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Review

POLYCHLORINATED BIPHENYLS A TOXICOLOGICAL REVIEW

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Summary

Polychlorinated biphenyls (PCBs) are a class of compounds which have, for nearly 60 years, been used as insulating fluids, hydraulic and lubricating fluids, heat exchanger fluids and as additives in adhesive inks and paints. The very properties that made PCBs attractive to industry, such as resistance to fire and persistence in the environment, are the same properties that have resulted in their perceived toxicological problems. Mixtures of these compounds which have great environmental persistence and are contaminated with other agents, have been shown to produce adverse organ and system effects on a variety of animals. Since the mid 1970's, production and use of PCB's have been curtailed based on chronic animal toxicity data and concern about the environmental persistence of these highly lipophilic compounds which tend to bioaccumulate in living tissues and the food chain.

This report discusses the chemical and physical properties of PCBs, their biological disposition, and their reported toxicologic effects including carcinogenic potential. Specific comparisons are made between toxicity of PCBs in animals with effects observed in humans following exposure. Other areas covered include governmental regulation and permissible levels of exposure. Indeed, as a result of passage of the Toxic Substances Control Act in 1976, Congress singled out PCBs for regulation as required by law and the U.S. EPA banned further production in 1979.

It is concluded that there are significant adverse effects of PCBs when administered to animals under laboratory conditions. However, with the exception of the development of chloracne, there is little evidence suggesting significant toxicity to man including carcinogenic effects resulting from the chronic exposure to PCBs in the workplace or environment.

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1. Introduction

1.1 History

Polychlorinated biphenyls, PCBs, are chlorinated aromatic hydrocarbons which were discovered in 1881. Effects of PCBs on the environment were noted more than 75 years later when accumulations of PCBs were found in aquatic life of the Baltic Sea [1]. The commercial production of PCBs began in 1929, and during the following decade, cases of poisoning were reported among workers involved in the manufacturing of PCBs [2]. Ensuing safety precautions prevented further PCB poisoning until 1953 when cases were reported in Japanese factories.

Widespread distribution of PCBs in the environment was not recognized until 1964 when S. Jensen began to search for an explanation for appearance of mysterious elution peaks during gas–liquid chromatographic separation of organochlorine pesticides from environmental samples [3]. He later attributed these peaks to the presence of PCBs in the samples which resulted in

world-wide studies that revealed the widespread distribution of PCBs in the environment.

More recent outbreaks of poisoning in men and domestic animals from accidental food contamination with PCBs stimulated an interest in the toxic effects of PCBs and have resulted in the cessation of the commercial production of PCBs and a regulation of their residues in food.

2. Commercial production and applications

The basic structure of PCBs is as follows:

PCBs have the general formula $C_{12}H_{10-x}Cl_x$ where the number of chlorines substituted on the biphenyls can range from one to ten resulting in ten forms of polychlorinated biphenyls. Two-hundred nine PCB isomers are theoretically possible (Table 1). The number of chlorines in each isomer determines its classification and nomenclature.

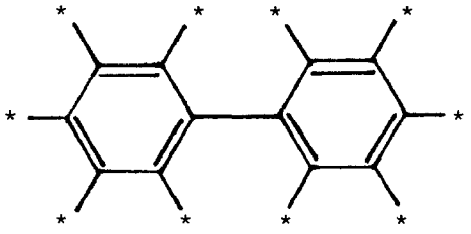


Fig. 1. General structure of poly chloro biphenyl; * denotes position occupied by either a hydrogen or chlorine atom.

TABLE 1

Isomers of PCBs

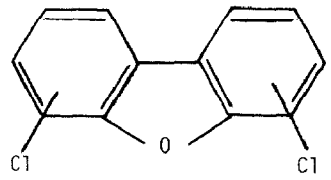
Empirical formula	Molecular weight	Percent chlorine	No. of isomers
$C_{12}H_{10}$*	154	0	1
$C_{12}H_9Cl$	188	18	3
$C_{12}H_8Cl_2$	222	31	12
$C_{12}H_7Cl_3$	256	41	24
$C_{12}H_6Cl_4$	290	48	42
$C_{12}H_5Cl_5$	324	54	46
$C_{12}H_4Cl_6$	358	58	42
$C_{12}H_3Cl_7$	392	62	24
$C_{12}H_2Cl_8$	426	65	12
$C_{12}HCl_9$	460	68	3
$C_{12}Cl_{10}$	494	79	7

*Not a PCB: not added in total.

Table Source: Durfee et al. [4].

