption data have a significant effect on daily intake calculations, an overall estimate in the order of 5-10 μg/day PCB dietary intake of PCBs for the general public seems reasonable. This figure would not be applicable to diets which may include regular consumption of fish from certain locations with high PCB levels.

PCB Residues in Fish

Review of the data gathered by various agencies on fish residues indicates a serious incompatibility of sampling programs for obtaining data which reliably define trends in PCB levels. The Food and Drug Administration's primary concern is the levels which exist in the edible portion of commercially imported fish which are marketed interstate. Therefore, in most cases, the heads, entrails, skin, and fins are excluded. Furthermore, FDA sampling has not included fish which are caught and consumed locally (freshwater fish) and the sampling has dealt with the most important consumption species which are primarily of marine origin and which generally do not contain PCB levels as high as freshwater species from certain locations.

In order to determine the human exposure to PCBs through dietary fish, one must know the levels of PCBs residues in the edible portions of fish, and the amounts of the various kinds of fish consumed by the population at large, and by special subpopulations. Information has recently been compiled by the National Marine Fisheries Service-NOAA (3) on the PCBs levels of these residues in marine and freshwater fish and shellfish, and on dietary habits.

Table 1 lists the 20 most important types of fish eaten in the U. S. today and the mean daily amount of each type eaten by the subpopulations of actual users. Table 1 includes all dietary fish, from sport fishing and from domestic and imported commercial fishing. These 20 items comprise 95% of the fish products eaten. The results are taken from information in a recent seafood consumption study, sponsored by the Tuna Research Foundation, by the National Purchase Diary of Schaumburg, Illinois (4), and National Marine Fisheries Service data on the amount of fish and shellfish processed and distributed in the U. S. Several items in Table 1 are worth noting for purposes of the present analysis. Although 93% of the U. S. population (197 million) eat fish, the average annual per capital consumption of fish is small: 15.0 lb/year; a large "unclassified" fish fraction exists in the U. S. diet, ranking just below tuna in importance; the major portion of many of our most familiar types of seafood is imported; and freshwater species, led by trout, bass,

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and catfish, comprise about 9% of our total fish diet.

A compilation of PCB data, representing the results of all the measurements known to NMFS of PCBs in fish used in the U. S. diet is presented in the Compendium of PCB Data (*4*). It includes data from government reports, and state and private publications. An effort was made to include current, unpublished data from marine laboratories. The compilation includes the results of a comprehensive literature search by the NOAA-Environmental Data Service (EDS). An EDS-ENDEX data search for unpublished data and a EDS-OASIS search were made, crossing marine food species with PCBs.

Two significant sources of data—the 1975 FDA-Market Basket results, and the results of the extensive analyses by the New York State Department of Environmental Analyses (*5*)—were not available to NMFS at the time the Compendium (*4*) was published. However, FDA has indicated that the 1975 Market Basket results do not differ dramatically from 1973/4 data. Preliminary results of the New York study are included in Table 3 below.

Table 2 summarizes the PCB information assembled in the Compendium relating to the 20 most important kinds of dietary fish identified in Table 1. Although at one time or another, some PCB measurements have been made on many fish, Table 1 points out the inadequacy of information on PCB residues in the most important items in the fish diet. Sampling and analysis have been sporadic and not designed to monitor trends in human exposure. Systematic surveys of neither the important items nor the species most likely to be contaminated have been undertaken. Very few recent measurements have been reported.

However fragmentary the data on PCB levels may be, they do not include a single measurement exceeding 1 ppm in any of the ten most important fish foods, except for Dover sole and crab taken in the immediate vicinity of Los Angeles sewerage outfalls, and crab living on contaminated sediments in Upper Chesapeake Bay. No more than 1.6 ppm has been reported in items 11 through 20 in importance, with the exception of freshwater bass and catfish living in river and lake areas known to be contaminated with PCBs. Nonetheless, as emphasized in Table 2, there have been no PCB measurements on the important unclassified dietary fish items, and the analytical information is in no instance systematic enough to permit an estimate of the actual mean PCB values, hence human exposure. The strongest statement that can be made, based on the incomplete data summarized in the Compendium (*4*), is the most of the important fish

Table 1. Fish and shellfish consumption in the United States (September 1973–August 1974).[a]

	Rank	Amount, 10^6 lb/yr	Percent of total by weight	Number of actual users (millions)	Mean amount per user, g/day
Total		2957	100.	197	18.7
Tuna (mainly canned)	1	634	21.4	130	6.1
Unclassified (mainly breaded, including fish sticks)	2	542	18.4	68	10.0
Shrimp	3	301	10.2	45	8.3
Ocean perch[b]	4	149	5.0	19	9.7
Flounder	5	144	4.9	31	8.6
Clams	6	113	3.8	18	7.6
Crabs/lobsters	7	110	3.7	13	10.6
Salmon	8	101	3.4	19	6.7
Oysters/scallops	9	88	3.0	14	7.8
Trout[c]	9	88	3.0	9	12.3
Cod[b]	11	78	2.7	12	8.1
Bass[c]	12	73	2.5	7.6	12.0
Catfish[c]	12	73	2.5	7.5	12.1
Haddock[b]	12	73	2.5	11	8.6
Pollock[b]	15	60	2.0	11	6.8
Herring/smelt					
Sardines	16	54	1.8	10	6.7
Pike[c]	17	35	1.2	2.5	17.4
Halibut[b]	18	32	1.1	5.0	8.0
Snapper	18	32	1.1	4.3	9.3
Whiting	20	25	0.9	3.2	9.7
All other classified		152	5.1		

[a] NMFS data (*3*).
[b] Mainly imports.
[c] Fresh water.

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meat items eaten in the U. S. probably contain mean PCB residue levels well below 1 ppm.

Fragmentary evidence also leads to the conclusion that the PCB levels in fish liver, roe, and oil are approximately ten times that in the edible muscle and the PCB concentrations are greatest in the older, larger, oily fish, especially those that spend part or all of their lives in contaminated lakes, rivers or estuaries.

Table 3 lists the location of the species in which

Table 2. Maximum reported PCB residue levels in fish muscle (white meat).

Rank[a]	Kind	Range and max. level reported, ppm		Mean level in the U. S. diet
1	Tuna	0–0.49	(1973)	Unknown[b]
2	Unclassified (mainly breaded)	no data		Unknown
3	Shrimp	0–0.167	(1971)	Unknown
4	Ocean perch	0–0.25	(1974)	Unknown[b]
5	Flounder/sole	0.6.3[c]	(1972)	Unknown[b]
6	Clams	0–0.819	(1974)	Unknown[b]
7	Crabs/lobster	0–4.9[d]	(1972)	Unknown[b]
8	Salmon	0–0.5	(1974)	Unknown[b]
9	Oysters, scallops	0–0.43	(1974)	Unknown[b]
10	Trout (excluding lake trout)	0–0.56	(1972)	Unknown[b]
11	Cod	0–0.4	(1974)	Unknown[b]
12	Bass	0.3–8.4[e]	(1974)	Unknown[b]
13	Catfish	0–4.4[f]	(1974)	Unknown[b]
14	Haddock	0–1.16	(1974)	Unknown[b]
15	Pollock	0.0	(1974)	Unknown[b]
16	Herring/smelt/sardines (marine)	0–1.6	(1974)	Unknown[b]
17	Pike	0–0.65	(1974)	Unknown[b]
18	Halibut	0–0.149	(1974)	Unknown[b]
19	Snapper	0–0.1	(1974)	unknown[b]
20	Whiting	0.0	(1974)	Unknown[b]

[a] These 20 items compose 95% of the fish in the U. S. diet.