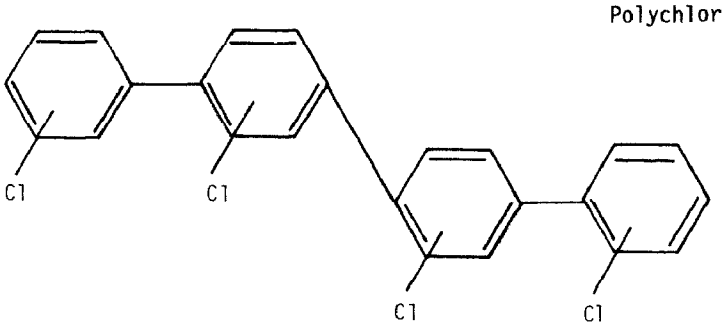
The commercial production of PCBs is carried out by the chlorination of biphenyls with anhydrous chlorine in the presence of a catalyst, usually from filings or ferric chloride. This reaction occurs at extremely high temperatures resulting in a crude product that must subsequently be refined by an alkali wash or sometimes be distilled [4]. The final commercial products are PCB mixtures that vary in chlorine concentration, PCB isomers as well as impurities. In addition, related chemicals, polychlorinated dibenzofurans (PCDF) and polychlorinated quaterphenyls (PCQ) are also formed (Fig. 2) and are present in some mixtures [5]. These different PCB mixtures have been marketed throughout the world under a variety of trade names: Aroclor, Chloretol, DyKanol, Inerteen, and Pyranol (United States); Phenochlor (France); Clophen (West Germany); Kaneclor and Satatherm (Japan); Fenclor (Italy); and Soval (Soviet Union). The varied compositions of isomers in the different PCB mixtures can be illustrated by two of the Kaneclor products. Kaneclor 500 is composed of 55% pentachlorobiphenyl, 26.5% tetrachlorobiphenyl, 12.8% hexachlorobiphenyl, and 5.0% trichlorobiphenyl while Kaneclor 400 contains 43.8% tetrachlorobiphenyl, 32.8% trichlorobiphenyl, 15.8% pentachlorobiphenyl, 4.6% heptachlorobiphenyl, and 3.0% dichlorobiphenyl [6].

Since the Monsanto Company began production of PCBs in 1929, they had been used in increasingly different capacities until the regulation of their use in 1971 [7]. There were three categories of PCB usage: closed uses, nominally



Polychlorinated dibenzofuran

(PCDF)



Polychlorinated quaterphenyl

(PCQ)

Fig. 2. Byproducts found in PCB mixtures.

TABLE 2

Type of systems in which PCBs have been employed

Applications of PCBs	Prior to 1971	After 1971
Closed electrical systems	61%	100%
Nominally closed systems	13%	0%
Open end applications	26%	0%

closed uses, and open-ended uses. The closed uses of PCBs include insulation for electrical wire, cables, and condensors as well as coolant/dielectric in transformers and capacitors. These applications isolate PCBs from the environment. The nominally closed uses of PCBs include hydraulic fluids, heat transfer fluids, and high pressure lubricants. These uses do not totally isolate PCBs from the environment, but for the most part do not allow direct contact. Open-ended uses of PCBs include additives to paints, ink dyes, platicizers, protective coatings for woods when low flammability is necessary, dedusting agents, adhesives, pesticide extenders, ink and dye carriers, and for microencapsulation of dyes for carbonless duplicating paper [1]. These applications resulted in the distribution of PCBs directly into the environment.

From 1971 until 1976, Monsanto produced an average of 27,000,000 lb/year (13,500 ton/y) of PCBs with sales to fewer than 40 customers. PCB production ceased in 1977, nearly 2 years before the Toxic Substances Control Act (TSCA) required it. Of the documented production of approximately 1.4 billion lb of PCBs in the United States (as of 1981), estimates are that 50 million lb have been destroyed, 300 million lb are in landfills, 156 million lb are in the environment, 150 million lb were exported, and 750 million lb are still in use [8].

In 1971, U.S. producers voluntarily limited the sale of PCBs to those applications that minimized introduction of the chemicals into the environment. Table 2 illustrates that applications of PCBs have been limited to closed systems since 1971 [1].

The major producer of PCBs in the U.S. was the Monsanto Industrial Chemical Co. which had two plants, one at Anniston, Alabama (closed in 1970) and the second at Sanget, Illionois. The Sanget plant produced 99% of the PCBs (trade name, Aroclor) used in U.S. industry. Seventy percent of these PCBs were used in capacitors while the remaining 30% were utilized in transformers [9].

2.1 Regulation

Despite uncertainty about health effects, Congress elected to regulate PCBs under the Toxic Substances Control Act (TSCA) of 1976. In 1979, the U.S. EPA banned further production of these compounds. However, utilities were

allowed to continue to use existing transformers and capacitors containing PCBs for the duration of their normal service life, although certain uses have been banned.

Under new rules issued by the U.S. EPA in July, 1985, utilities must phase out the use of PCB transformers in or near buildings by 1990. Ultimately, they must destroy all PCBs in equipment and clean up or contain any PCB-contaminated sites that are environmental hazards.

Disposal regulations for PCB's are quite restrictive. In the 50 to 500 ppm range, the U.S. EPA allows landfilling. However, when PCB levels are greater than 500 ppm, in liquids, the waste must be incinerated. Below the 50 ppm level, disposal is unregulated by the U.S. EPA, but, States' rules may mandate otherwise.

Ironically, PCBs are still manufactured by Germany, France, Spain, and Italy and certain Eastern European countries and they continue to be used throughout the world [8].

3. Physical and chemical properties

PCBs have physical and chemical properties that make them valuable in the previously mentioned applications of electrical insulations, i.e. stability and fire resistance. Pure PCBs are solids at room temperature (25°C), and their melting points range from 54°C for 2-chlorobiphenyl to 310°C for 2,3,4,5,6,2′,3′,4′,5′,6′ decachlorobiphenyl. Generally, PCB melting points increase with the complexity of the compound. The chemical mixtures of PCBs used in industry are usually colorless to lightly tinted oils. Densities of such mixtures as Aroclors and Kaneclor are approximately 1.2 to 1.5 g/cm^3 and have refractive indices of approximately 1.62 [6].

PCBs are fat-soluble, water-insoluble, and very stable. They are very resistant to degradation, oxidation, and other chemical agents such as acids and bases. They can withstand extreme temperatures up to 1600°F (870°C) and are fire resistant [6]. PCBs may dimerize and when they do they form polychlorinated quaterphenyls (PCQs) (Fig. 2) [10]. Another property of PCBs that make them attractive to industry is their low vapor pressures. This property also reduces the probability of exposure even with concentrations of several thousand parts per million [11].

4. Environmental exposure

There is no evidence that PCBs occur naturally in the environment. Apparently, all PCBs present in nature can be attributed to dissemination by humans. The majority of PCBs in the environment is found in surface marine waters, mainly of the North Atlantic Ocean [1]. However, since restrictions of PCB use and production, the North Atlantic surface water has shown a 40-

fold decrease in PCB concentration since 1972. Tests in September, 1973 indicate a disappearance of 20,000 tons of PCBs in the upper 200 meters of water during that one year time span [1].

In 1972, the rivers of the United States were tested for presence of PCBs. The concentrations of PCBs found ranged from less than 0.01 to 0.45 μg/l [12]. These are low concentrations compared to that found in Japanese drinking water and North Atlantic surface water which contained 10–100 μg/l and 1–35 μg/l, respectively [7, 13] . The Hudson River is a prime example of PCB pollution as a result of unregulated discharge. Between 1942 and 1970, two General Electric plants (Fort Edward and Hudson Falls) discharged an average of 14 kg of PCBs per day into the river. Sediment samples from the river bed have been found to contain concentrations of 540 to 2,980 μg/kg. Fish taken from the river demonstrated PCB concentrations of 62 to 135 mg/kg [14]. These concentrations have greatly decreased since the cessation of PCB discharge into the river.

Sedimentation testing during the early 1970's in Lake Erie (1971), Lake St. Clair (1970 and 1974), and the Detroit River (1974) revealed residues of PCBs which were 3 times higher than those of all organochlorine insecticides. These levels have also decreased since the restrictions of PCBs [15].

An important environmental concern about PCBs is their incorporation into the food chain. Benthic invertebrates feeding on the lake bottom consume PCBs and later pass them on the food chain to fish, birds, man, and other creatures. As PCBs pass through the food chain, concentrations accumulate and are transferred from one organism to another. As a result, the upper trophic levels are most prone to PCB accumulation [1], and freshwater fish are the major source of PCBs in the diet of humans [4]. It has been indicated that adults consuming 150 g per week of Coho salmon from Lake Michigan also are ingesting 15 mg/kg of PCBs whereas in Japan, 80 g of fish contains the same quantity of PCBs [7]. Studies of 70–79 year old Japanese men revealed 5.1 mg/kg of PCBs in fat tissue. Japanese women of the same age bracket had 2.4 mg/kg PCBs in fat tissue [16]. A 1972 survey by Yobs of 637 Americans from 18 states indicated that 26% had 1–2 mg/kg PCBs in fat tissue [17]. In the same year, a report by the U.S. Department of Agriculture listed PCB presence in many common foods such as cheese (0.25 mg/kg), milk (2.27 mg/kg), and eggs (0.55 mg/kg) [6].