[b] Probably well below 1 ppm.

[c] Single Dover sole taken near Los Angeles municipal sewerage outfall. The mean value of sole samples taken in this vicinity was 1.3 ppm in 1975. Mean values of other samples taken away from outfalls were less than 1 ppm in 1975. In any case, although Dover sole is an important food fish in Northern California, it is not taken commercially in Southern California waters.

[d] Single yellowneck crab taken near Los Angeles outfall-mean of group including this crab was less than 1 ppm. A composite of Upper Chesapeake Bay crabs contained 1.2 ppm in 1974.

[e] Taken in 1974 from St. Croix River, Wisconsin; mean of four white bass was 6.2 ppm.

[f] Taken from Mississippi River, Minnesota, mean of a sample of five catfish was 2.5 ppm.

Table 3. Areas where at least one example of high PCB residue levels (> 5 ppm) levels have been reported in the listed species.[a]

Species	Location
Striped bass	Hudson River, N. J.
Chub	Lake Michigan
Carp	Mississippi River, Minn., Lake Onandaga, N. Y.
Chain pickerel, alewife	Hudson River
Coho salmon	Lake Michigan, Lake Ontario, Hudson River
Chinook salmon	Lake Michigan, Lake Ontario, Hudson River
Steelhead trout	Lake Michigan, Lake Ontario
Lake Trout	Lake Michigan, Lake Ontario, Lake George, N. Y.
Smallmouth bass	Lake Onandaga, Genessee River, N. Y. Hudson River, Mohawk River, St. Lawrence River
White perch	Lake Onandaga, Hudson River
Alewife	Hudson River
White sucker	Hudson River, Mohawk River
Walleye	Hudson River, Mohawk River, Black River, N. Y.
Largemouth bass	Hudson River, Mohawk River
Yellow perch	Hudson River
American eel, crabs, sturgeon	Hudson River
Rock bass, catfish	Hudson River
Bluefish	Long Island Sound (muscle from one large oil fish contained 8 ppm)

[a] Includes recent data from New York State Department of Environmental Conservation not included in the NMFS compilation. The Hudson River above Fort Edward, N. Y., is not contaminated with PCBs, and the residue levels in fish are quite low.

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high PCB levels, exceeding the FDA 5 ppm guideline, have been reported. Although the trout, salmon, and chub in Lakes Michigan and Ontario and the Hudson River bass, perch, and eel constitute only a few percent at most of the national fish diet, in some areas they are a significant part of the fish diets.

In order to discover what is presently known about U. S. fish consumption habits, numerous government and private sources were consulted. A number of pre-1970 studies are available, including a 1969 NMFS Survey of Fish Purchases (*6*) and a 1968-70 HEW Ten State Nutrition Survey (*7*). In addition, a few specialized reports have been published, including annual FDA Regional Basket Surveys (*8*) that do not include fish eaten in restaurants and institutions or by sport fishermen, and surveys by the Sport Fishing Institute (*9*) and a 1974 Texas A&M Analysis of Seafood Consumption Patterns in Texas (*10*). However, the most up to date and comprehensive data are available in the previously mentioned 1973-74 Seafood Consumption Study by the National Purchase Diary (*4*).

Table 4 summarizes results of fish consumption demographic information that defines the number of U. S. consumers who would exceed an arbitrarily set dietary microconstituent level. To date, this kind of information is available only for total dietary fish and one subcomponent, tuna. Table 4 indicates that 75 million U. S. consumers eat more than the national average of 18.7 g fish per day and 29 million would exceed the present dietary intake limit of PCB (175 μg/day) if the 35 or more g/day of fish eaten was contaminated on average to 5 ppm, the current FDA guideline level. There is, of course, no evidence that the mean PCB level in fish is anywhere near 5 ppm. Nonetheless, should it in the future reach 1 ppm, then by an extrapolation from Table 4, an estimate can be made that about 200,000 U. S. consumers would be exceeding the 200 μg/day FDA limit. As another hypothetical case, if the PCB level in tuna should ever reach 1 ppm, then about 5,000 tuna fish consumers, those who eat in excess of 175 g/day, would exceed the 200 μg/day limit from tuna alone.

Table 4. Distribution of fish consumption by U. S. consumers.[a]

Level of consumption, g/day	Number, thousands of consumers	
	Total fish	Tuna
0	197,000	130,000
18.7 (national avg.)	75,000	5,700
35	29,000	1,300
50	14,000	400
100	2,000	43
150	400	10

[a] Derived from graphs on pp. 21 and 23 of the Seafood Consumption Study (*4*).

Survey data do show that in general U. S. fish eaters include a wide variety of fish items in their diet. Thus, even if certain items contain toxic micro-constituents at or near FDA guideline level, the great majority of consumers would receive only a small fraction of their average dietary intake from these sources.

Clearly, there is a need for demographic information, similar to that available on total fish and tuna, on the other principal foodfish items in the U. S. diet; and a need to extend and better measure the high-consumption tail of the distributions, to get a correct picture of the number and type of consumers eating in excess of 100 g/day of any single fish product.

Human Exposure from Eating Fish

At present, it is difficult to estimate human exposure to PCB from eating fish, either for the population as a whole or for subgroups at higher risk. Fragmentary evidence suggests that the exposure to the population as a whole from PCB residues in ingested fish is probably well below 19 μg/day-consumer, based on PCB levels which are probably well below 1 ppm and 19 g fish consumed/day.

Although it is important to know the total population exposure, the first priority should be given to defining the dietary intake of PCBs in special subpopulations at high risk by reason of high consumption of fatty fish or high sensitivity to the toxic action of PCBs. Such populations might include pregnant women and young children, dieters, low income groups, and sport fishermen living in coastal and lake regions where there is known PCB contamination. Primate studies suggest that pregnant women, young children and dieters, will be particularly sensitive to PCBs and in some areas low income groups may rely heavily on fish for food. For each subpopulation, the amount and kind of fish in the diet and the PCB residue levels in the fish eaten must be obtained in order to determine exposure. None of the necessary information to define the human PCB exposure in subpopulations is presently known.

The first priority in systematically monitoring and analyzing for PCB residues is fish should therefore be among the oil fish such as salmon, trout, mackerel, shad, sardines, herring, bluefin tuna, sable fish, whitefish, striped bass, and bluefish, that have been identified as significant food items in the diets of special subpopulations of consumers.

Although only minimal dietary exposure to PCBs may occur through food, there is evidence of potentially significant exposure in those subgroups of the population who regularly consume freshwater fish from waters which are contaminated with PCBs

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at levels which exceed the FDA temporary tolerances. These subgroups of the population would include sports fishermen and others who consume locally caught freshwater fish.