There are four major routes by which PCBs enter the environment: industrial accidents or discharges, incomplete destruction of PCB containing products, natural weathering of PCB containing products, and leaking from landfills [6]. Most PCB leaks result from pump leaks into the cooling water used in capacitor and transformer production resulting in the introduction of the PCBs into municipal sewers [9]. Once in the environment, PCBs can be transported by leaking, diffusion, rain, snow, and dust [6].

Domestic sources of PCBs in the U.S. are: 1) industrial and municipal sew-

age disposal, 2) paper recycling plants, 3) PCBs in the soil, 4) incineration, and 5) municipal (solid waste) landfills. The PCBs put in carbonless copy paper from 1957 to 1971 contaminated the paper products which have subsequently been recycled and put back into the environment. PCBs have found their way into soil from disposal sites and equipment servicing as well as oils used in dust control which may have been contaminated with PCBs.

Incineration is probably the best method for destruction of PCBs, but if not properly executed, incineration can release PCBs and their by-products back into the environment. Incineration can be accomplished in a number of thermal devices including industrial boilers, cement kilns, and hazardous waste incinerators. All appear, if properly operated, to satisfactorily destroy the chemical [18]. U.S. EPA regulations governing incinerators require 99.9999% destruction, thus allowing a maximum of 10^{-4}% to escape. Chemical landfills are presently effectively used to isolate PCBs from the environment, but the danger of erosion and leaking is present [4]. PCBs are also introduced into the U.S. by atmospheric currents from other parts of the world, but the amounts are nominal compared to domestic sources [1].

5. Bioaccumulation/distribution in animal tissues

Environmentally, the bioaccumulation of PCBs is very important. Due to their low solubility in water and high accumulation coefficients, PCBs display high bioaccumulation values in animal tissue. Aquatic organisms, such as fish, experience the greatest amount of PCB accumulation. For instance, the concentration of PCBs in Lake Michigan averages approximately 0.008 μg/kg while PCB concentrations found in the lake trout are approximately 28 mg/kg [19]. This concentration is over 3 million times that of the external environment.

Different species of fish collected from the same environment in Lake Michigan contained different amounts of PCBs. Lake trout and carp both have approximately 10% body fat and contained more than five times as much PCB as yellow perch with only 4% body fat. It appears that species of fish with higher amounts of body fat (such as carp or catfish) contain more PCBs than other species of fish having less body fat (such as yellow perch or northern pike) [20]. This difference in the bioaccumulation of PCBs is mainly dependent upon adipose tissue and under stress this may present a release mechanism as PCB-containing lipids are mobilized [1]. PCBs also may accumulate in skin and muscle tissue. After PCBs reach the bloodstream, they become located within the liver and muscle. From these locations they are redistributed and become incorporated within other tissues such as adipose tissue and skin which, although they have lower blood perfusion rates [21], also have higher affinities for PCBs.

This distribution of the PCBs primarily in adipose tissue is displayed in feeding experiments with Sherman rats [22]. These rats were fed a diet of 500

ppm of Aroclor 1254 for 6 months. After 10 months, the rats were sacrificed and PCB concentrations were determined. Adipose tissue contained 1200 ppm of PCBs while liver tissue contained only 22 ppm [22]. In another such feeding experiment, rats were fed diets of 1000 ppm Aroclor 1254 for 98 days. The adipose tissue contained 11,278 ppm while other tissues had less than 200 ppm [23]. Experiments with pheasants indicate that as much as 82% of the PCBs are absorbed via the gastroenteric tract [24]. Additional absorption, though reduced in amount, is by way of the respiratory tract [25]. In considering the effects of absorption and bioaccumulation of PCB's in man, it is calculated that ingestion of 2 liters of water per day containing 10 μg/l (10 ppb) would result in a 70 year lifetime burden of 7 mg/kg assuming 100% absorption and zero excretion or metabolism. This level is three orders of magnitude lower than the average LD_{50} (Lethal Dose at which 50% deceases).

5.1 Excretion/metabolism

Although adipose tissue accumulates more PCBs than other tissue types, the liver still must be considered an important target organ because of its importance in the excretion of such toxins in the body. Furthermore, liver tissues still can accumulate concentrations of PCBs at levels twice that seen in the rest of the body [26]. Microsomes of the human liver transform certain PCBs into less lipophilic compounds to facilitate excretion [27, 28]. However, the nature of the PCBs in question dictates the fate of these toxins because their excretion is associated not only with the rate of metabolism, but also with their lipophilicity.

In vitro experimentation involving the metabolism of PCBs by human liver microsomes indicates that PCBs must have two adjacent unsubstituted carbons to be metabolized. Any unmetabolized PCBs appear to accumulate in adipose tissue [27, 28].

The number of chlorine atoms on the biphenyl compound also affects the rate of metabolism [27]. In mice, the rates of metabolism and excretion of orally administered PCBs appears to decrease as chlorination increases [21]. Similarly, studies by Bunyan and Page dealing with quail suggest that absorption, metabolism and excretion become increasingly impaired as chlorination increases on the biphenyl compounds [29]. However, the extent of chlorination alone is not the only thing to affect metabolism as different isomers have been demonstrated to be metabolized differently by hepatic enzymes. One study indicated that 2,2′,4,4′,5,5′ hexachlorobiphenyl is not metabolized and it tends to accumulate in human adipose tissue [27]. This indicates that not only the number of chlorine atoms but also the location of the chlorine on the biphenyl ring affects its disposition. Thus, PCB isomers differ sufficiently to warrant individual evaluation of each isomer with respect to its metabolism. The extent of PCB metabolism also depends upon the animal species [30].

Testing with rhesus monkeys demonstrated that the majority of PCBs from

a diet of Aroclor 1248 accumulate within liver and adipose tissue and decrease slowly following discontinued exposure. In fact, the PCBs appeared to have a half-life of at least 3 to 4 months.

Beagles were used in an experiment in which both 2,3,6-heptachlorobiphenyl (HCB) and 2,4,5-heptabromobiphenyl (HBB) were given in 0.6 mg/kg doses. The results indicated that 70% of the 2,3,6-HCB was excreted in 3 days while only 14% of the 2,3,5-HCB was excreted in 20 days. The 2,4,5-HCB was 66% excreted in 15 days while only 8% of the 2,4,5-HBB was excreted in 25 days [31]. Thus, the rate of elimination was also determined to be affected by chlorine position, probably by controlling the rate of metabolism. Additionally, the extent of metabolism and rate of excretion is also determined by the specific halogen.

Another experiment involved beagles treated with an intravenous dose of 0.6 mg/kg of ^{14}C labelled 4,4′-PCB. Excreta, bile and tissues were collected from 15 minutes to 28 days following treatment. These specimens oxidized and $^{14}CO_2$ was quantitated by scintillation counting. The results indicated that 50% of the dose of 4,4′-PCB was excreted as metabolites within the first 24 hours. Urine contained 7% of these metabolites, while feces contained the remaining 43%. Any remaining ^{14}C in the dogs was present mostly in fat, muscle and skin. By 5 days after the termination of exposure, more than 90% of the original dose of the 4,4′-PCB was excreted. Cynomolgus monkeys were exposed to PCBs in an identical experiment. However, only 15% of the dose was excreted within the first 24 h. At 24 h, the blood and bile contained 75% and 100%, respectively, of their original values. The remaining PCBs were located mainly in the adipose tissue (33%) as the parent compound. Skin and muscle contained lesser amounts. After 28 days, only 59% of the dose was excreted. Hence, with 4,4′-PCB, beagles appear to be capable of eliminating highly chlorinated PCBs more quickly than monkeys due to metabolic differences between the two species [32].

5.2 Mechanism of metabolism

Polychlorinated biphenyls are metabolized via dechlorination and arene oxide formation resulting in metabolites which are more polar and water soluble thus facilitating excretion. The enzyme system responsible for dehalogenation is the hepatic mixed function oxidase system which upon exposure to PCB's and polychlorinated dibenzofurans responds with the subsequent induction of specific P-450 isozymes. This induction resembles the process observed following chronic treatment with phenobarbital and methylcholanthrene [33]. Arylhydrocarbon hydroxylase induction occurs upon PCB exposure and it has been suggested that toxicity to PCB's is correlated with induction potency [120]. It has also been suggested that toxicity to PCB's is related to increased intermediary metabolism (i.e. steroids) as well as enhanced metabolism of

xenobiotics. Genetic variations exist among humans with respect to arylhydrocarbon hydroxylase responsiveness and individuals with high AHHase inducibility may be more sensitive to toxic effects of PCBs [34].

Biphenyls are hydroxylated then conjugated before incorporation in rat bile for excretion. After doses of 2,2′-; 2,4-; 2,3-; 3,4-; 3,3′-; and 4,4′-dichlorobiphenyls, the primary metabolites were dichlorodihydroxybiphenyls [22]. PCBs have been indicated in some cases as the toxins responsible for mutagenicity and liver damage in animals and humans. It seems that these adverse effects result from electrophilic intermediated produced during the metabolism of PCBs [28, 35]. Hydroxylation, the major pathway of metabolism for PCBs, may sometimes involve arene oxides as intermediates. Arene oxides may lead to carcinogenic, cytotoxic, or mutagenic effects. Increased arene oxide production may be due to the activity of both PCBs and PBBs working additively together [36]. Furthermore, hydroxylated chlorobiphenyls are more hazardous than the starting PCBs [1]. It also has been indicated that rats exposed first to PCBs or PBBs have an increased likelihood of toxicity from other chemicals such as carbon tetrachloride, chloroform, and bromobenzene. Certain insecticides are also more toxic when given with PCBs [37–39].