In surveys conducted by the State of New York and FDA, samples of 17 species of fish were collected from 10 points on the Hudson River between Glens Falls and Alpine, 13 samples were collected at Glens Falls and 68 samples below Glens Falls. The data from these surveys indicate that 53 out of 68 samples of fish collected at or below Fort Edward (approximately 7 miles below Glens Falls) contained PCBs in excess of 5 ppm. The average level of PCB contamination in these 68 samples was 31.3 ppm. In contrast, only trace levels were found in the 13 samples obtained at Glens Falls. A high proportion of finfish and eels from all sampling points below Glens Falls contained PCB levels in excess of 5 ppm. The Fort Edward sampling point had the highest levels for the species examined, with individual samples ranging from 20.1 to 178 ppm.

Twenty-eight of the 33 samples of coho and chinook salmon from Lake Ontario exceeded 5 ppm, with a range from 21 ppm to 24.6 ppm. Of the 4 samples of lake trout tested, results were in the range of 10 to 15 ppm. All other species of fish sampled from Lake Ontario were at 5 ppm or less PCBs.

The Great Lakes represent another area of the nation contaminated with PCBs. The Michigan Water Resources Commission (*11*) has reported that many surface water samples contained PCBs at concentrations above the detection limit of 10 ppt. Ten significant levels of PCBs have been found in rivers and streams discharging into the Great Lakes. Effluents from wastewater treatment plants servicing industrialized communities have been found to be highly contaminated.

Sampling surveys of Great Lakes fish have shown that most species tested contained detectable levels of PCBs and that residue levels were generally proportional to fish size (age) and highest in the predator species. Except for whitefish, the species of commercial or sport interest (trouts and salmons) from Lake Michigan were found to be highly contaminated with PCBs. Data obtained from lake trout collected from various areas of Lake Michigan show mean PCB levels ranging from 3.06 ppm to 11.93 ppm.

The Michigan Department of Public Health has recently completed a study (*11*) which attempted to assess some of the consequences of human exposure to PCBs from the consumption of sportsfish caught in different areas of Lake Michigan. The study included exposed and control subjects from five areas of Michigan bordering on Lake Michigan. Exposed study subjects were those individuals who consumed at least 24 to 26 lb of Great Lakes fish per year. Control subjects were those individuals who consumed less than 6 lb of Great Lakes fish per year.

A preliminary assessment of the findings in the study indicate that the most frequently recorded quantity of fish consumed by the study participants was in the 24–25 lb/yr range. The highest recorded fish consumption over the two-year period of the study was 180 lb/yr and the highest single-season consumption was 260 lb. Mean PCB levels in whole lake trout are reported as 18.93 ppm in 1973 and 22.91 ppm in 1974, and 12.17 ppm in Coho Salmon in 1973 and 10.45 ppm in 1974.

However, comparisons of PCB levels in raw vs. cooked fish indicate that actual human exposure to PCB from fish consumption is less than might be expected from the raw fish data. This is not unexpected, since preparation (trimming away fatty tissue) and cooking have been shown to decrease the concentration of PCBs. For example, the PCB level in cooked Lake Trout consumed by the study participants ranged from 1.03 ppm to 4.67 ppm; in cooked salmon from 0.48 ppm to 5.38 ppm; and in other cooked fish from 0.36 ppm to 2.06 ppm. These levels are decidedly lower than the level of PCB contamination reported in raw trout and salmon.

PCBs were found in 501 blood and breast milk specimens collected from study participants during the study. The values ranged from a low of 0.007 ppm in blood in the control group to a high of 0.366 ppm in the exposed group. Although there was a wide range of blood values for each quantity of fish consumed, there was a highly significant correlation between the reported quantity of Lake Michigan fish consumed and the concentration of PCB in the blood of study participants. Using a natural log transformation of PCB values, the correlation between amount of fish consumed and PCB blood levels was significant ($t = 6.24$, $p < 0.0001$), with higher reported fish consumption being associated with higher blood PCB levels.

No annual variation in PCB blood levels in humans could be demonstrated. The mean PCB blood values for the control and exposed groups did not appear to change markedly from 1973 to 1974. In addition, abstinence from Lake Michigan fish consumption for a period of 90 days or more did not change the PCB blood levels significantly. PCB blood levels over the abstaining period shows variation but no steady decline in PCB. In fact, more subjects showed no change or a rise than showed a decline in PCB blood levels over time.

The calculated quantity of PCB ingested by eating

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Lake Michigan fish averaged 46.5 mg/yr and ranged from 14.17 to 114.31 mg/yr. PCB ingestion for each individual was determined by proportioning the reported annual fish consumption by frequency of species eaten and the cooked fish PCB levels for those fish. The community average for cooked fish was used in instances were cooked fish determination were not available for a study participant. Because fish consumption was found to vary from year to year, the average annual consumption for each individual for the two baseline years of study was used in each case.

Results from this study indicate the strong likelihood that the maximum allowable ingestion of 1 μg/kg body weight per day recommended for protracted exposure to PCB is being exceeded by the majority of the exposed group participants, and by inference, by a substantial number of individuals participating in sport fishing and who consume quantities of contaminated fish. The calculated mean daily dose received by the exposed group is 1.7 μg/kg-day and ranges from 0.49 to 3.94 μg/kg-day. If the average annual rate of PCB ingestion from fish indicated by these study results were continued over the years, and if net accumulation occurs, the average sports fisherman consuming contaminated fish could receive a total PCB dose equal to the 200 mg safety limit in approximately 4.3 yr. Under the same set of assumptions, individuals consuming greater than average amounts of contaminated fish would reach the total dose level sooner.

No adverse health effects or group of symptoms could be identified in the exposed group that were clearly related to PCB exposure. This implies that exposure to PCBs from eating contaminated fish at the levels observed and the presence of PCBs in these exposed persons has not caused any observable adverse health effects at the time of the study. However this does not exclude the possibility that effects too subtle for detection are occurring or the possibility of long-term adverse health effects.

Yusho

Considerable scientific interest has centered on the Yusho incident in Japan, where in 1968 human intoxication with Kanechlor 400, a PCB manufactured in Japan, was noted when a heat exchanger leaked this PCB into rice oil ("Yusho" oil) which was consumed by Japanese families.

The typical clinical findings included chloracne and increased pigmentation of the skin, increased eye discharge, transient visual disturbances, feeling of weakness, numbness in limbs, headaches, and disturbances in liver function. Most of the babies born to mothers with Yusho had skin discoloration which slowly regressed as the children grew in size. Adult Yusho patients had protracted clinical disease with a slow regression of symptoms and signs, suggesting a slow metabolism and excretion of the PCB in humans, probably resulting from a long biological half-life.

A review of the literature extent in 1972 led to the following facts with respect to this tragic incident in Japan. The average PCB content of the rice oil in the dose–response epidemiologic study was 2500 ppm. In this dose–response epidemiologic study, the average cumulative intake of PCBs, leading to overt symptomatology, was 2000 mg. In this same study, the lowest dose leading to overt symptomatology was 500 mg. The toxicity seen was the result of the ingestion of the PCBs contaminant in the rice oil.

A summary updating of the Yusho incident was presented by Kuratsune in 1975 (*12*). This report affects the original conclusions enumerated above.