Since degree and position of chlorination dictate the rate of PCB metabolism, it may suggest that the limiting factor is the rate at which arene oxide intermediates are produced [40]. The production of these highly reactive, electrophilic arene oxides may be due to the activity of hepatic and extrahepatic arylhydrocarbon hydroxylase (AHH). The metabolism of 4-dichlorobiphenyl often yields 4,4′-dichloro-3-biphenylol which is probably due to a rearrangement of a 2,3-epoxide or a 3,4 epoxide using an arene oxide as an intermediate. If a 2,3-epoxide is rearranged, the metabolite is 4,4′-dichloro-2-biphenylol. However, if a 3,4-epoxide is rearranged then a 3,4′-dichloro-4-biphenylol is the metbolite [15]. A mixture of the two is most probable.

A major concern with PCB metabolism is the effect resulting metabolites may have on the young of exposed pregnant adults. Aroclor 1254, in doses of 10 or 50 mg/kg, was administered to rats from the 7th to the 15th day of pregnancy [23]. These doses resulted in average PCB concentrations in fetuses excised on the 20th day of 0.63 and 1.38 mg/kg for the above doses, respectively [23]. These values, although low, indicate a definite transfer occurring from parent to fetus. Laboratory studies indicate that greater quantities of PCBs are transferred by breast feeding after birth than prenatally through the placenta. This may be due to the fact that PCBs accumulate more readily and in greater quantity in the fat of maternal milk rather than in maternal serum [41]. Tests of blood, milk, and adipose tissue of infants and mothers yielded data which demonstrate that the leading maternal source of PCBs for infants is, in fact, maternal milk fat (Table 3). Additionally, the fetus accumulates the majority of PCBs in adipose tissue.

TABLE 3

Maternal sources of PCBs and distribution found in infants

Biological source	Concentration of PCBs (ppb)
Maternal milk	13
Maternal milk fat	350
Maternal blood	1.4
Infant blood	2.5
Fat only	470
Total adipose tissue	150
Liver	7.3
Adrenal	26

6. Toxicity and effects of PCBs

Acute toxicity is a valuable consideration when considering toxic effects of any chemical on living organisms. The lethal doses of PCBs such as Aroclor 1242 and Aroclor 1260 administered orally are 4.25 g/kg and 9.5 g/kg, respectively [42a]. Some of the toxicity to PCBs such as hepatic injury appear to result from electrophilic intermediates formed during metabolism [35]. In laboratory rats, oral toxicity decreases with increased chlorination; however, there is no similar correlation with rabbits and toxicity [42, 43]. The exact effects of PCBs are difficult to ascertain because the mixtures often contain impurities. PCB mixtures have also been demonstrated to contain several other types of chlorinated compounds such as polychlorinated naphthalenes and polychlorinated dibenzofurans (PCDFs) [44]. The presence of these PCDFs in PCB mixtures may arise from the distillation process during purification (Fig. 3) [1].

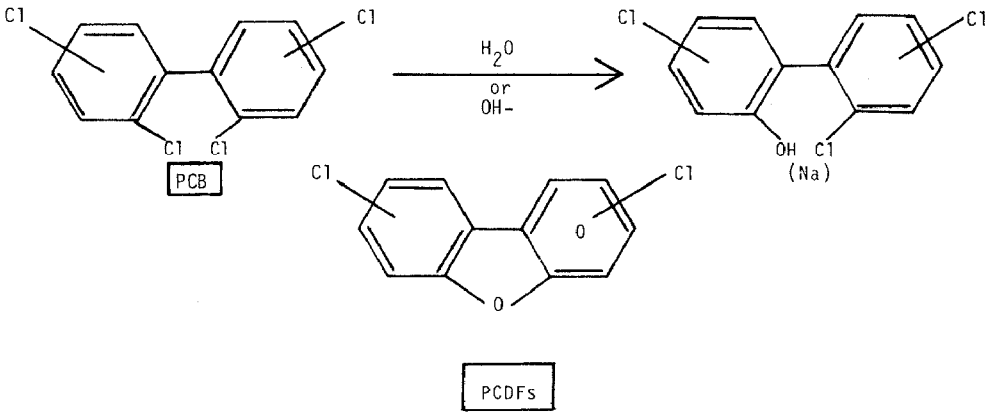


Fig. 3. Conversion of PCBs to PCDFs during purification process.

6.1 PCDFs

The effects of PCDFs have been widely studied because of their possible connection with PCB toxicity. Rats on diets of PCDFs displayed inhibition of food consumption. PCBs also caused reduced food consumption but the decrease was far less than that demonstrated by PCDFs. In addition, chloracne-like lesions appeared on the ears of these rats. Low levels of PCDFs cause the hemoglobin hematocrit and mean corpuscular volume to decrease. At higher concentrations, 10 ppm or more, PCDFs cause additional erythrocyte count decreases [45]. PCDFs have also been demonstrated to decrease serum glutamic-pyruvic transaminase activity as well as testosterone concentrations within the testes. Concurrently, an increase in serum glutamic-oxaloacetic acid transaminase activity is typical for these PCDF treatments. Mixtures of PCBs and PCDFs cause a variety of symptoms in treated animals including increased serum cholesterol levels, elevated cholinesterase activity, and decreased triglyceride and aminopeptidase activity [46].

6.2 ATPase enzyme activity

PCBs are also capable of altering ATPase enzyme activity in organisms. It appears that the lipophilic properties of PCBs are the dominating factor in PCB inhibition of ATPases. The inhibitory activity of PCB decreases as its aqueous solubility increases. It seems that the lipid portion of the ATPase enzyme readily associates with PCBs. An allosteric change probably occurs in the ATPase enzyme by the lipophilic separation and results in decreased activity of this ATPase [47]. In fact, studies by LaRocca and Carlson indicate Aroclors and other chlorinated hydrocarbons are equally capable of inhibitory activity on both Mg^{2+}- and Na^{+}/K^{+}-adenosine triphosphatases (ATPases). More specifically, it was determined with *in vitro* experimentation that a concentration of 30 ppm of PCBs inhibits the MgATPase activity of brain and heart tissue [48–52]. The activity of each of the 209 isomers of PCB as ATPase inhibitors varies according to each compound and its corresponding association with a given ATPase [47].

6.3 Chloracne

Chloracne, a common symptom of human PCB poisoning, is a skin disorder associated with poisoning by any chlorine-containing compound. It occurs as severe acne but does not disappear as quickly as it appears and can be severe enough to leave facial scarring. The effect of PCBs on skin is manifested as typical chloracne in addition to hyperpigmentation, loss of hair, and porphyria [53]. The acneiform eruptions of chloracne form both closed comedomes (cysts) and open comedomes. The cause of these acneiform eruptions appears to be the follicular excretion of PCBs with the sebum. These excretions continually stimulate the skin and result in the acneiform characteristic of PCB poisoned patients [54].

6.4 Animal experiments

On the Acute Toxicity Chart, PCBs are only ranked slightly toxic to non-toxic [11]. Recent studies indicate that short-term exposure to PCBs does not seem to be particularly toxic [55]. The short-term toxic effects seen in laboratory animals would appear to require dosages in terms of pints or quarts to cause corresponding effects in humans [56].

Experiments with rhesus monkeys on a diet of 300 ppm of Aroclor 1248 resulted in chloracne, loss of eyelashes, and subcutaneous edema [57]. Longer terms of exposure in male monkeys resulted in slight periorbital edema and erythema [58]. Oral administration of a 65% chlorinated biphenyl to laboratory animals resulted in atrophy and lesions of the liver [59]. More specifically, male dogs on a diet of 100 μg/g of PCBs have experienced observable reductions in growth rates while displaying an enlargement of the liver. Serum levels of alkaline phosphates are also elevated [60]. Studies on the effects of PCBs on microorganisms such as the *Euglena* and the *Scenedesmus* also demonstrate reduced growth rates. Other microorganisms that contain chlorophyll, the *cyclosterium* and *thalossiosioa,* also display suppressed growth [61–64].

Guinea pigs, rats, and rabbits that were topically treated on a daily basis with 0.025 ml (34.5 mg) of undiluted chlorinated biphenyl all demonstrated fatty degeneration and central atrophy of the liver. In addition, the epidermis thickened at the site of application [25]. Testing with Wistar rats fed 1000 ppm of Kaneclor 300, 400 or 500 resulted in the development of cholangiofibrosis. Lower doses did not display such symptoms. In addition, increasingly larger concentrations of PCBs with greater chlorination caused higher occurrences of medullar hyperplasia [65]. Sherman rats fed high doses of Aroclor 1254 exhibited adenofibrotic lesions.

Mice also demonstrated liver changes when given highly chlorinated compounds in concentrations of 300–500 μg/g [1]. A 300 ppm dosage of Aroclor 1254 was administered to two groups of mice. Group one was exposed for 11 months while group two was exposed for 6 months. Histological examinations of these mice indicated that one of the 24 mice in group two developed hematomas. Furthermore, of the 22 mice in the first group, all displayed adenofibrosis [66].