PCBs Content of Yusho Oil. The first reported PCB determination was made on a canned contaminated rice oil produced on February 5, 1968, consumption of which was associated with overt symptomology. One group of Yusho patients was associated with ingestion of this contaminated canned rice oil produced or shipped on February 5 and 6, 1968 (*13*).

The detailed epidemiologic studies are given in the papers by Kuratsune et al. (*14*) and Yushimura (*15*) and summarized in English by Kuratsune et al. (*13, 16, 17*). Of 325 patients queried, 166 of 170 used canned rice oil produced or shipped on February 5 and 6, 1968, and 143 of 155 used bottled rice oil shipped from February 5 to 15, 1968. Tusukamoto et al. (*18*), determined that the organic chlorine content of canned rice oils produced or shipped on February 5, 1968, was 1000 to 1500 ppm, by chemical and activation analysis. Since Kanechlor 400 had a 48% chlorine content, if one attributed all the organic chlorine to this specific chlorinated biphenyl, then this canned rice oil contained, as an average, 2500 ppm PCBs. Kuratsune et al. (*14*) reported that a qualitative GLC survey of 109 samples of bottled rice oil shipped between October 1967 and October 1968 showed "significant" PCBs content only in those samples between February 7 to 10, 1968. The largest amount was reported in the sample of February 7, 1968, but the quantity was not given. No bottled rice oil samples were available for February 5 and 6, 1968. However, in the paper by Kuratsune et al. (*17*), the most marked contamination of bottled rice oil was for that shipped on February 7, 1968; and the maximum chlorine content was 462 ppm. One may assume that this

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number applies to the sample of bottled rice oil of February 7, 1968, giving this sample a PCBs content of 924 ppm. Kuratsune et al. (*12*) reporting the work of Nagayama et al. (*19*), gives the PCBs analyses for three samples of toxic Yusho oil, used by three independent families with Yusho, as approximately 800 to 1000 ppm. These were GLC/MS measurements. Nagayama et al. (*19*) described these samples as follows: "Rice oil used by patients with Yuso ("Yusho oil"): 3 samples of rice oil used by 3 independent families with Yusho in 1968. These samples had been kept in glass bottles with glass stoppers at room temperature in our laboratory until 1974 when the analysis was made." Kuratsune (*13*) pointed out that these three samples were canned oil and considered to have been produced and shipped on February 5 or 6, 1968. It was reported previously that, based on organic chlorine determinations, Tsukamoto et al. (*18*) reported an average PCB content of the canned oil of February 5, 1968, to be 2500 ppm. Now, based on GLC/MS, we have a PCB content of ca. 1000 ppm for the canned oil sample of February 5 or 6, 1968.

What are the possible explanations for this discrepancy in values? One possibility is based on the assumptions associated with the method of measurement by Tsukamoto et al. (*18*); namely, determination of total organic chlorine. Thus, any organic chlorine present in the rice oil, which was not a chlorinated biphenyl, would be included in the PCB analysis. Some possibilities include: chlorinated dibenzofurans, chlorinated naphthalenes, chlorinated paraffins, other chlorinated aliphatics, and nonbiphenyl aromatics.

Another possibility is related to the distribution, with time, of the contaminated rice oil samples. February 5, 1968, occurred on a Monday. The first rice oil samples reported to contain PCBs were produced on this date (*18*). If the leak first occurred sometime over the weekend (February 3 and 4, 1968), and production was resumed Monday morning, February 5, 1968, then one would expect the samples of this date to be higher in PCB content.

Therefore, one would expect the first batches Monday morning to be highest with a diminution of PCB content with time. Tsukamoto (*18*) reported the organic chlorine content of six canned oils produced Monday, February 5, 1968, as follows: 1020, 1170, 1070, 1080, 1030, and 1500 ppm. In the survey of bottled oils, Kuratsune et al. (*14*) reported that for those samples where PCBs were found, the greatest amount was in the samples of February 7 (Wednesday); and after February 11. It was inferred from the paper by Kuratsune et al. (*17*) that the PCB content of the bottled rice oil samples of February 7, 1968, was 924 ppm. In addition, Kuratsune et al. (*12*) gave a value of 134 ppm PCB for a rice oil produced on February 10, 1968. Thus, the available data does confirm a diminution of PCB contamination of the rice oil with time. This is summarized in Table 5.

Table 5.

Date	Source	PCB content, ppm	Method
Feb. 5, 1968	Canned oil	2000–3000	Organic Cl
Feb. 5 or 6, 1968	Canned (?) oil	ca. 1000	GLC/MS
Feb. 7, 1968	Bottled oil	924	Organic Cl
Feb. 10, 1968	Bottled oil	134	?
After Feb. 11 1968	Bottled oil	Just detectable	GLC (?)

The resolution of the varying PCB values for the canned oil cannot be made. However, Kuratsune (*7*) (1976) confirmed that the production of rice oil had been suspended for an unknown period of time prior to February 6, 1968, when it resumed.

Dose–Response. There were 1291 Yusho patients as of April 30, 1975 (*20*). Of this total group, the dose–response relationship was developed from a detailed analysis of 146 patients (*15*, *16*). These 146 patients all consumed contaminated canned rice oil produced on February 5, 1968 containing 2000–3000 ppm PCBs as Kanechlor 400 (*18*). Tsukamota et al. estimated that the lowest dose producing symptoms was 0.5 g.

If the PCB content of this canned oil was ca. 1000 ppm, as discussed in the previous section, then the average dose producing an overt effect was 0.8 g, and the lowest dose producing an overt effect was 0.2 g.

Causative Factors. Originally, rice oil contaminated with a heat exchanger, Kanechlor 400, a polychlorinated biphenyl, was associated with Yusho symptomatology. PCBs were identified in the contaminated rice oil consumed and in the blood and tissues of Yusho patients. Therefore, the effects seen were attributed to PCBs.

In the review by Kuratsune et al. (*12*), a new factor was introduced into the system; namely, the canned rice oil was also contaminated with chlorinated dibenzofurans to the extent of 5 ppm. In addition, in this same paper Kuratsune presented data of Nagayama et al. (*19*) showing polychlorinated dibenzofurans to be present in the liver and adipose tissue of Yusho patients, while none was found in that of a control group. The ratio of PCBs to PCDFs in Kanechlor 400, a Yusho oil of February 5 or 6, 1968, in adipose tissue and liver from a Yusho patient were 50,000, 200, 144, and 4, respectively. Thus, relative to Yusho oil, the liver with a PCB/PCDF ratio of 4 and 1 appears to concentrate PCDFs selectively relative to PCBs.

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Relative to PCBs, PCDFs are about 250 times higher in the rice oil than in Kanechlor 400 (*12*, *19*). (It should be noted that we are comparing chlorinated dibenzofuran content of an unused Kanechlor 400 to that after prolonged use in a heat exchanger.) PCDFs may also be a factor in Yusho disease. In another paper Nagayama et al. (*21*) reported that it is said that the toxicity of PCDF is said to be from 200 to 500 times that of PCB. At the lower factor (200), contaminated rice oil would be expected to be twice as toxic as Kanechlor 400. Also, in this same paper Nagayama et al. stated that the symptoms seen in Yusho patients seemed to be more severe than would be expected just from the PCB intake associated with the oil.

If PCDF is 200 to 500 times more toxic than PCB, then contaminated rice oil would be 2 to 3.5 times more toxic than that expected from its PCB content alone. Kuratsune et al. (*13*) estimated that if the average amount of contaminated rice oil ingested by a Yusho-exposed person, is related solely in terms of its PCB equivalent, then the amount of oil needed to be ingested, on that basis, would be 1600–2800 ml. At a PCB content of 2500 ppm, this is an ingestion of 4 to 7 g of PCBs equivalent: whereas at a PCB content of 1000 ppm, this is an ingestion of 1.6 to 2.8 gm of PCBs equivalent.

The complexities and uncertainties associated with the most recent reports of the Yusho incident in Japan, make it extremely difficult to quantify possible human health effects resulting from exposure to PCBs alone.

Occupational Exposure to PCBs

The earliest reports of adverse health effects due to exposure of workers to PCBs in this country are probably those of Schwartz (*22*), who described skin lesions and symptoms of systemic poisoning among workers who were said to have inhaled chlorodiphenyls; their complaints included digestive disturbances, burning of the eyes, impotence, and hematuria. Patch tests with the chlorodiphenyls were negative, and Schwartz speculated that mechanical plugging of the follicles of the skin as the fumes solidified on it were responsible for the skin lesions. The chlorine present in the products was thought to then exert an irritating effect on the plugged follicles and to thus cause suppuration. No quantitative data were reported, but a number of preventive practices were recommended.

There have been numerous reports over the ensuing years (*23–28*) of cutaneous eruptions and of systemic manifestations (sometimes fatal) as well, among marine electricians, machinists, capacitor and transformer manufacturing workers, and others occupationally exposed to PCBs. However, in many of these reports the exposures are described as having been to mixtures of chlorinated hydrocarbons, quite often of chlorinated naphthalenes and PCBs.

The skin lesions described by Schwartz (*22*) have come to be designated generally as chloracne. Chloracne can be produced by a number of chemical compounds, including chlorinated dibenzofurans and certain isomers of the chlorinated dibenzodioxins (*29*). Oily skin and large pores seem to predispose to the disease, while the opposite is the case for smooth, tender skin (*30*). Chloracne also has occurred among workers engaged in the production of 2,4,5-T (*31*).

Part of the chloracne lesion resembles adolescent acne, but it is generally more severe, and lesion distribution is inconsistent with, although it may be superimposed upon, adolescent acne. It is known that chloracne can be produced by either the systemic absorption of chlorinated biphenyls or the direct application of chloracnegenic compounds to the skin. Systemic effects sometimes result after occupational chloracne has manifested itself; these may include loss of appetite, nausea, edema of the face and hands, abdominal pain, vomiting, and burning and soreness of the eyes. No fully satisfactory explanations have been made of the development of chloracne. Chloracne is generally very persistent, and there is no preferred control measure. An excellent review of this subject is that by Crow (*32*).

The U. S. occupational standards for PCBs are: 8-hr time-weighted average exposure limits of 1 mg/m^3 (skin) for the 42% chlorinated product, and 0.5 mg/m^3 (skin) for the 54% chlorinated product (CFR, Title 29, Part 1910.93). The National Institute for Occupational Safety and Health has underway the preparation of criteria for a recommended standard for occupational exposure to polychlorinated biphenyls. In addition to an environmental exposure limit, this document will provide comprehensive recommendations for medical surveillance, safe work practices, and engineering controls to ensure employee protection during occupational exposure over a working lifetime; it is scheduled for transmittal to the Department of Labor in late 1976 or early 1977. NIOSH also is undertaking certain studies of employee populations (mainly in U. S. capacitor factories) in order to better define the nature and extent of any chronic and/or life-shortening effects of exposure to PCB.

Practically all of the currently available information on worker health and PCB exposure is found in foreign literature. For example, Karppahen and Kolho (*34*) reported on relationships between the

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concentration of PCBs in the blood of all, and in the adipose tissues of some, of 29 persons in "good health" from three different employee groups in Finland. [Kolho has stated that the capacitor plant workers received quarterly health examinations, and, in addition to the clinical examination made at the time of the investigation, serum alkaline phosphatase, GOT, and GPT activities were determined; the six employees with the highest blood concentrations of PCBs also had BSP excretion tests performed. All results were normal. In view of claims based on animal experiments that PCBs can induce liver microsomal enzyme activity, the authors also determined the half-time of antipyrin before and after phenobarbital induction (1 mg phenobarbital/kg body weight/day/3 days) for six capacitor plant employees and six controls; no enzyme induction was observed. Further, because of claims that PCBs have effects on steroid metabolism, four capacitor plant workers were tested for ACTH (serum, presumably); all results were reported to be within the normal range (letter from S. Hernberg to A. C. Kolbye, Jr., 12/23/75)].

Nine of the employees had no history of occupational exposure to PCBs, six of them had handled PCB samples in an analytical laboratory, and the other eleven of them had been employed for 6 years in a capacitor factory where Aroclor 1242 was used as the impregnating fluid. It was stated that average PCB concentrations in the air of the capacitor factory had not exceeded "internationally accepted limits," and that special attention had been given to skin protection. [The Joint ILO/WHO Committee on Occupational Health, in its sixth report (*36*) recommended for international adoption a "safe concentration zone" of 1 mg/m³ for chlorinated derivatives of diphenyl.]

Table 6 shows the observed tissue concentrations of PCBs; the authors were unable to detect any biological effects of the approximately 50-fold larger PCB concentrations in the blood of the capacitor plant employees, compared to the "unexposed" control group.

Ouw et al. (*35*) conducted a survey to determine the degree of absorption and the health effects of exposure to "electrical grade" Aroclor 1242 (that "did not contain any impurities") for varying periods of time. PCB concentrations in the air of a capacitor factory in New South Wales, Australia, were measured, and 34 occupationally exposed employees (15 males, 19 females, ranging in age from 33 to 55 years) were examined and compared with volunteer controls (23 males, 7 females ranging in age from 20 to 50 years) having no history of occupational exposure to PCBs. It is noteworthy that Aroclor 1242 is not manufactured in Australia.

Table 6. Concentration of PCBs.[a]

Subjects	PCBs in blood (fat basis), mg/kg		PCBs in adipose tissue (fat basis), mg/kg[b]
	Average	Range	
Workers in capacitor factory	313	100–700	200
			11
			160
			285
			635
Persons handling PCBs in analytical laboratory	53	33–71	Not analyzed
Persons without any special exposure to PCBs	5.4	3.6–9.9	2.3
			1.5

[a] Data of Karppanen and Kolho (*34*).
[b] Individual samples.

Study parameters included occupational and medical histories, PCB-in-blood concentration estimates, and liver function (serum bilirubin, alkaline phosphatase, total protein, and GPT, and BSP excretion) tests. The authors noted that exposed workers tended to complain of eye, face, and skin "burning," that the PCB "fume" . . . has a pungent smell which often causes persistent body odor, and that the employees with higher blood concentrations of PCBs complained most often of the skin lesions (one case of chloracne, five cases of "an eczematous rash on" the legs and hands), although there apparently was poor correlation of blood PCBs with the severity of the complaints. No significant health effects were observed among those of the 34 workers whose blood PCB concentrations were below 200 ppb. There was a statistically significant difference between the blood PCB concentrations of the exposed group and the control group ($p < 0.01$). Table 7 shows the concentrations of Aroclor 1242 in the capacitor plant air prior to and after exhaust ventilation system "improvements" had been made. [The Australian National

Table 7. Aroclor 1242 concentrations in the air inside capacitor plant before and after improvement of exhaust ventilation system.[a]

No.	Area in the impregnation room	Aroclor concentration, mg/m³	
		Before	After
1	In unloading tank in front of exhaust register from operator's breathing zone	1.44	0.75
2	In unloading tank not in front of exhaust register	2.22	0.7
3	General atmosphere near tank	1.08	0.18
4	Soldering area	0.32	0.08

[a] Data of Ouw et al. (*36*).

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Health and Medical Research Council recommended (*37*) exposure limit values of 1.00 mg/m³ for PCBs of 42% and 54% chlorine content, respectively]. Table 8 shows that there was no lowering of blood PCB concentration among those workers tested two months after the installation of a more efficient exhaust ventilation system and the concomitant recommendation to wear "suitable impervious gloves" in order to reduce PCB absorption through the skin. The authors suggested that a failure to adhere strictly to the glove recommendation might explain the continued elevation blood PCB levels. Another possibility might be that PCBs were continually mobilized from storage in adipose tissues.

Table 8. Mean blood Aroclor 1242 levels before and after improvement of exhaust ventilation and the recommendation to use suitable gloves.[a]

Retention times relative to Aldrin 1	Mean blood Aroclor level, pbb		Statistical difference
	Before	After	
0.69	281.6	477.2	None ($p < 0.01$)
1.31	135.1	225.4	None ($p < 0.01$)
1.41	58.41	524.7	Significant ($p < 0.05$)

[a] Data of Ouw et al. (*36*).

The Japanese Ministry of Labor (Regulation for the Prevention of Disturbances due to Specified Chemical Substances, under the Act for Safety and Health of Workers, of April 28, 1971) established an occupational environmental exposure limit for PCBs of 0.5 mg/m³ at 25°C/1 atm (*38*). Japanese import of PCBs commenced around 1950, and early uses were as dielectrics in capacitors and transformers. In 1954, Kanegafuchi Chemical Industry Co., Ltd. started PCB production in Japan, and it was at about this time that chloracne eruptions among workers were first reported. Slightly earlier (1953) incidents of changes attributable to PCBs in blood and urine findings among capacitor factory workers, however, were reported by Hara (*39*).

According to an Ad Hoc Committee sponsored by the Japanese Environmental Agency (*38*), PCB concentrations in the air of a Japanese capacitor factory (where the major PCB constituent was "diphenyl pentachloride") were found to range from 0.37 to 6.75 mg/m³; this was between the years 1953 and 1957, and prior to the date when the aforementioned occupational exposure limit was promulgated. The highest concentration was measured where PCBs were heated to drive out entrained/dissolved air. Admittedly, the analytical methodology for PCBs in those years was not as refined as that now in use, but it is thought likely that some employees were exposed continually at concentrations of several milligrams per cubic meter.

The Japanese literature is said to have contained no further reports on measurements of PCB in air until the spring of 1972, just prior to the suspension of their usage. The production of PCBs was discontinued in Japan in June 1972, and their importation was discontinued in the following September. At that time Hasegawa et al. (*40*) reported PCB measurements in the air of one PCB production plant (Kanechlors 200–600, 0.005–0.02 ppm), four capacitor manufacturing plants (Kanechlor 300, 0.01–0.05 ppm), and one plant where PCBs (Kanechlor 300) were used as a heat exchange medium (0.002 ppm). Peak values of 0.17 ppm and 0.67 ppm, respectively, were found in a capacitor plant "air-riddance" process area and in a capacitor impregnating area where tank leakage had occurred. Estimated (presumably 8-hr work day) time-weighted average exposures of affected employees were 0.02–0.03 ppm. Airborne PCBs in the capacitor plants were reported to consist of 70–80% vapor for material corresponding to Kanechlor 200, and of particulates larger than 0.1 μm for Kanechlor 300. The authors attributed the 3:1 vapor: particulate mix to selective evaporation of low boiling components of Kanechlor 300.

Although no measurements were available, Hasegawa et al. (*40*) estimated that environmental conditions in carbonless copy paper manufacturing facilities (using Kanechlor 300) were roughly similar to those found in capacitor factories. Beginning in February 1971, PCBs were phased out as the microcapsular solvent in this process, being replaced by SAS or KMC-oil; however, during the period from November 1972 to January 1973, when occupational health surveys were being performed relative to SAS or KMC-oil toxicity, PCB concentrations of 0.013–0.4 ppb were measured in the environments of these facilities. General environmental concentrations of PCBs at that time were less than 0.0005 ppb, and outdoor PCB concentrations around the facilities were 0.0043 ppb (*40*) and 0.009 ppb (*41*). In an office room where carbonless copy paper was used, an air concentration 1.1 μg/PCB/m³ was measured, and in the carbonless copy paper storage area of a post office, PCB concentrations of 8.7–21.1 μg/m³ were detected (*42*).

The Japanese Ministry, in its Regulations for Physical Examinations for the Prevention of Disturbances due to Specific Chemical Substances (October 14, 1971), advised PCB users to examine employees for dermal and hepatic "symptoms" and their anamnesis, "subjective symptoms" such as

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anorexia and asthenia, and urine urobilinogen, in the first (pre-employment?) physical examination, and to "survey" working conditions, blood tests and liver function tests in the "secondary" (periodic re-?) examination. A 1973 notice advised those users of PCBs as heat exchange fluids to perform comprehensive health surveillance (*38*). Yamamoto (*43*) reported "positive" findings in 37 employees of 323 (total employment = 706 in 51 establishments) who were given "special" physical examinations in 1971.

Hara (*39*) reported a 20–30% incidence of dermal "symptoms," consisting of "distinctive hair follicles" in exposed areas such as the face, neck, and forearm, and pimplelike skin eruptions of the face and neck, among employees in a capacitor factory that had been in operation between 1953 and 1963 (pentachlorobiphenyls, 1953-1957; Kanechlor 300, 1958-on). No other (e.g., hepatic) dysfunction was observed, and no quantitative information was reported in the reference from which the preceding report was obtained; however, in a follow-up survey of workers in capacitor factories, Hara et al. (*44*) reported that one year after the suspension of PCB usage skin findings had become milder.

Hasegawa et al. (*40*) reported on a 1972 survey of capacitor factories, in which they noted that persons working in environments that contained 0.2–0.3 mg PCB/m^3 (0.02–0.03 ppm) showed dermatologic ailments that included "brown chromodermatosis" of the dorsal joints of the hands and fingers and nail bed, and "acneform exanthema." Several cases of comedo or acneform exanthema of the jaw, back, and thighs were seen also. These signs were no longer observed one month after the cessation of the handling of PCBs.

In a factory where Kanechlor 300 was employed as a heat exchange medium, the environmental concentration of PCBs was reported to be 0.02/mg/m^3, and no dermal manifestations were observed among its employees (*40*). Nor did Hashimoto (*45*) observe any abnormalities among 236 workers in such a facility, to whom he administered "examination centered around liver function tests."

In 1972, when Hasegawa et al. (*40*) performed a health survey of workers in carbonless copy paper factories (2 years after the use of PCBs in such processes had ceased) they noted no dermal effects, and no liver function, blood, or urine test abnormalities were seen, with the exception of "slight abnormalities" in lipid metabolism. PCB levels in the blood of these workers were reported as "approximately 0.01–0.02 ppm," or what amounted to a decrease to 10% of the levels during the period of PCB usage. The data indicated that PCBs collected from the work atmosphere had apparently degraded to a product containing one less chlorine atom than the average number of chlorine atoms in the PCBs handled in the factory, and that, conversely, the PCBs found in the workers' blood contained one more chlorine atom than did the PCBs handled in the factory, i.e., if the PCBs found in the workers' blood were inhaled at the workplace, it can be surmised that the di- and trichlorobiphenyls disappeared rapidly from the body, whereas the tetrachlorobiphenyl was metabolized slowly.

Hasegawa et al. (*40*) concluded that blood analysis is a feasible method for determining body burdens of PCBs, and "probably more useful than the technique presently used by extracting adipose tissue and using it for PCB;" urinalysis for PCBs did not appeal to them as a viable monitoring method. They noted, however, that there was no correlation between length of employment (and presumably, duration of exposure) and the amount of PCBs accumulated in the blood, i.e., with continued exposure, PCB levels in the blood did not increase linearly; in light of the demonstrated slow excretion rate of PCBs from the body, the authors conjectured that some different biotransformative mechanism comes into play after blood PCB levels exceed approximately 1 ppm (perhaps fat storage). This would seem to belie their confidence in blood analysis as a reliable index of exposure.

Kitamura et al. (*46*) reported that the mean PCB level in the blood of ten capacitor factory workers was 0.82 ppm (0.32–2.1 ppm) immediately after the cessation of PCB usage and 0.31 ppm 3 months later, when almost all of the subjects were observed to have skin signs. It seems significant that the blood PCB concentrations observed in this study were several fold higher than those seen by Hasegawa et al. (*40*). Kitamura et al. (*46*) attributed the skin effects to PCBs accumulated in the workers' bodies during the period of PCB usage. No other abnormalities were reported.

Sagami et al. (*47*) reported the case of a housewife in whom they observed skin effects several years after she had left 6 years of employment in a capacitor factory. She was found to have PCB concentrations of up to 0.13 ppm in her blood and of 42 ppm in samples her subcutaneous adipose tissue; this contrasted sharply with the findings of Hara et al. (*44*) that the blood PCB levels of three workers who remained at the same factory had decreased to $\leq$ 0.05 ppm one year after the cessation of PCB usage [from levels of 0.05-0.3 ppm during the time of PCB usage (*40*)].

Some capacitor manufacturers in the U. S. use epoxide-type alkylating agents as additives to prolong the service life of PCBs. EPA sec. 308 responses from the General Electric Co., probably contain identifying data.

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Air and Water Exposure to PCBs

As indicated previously, nominal human exposure to PCBs in the U. S population may occur from air and water. Samples of ambient air were collected in suburban areas of Miami, Florida; Jackson, Mississippi; and Fort Collins, Colorado. Preliminary results (*48*) for samples taken in April, May, and June of 1975 show that PCBs were present at all locations. Although the data varied, the average concentrations at each of the three locations was approximately 100 ng/m^3. Initial identification of the PCBs indicated that they were most comparable to the Aroclor 1254 standard.

Dennis (*49*) has reported that data gathered from monitoring activities of surface waters and bottom sediments of the major drainage basins of the United States indicate the widespread occurrence of PCBs in both surface water and bottom deposits. A preliminary assessment of PCB levels shows mean residue levels in water ranged from 0.01 to 0.05 μg/l. The 0.05 μg/l. were found in the South Atlantic Slope and Eastern Gulf of Mexico drainage basin. In general, the lowest PCB residue levels were found in drainage basins west of the Mississippi.

Kleinert (*50*) has summarized the work completed by the Wisconsin Department of Natural Resources to identify some PCB sources in the environment in Wisconsin. Effluents from cooling water in aluminum foundries contained PCBs ranging from 11.5 to 335 ppb. Investigations revealed the common source to be leaking hydraulic fluids containing PCBs which were used in die cast machines. Effluents from paper mills that recycle wastepapers has measurable discharges ranging from 0.01 to 25 ppb.

Snow samples (*50*) were collected early in 1975. Analysis of the snow melt water from Racine, Kenosha, Madison, and Milwaukee revealed concentrations from 0.17 to 0.24 ppb. The author concludes that these values suggest that fallout of PCBs from the air may be a principal source of PCBs entering the waters of the state.

Hesse (*51*) indicates that, similar to the studies in Wisconsin, not all industrial effluents tested in Michigan contain measurable PCB levels. In testing over 900 industrial samples, approximately 40% contained PCBs above the 0.1 μg/l. laboratory sensitivity limit. Of the industries tested, 23% had greater than 0.5 μg/l., 18% greater than 1 μg/l., 6% greater than 10 μg/l., and 2% greater than 100 μg/l.

Although much of the PCBs entering municipal waste treatment facilities are removed and become incorporated into the waste sludge, a sampling of 58 municipal wastewater treatment plant effluents throughout Michigan in 1973 showed an average concentration of 0.52 μg/l. Concentrations of PCBs are much higher in the sludges. The average for all plants was 15.6 mg/kg with individual values as high as 350 mg/kg. Since sewage sludges are commonly disposed of by incineration, spreading on agricultural land, or placing in landfills, the addition of PCBs to the environment is obvious.

Residues of PCBs in Human Tissue and Milk

Yobs (*52*) has reported that 31.1% of 637 samples of human adipose tissue collected from the general population as part of the Human Monitoring Survey during 1971 were positive for PCBs in measurable amounts. These samples were collected in 18 states and the District of Columbia and positive samples were obtained from each of the sampling states and District. The distribution of PCB levels ranged from 34.2% none detected, 33.3% < 1 ppm, 27.3 % 1–2 ppm, and 5.2% > 5.2 ppm.

Kutz and Strassman (*53*) have described the results of PCB monitoring during fiscal years 1973 and 1974 in which 35.1% and 40.3%, respectively, of the tissues collected contained levels of 1 ppm or more of PCBs on a net-weight basis. Analysis of the tissue revealed that the compounds found in adipose tissue were most comparable to those prevalent in Aroclor 1254 and Aroclor 1260. Additional analysis indicated that the most frequently encountered PCB residues were penta-, hexa-, and heptachlorobiphenyl compounds.

Residues of PCBs have also been detected in a study of human milk collected in Colorado where 8 or 40 samples contained residues ranging from 40 to 100 ppb (*54*).

A study of adipose tissue samples collected at autopsy from Canadians (*55*) indicates that the majority of Canadians have adipose tissue residues of 1 to 2 mg/kg of PCB. All adipose tissues had detectable levels of PCBs and 30% of the samples had PCB residues greater than 1 mg/kg with a range of 0.11 to 6.60 mg/kg. PCB residues in human milk from Ontario residents were found to be approximately 1 mg/kg on a fat basis.

Polybrominated Biphenyls

Introduction and Background

The polybrominated biphenyls (PBBs) in this report refers to either FireMaster BP-6 or hexabromobiphenyl manufactured by Michigan Chemical Corporation for use as a flame retardant for thermoplastics. This product is a mixture of brominated biphenyls with an average bromine content

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equivalent to about six bromine atoms per biphenyl molecule. FireMaster BP-6 is a mixture of the following brominated biphenyls: tetrabromobiphenyl, 2.0%; pentabromobiphenyl, 10.6%; hexabromobiphenyl, 62.8%; heptabromobiphenyl, 13.8%; other bromobiphenyls, 11.4%.

The Michigan Chemical Corporation has stated (56) that, to their knowledge, FireMaster BP-6 is the only polybrominated biphenyl produced in commercial quantity in the U. S. Their production estimates are: 1970, 20,000 lb; 1971, 200,000 lb; 1972, 2,300,000 lb; 1973, 3,900,000 lb; 1974 (projected) 4,800,000 lb.

Firemaster BP-6 has been used as a flame retardant in the manufacture of typewriter, calculator and microfilm reader housings, radio and TV parts, miscellaneous small automotive parts and small parts for electrical applications. The use of FireMaster BP-6 has been restricted to those applications where the end-use product is not exposed to either animal feed or food and there is no known use in flame retarding fabrics where human exposure would occur.

The ultimate disposition of FireMaster BP-6 upon burial is uncertain. The Michigan Chemical Corporation has stated that in their opinion this material will eventually undergo oxidative/biological degradation forming carbon dioxide, water and bromide ion.

Human Exposure

In October of 1973, adverse health effects were observed in cattle in several dairy herds in the State of Michigan. At that time, the cattle refused to eat manufactured feed; milk production decreased; there was a loss in body weight and the cattle developed abnormal hoof growth with lameness; cattle and swine aborted; and farmers reported the inability to breed heifers after they consumed feed manufactured by Farm Bureau Services. A herd of some 100 head of cattle sent to slaughter during this time period exhibited enlarged livers.

Analysis of samples of the suspected feed by laboratories of the U. S. Department of Agriculture at Beltsville, Maryland, revealed that the feed was contaminated with a flame retardant chemical, hexabrominated biphenyl. Subsequent investigation revealed that the Michigan Chemical Corporation manufactured magnesium oxide, a dairy feed supplement sold under the tradename NutriMaster, and a flame retardant, hexabrominated biphenyl, sold under the tradename FireMaster BP-6. Both of these products were distributed in brown paper bags with either the name NutriMaster or FireMaster stenciled across the top of the bag. When the top of the bag was torn off and discarded, identification was essentially lost.

As the result of a mix-up in bags, FireMaster BP-6 was mixed with animal feed in place of the NutriMaster, apparently in the same proportion of use for the NutriMaster. It appears that three kinds of feed were initially involved in this episode with PBB levels as follows: Feed No. 405, 2.4 ppm PBB; Feed No. 410, 1790 ppm PBB; Feed No. 407, 4300 ppm PBB.

Samples of milk collected from individual farms soon after the PBB was identified as the contaminant ranged from 2.8 ppm on a fat basis to 270.5 ppm on a fat basis. Other products seized and destroyed included: butter (1-2 ppm); cheese (1.4-15.0 ppm); canned milk (1.15-1.62 ppm).

It has been estimated that between the onset of contamination in the fall of 1973 and the establishment of the quarantine of affected herds and flocks in the spring of 1974 over 10,000 Michigan residents have been exposed to PBB through the consumption of contaminated milk, meat and other dairy products. There was probably considerable variation in both length of exposure and levels of exposure. As a group, the farm family members have been at greatest risk followed by those individuals who purchased dairy products from contaminated farms on a regular basis.

In order to determine whether or not persons exposed to PBB-contaminated products had suffered

Table 9. Distribution of PBB blood levels, Michigan, 1974.

	Quarantined farms				Nonquarantined farms			
	Adults		Children		Adults		Children	
PBB blood level, ppm	No.	%	No.	%	No.	%	No.	%
0	3	3.7	—	—	21	28.4	—	—
0.002–0.019	43	52.4	8	28.6	52	70.3	29	96.7
0.020–0.090	19	23.2	10	35.7	1	1.4	1	3.3
0.100–0.490	11	13.4	3	10.7	0	0	0	0
0.500–2.260	6	7.3	7	25.0	0	0	0	0
Total	82	100.0	28	100.0	74	100.1	30	100.0

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Table 10. Comparison of PBB concentrations in human breast milk and blood plasma.

Date	PBB levels, ppm	
	Breast milk	Blood plasma
12/74	10.800	0.082
6/74	22.700	0.252
10/74	1.800	0.014
3/75	0.210	0.003
3/75	92,660	1.068

Table 11. Comparison of PBB concentrations in human adipose tissue and blood plasma.

Date	PBB levels, ppm	
	Adipose tissue	Blood plasma
11/4	0.410	0.002
6/74–1/75	1.400	0.005
3/75	3.000	0.012
3/75	174.000	1.068
3/75	0.248	0.002
3/75	0.274	0.003
4/75	0.177	0.003
4/75	0.152	0.003
4/75	1.140	0.004
4/75	0.808	0.004
4/75	0.530	0.007
4/75	0.210	0.003
5/75	1.110	0.003

any acute adverse health effects, the Michigan Department of Public Health undertook a series of studies in the summer and fall of 1974. Study participants for the exposed group were dairy farm residents from farms which had been quarantined by the Michigan Department of Agriculture. The exposed subjects were limited to those who had lived or worked on the quarantined dairy farms for more than six months since May of 1973. Nonexposed subjects were randomly selected from a list of dairy producers in the same geographical area where farms had not been quarantined.

A total of 298 persons were interviewed in the study and physical examinations and/or blood samples were obtained for 110 persons in the exposed group and 104 persons from the control group.

The Michigan Department of Public Health has reported (57) that responses to a set of 24 specific medical conditions revealed that none of the health complaints occurred consistently in either of the study groups. Statistical analysis showed that none of the listed complaints was significantly more frequent in those persons with the highest PBB levels when compared to other study subjects. Physical examinations of adults and children showed no unusual abnormalities of the heart, liver, spleen or nervous system. Urinalyses and complete blood counts did not reveal a significant excess of unusual abnormalities related to exposure to PBB levels.

These studies showed that blood levels of PBB were significantly higher in the study subjects from quarantined farms as compared to those from the nonquarantined farms; although some subjects from the farm showed low PBB blood levels (Table 9).

Several exposed females delivered normal babies without complication. Tests showed concentrations of PBB in breast milk to be considerably higher than that found in paired blood plasma (Table 10).

Paired samples of adipose tissue and blood were collected in a group of 13 individuals entering the hospital for surgical procedures. The concentration of PBB in adipose tissue ranged from 61 to 370 times the PBB value found in blood plasma with an average ratio of 175 to 1 (Table 11).

Reports of health complaints such as numbness, stomach pain, headache, fatigue and anxiety continue to be reported in the various newspapers in Michigan. Reports have also appeared in the press that several physicians in Michigan have reported abnormal liver function tests in patients exposed to PBB. Attempts to verify these reports with physicians have been unsuccessful.

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