Birds also suffer adverse effects from long-term exposure to PCBs. For example, chickens display reduced egg production and fertility over long-term exposure to PCBs [67]. Chickens have also displayed slight morphological deformities and a decline in reproductivity which is accompanied by subcutaneous edema when doses of 20–50 μg/g of PCBs were administered [1]. Chickens treated orally with 100 ppm of Aroclors 1242 and 1254 display decreased rates of hatching eggs [68]. Quails exposed or 2 months to Aroclor 1242 showed discontinued production of eggs and displayed decreased levels of Vitamin A in the liver with as much as 50% of the original level of Vitamin A being de-

creased [69]. Wild fowl, in general, display reproductive changes when exposed to PCB concentrations of 50–200 μg/g [1]. American kostiels exposed to PCBs demonstrated nominal increases in the thickness of egg shells. Higher doses of 80 mg/kg were necessary to cause decreased egg production and a 12% decrease in eggshell thickness. Ring doves fed 20 ppm of Aroclor 1254 displayed lower hatching rates. Cytogenetical testing on the embryos of these PCB fed doves yielded higher than normal chromosomal rearrangements and aberrations when irradiated with X-rays [70].

Of all bird species studied, ring doves appear to be the most susceptible to PCBs. A 10 mg/kg dose of PCBs has been reported to greatly increase embryonic mortality rates in the second generation as well as cause chromosomal aberrations. In addition, behavioral changes have been observed in the parent birds [71]. It is apparent that different species of birds have varying tolerance and reactions to PCBs.

Birds also demonstrate many symptoms exprienced by laboratory mammals. Chickens as well as other species show enlarged kidneys, splenic atrophy, and congestion and infiltration of fat in the liver [72, 73]. Pelicans have been shown to experience some hepatocellular alterations when exposed to PCB doses of 100 μg/g [1].

6.5 Vapor exposure

Vapor exposure to PCBs seems to result in an increase in the occurrence of adverse effects on animals. Vapor exposure of mice demonstrates that chlorinated diphenyls could cause injury when used in small concentrations. PCB exposure, in this fashion, may be more dangerous than exposure to chlorinated naphthalenes [62, 63]. However, guinea pigs that underwent vapor exposure to PCB concentrations of 816 μg/l of air for the 7 h/day over 14 days showed no toxic effects. This concentration was near saturation and did cause poor growth, but nothing so profound as indicated by the experiment with mice [62, 63].

Skin exposure, as mentioned previously, can cause chloracne. In addition, high doses of PCBs may cause systemic effects. These effects increase in severity with the amount of chlorination of the biphenyl [44]. Systemic effects were observed in rats given five skin applications of Aroclor (1 ml of 20% solution mixed in olive oil). These rats displayed general malaise, rough fur, loss of body weight, death with and without convulsions and coma [74].

6.6 Reproductive effects

One of the leading concerns regarding PCBs today is the effect on mammal reproduction and the reproductive system. With regard to the endocrine system, PCBs can cause irregularity in the menstrual cycle [53]. In monkeys, small doses of 2.5–5.0 μg/g will cause an erratic menstrual cycle as well as an increase in abortion rates [75]. Reproductivity tests in female rhesus monkeys

with PCB doses of 2.5–5.0 ppm were carried out over a 6 month period. The monkeys on the 5.0 ppm dosage demonstrated irregularities in the menstrual cycle. Six of the eight females tested were capable of conceiving. Of the six animals that conceived, five had abortions or experienced early fetal resorption. The eight females receiving dosages of 2.5 ppm were all capable of conceiving. However, three did not carry to full term and the surviving infants showed reduced size and dark skin pigmentation [57].

Studies by Kihlstrom et al. determined that a decrease in implantation capability occurred in mice when both the mother and father were nursed from PCB or DDT-treated mothers. When the mothers alone were treated with PCBs, implantations dropped to 75% from a control rate of 94%. The control rate dropped to 79% when the mothers were treated with DDT. However when only one parent was nursed from a treated mother, there was no noticeable decrease in the implantation rate. It seems that the milk on which the mice nursed, contained PCBs and was capable of increasing standard catabolism. The end result was an alteration of normal sexual development of these mice [76].

A similar experiment was carried out by Burke and Fitzhugh with rats. The rats were fed diets of Aroclors 1242, 1254, and 1260. Concentrations of 1, 10 and 100 ppm were administered. At lower concentrations of 1 and 10 ppm there were no noticeable effects. However, when dosages of 100 ppm of Aroclor 1242 were used, the animals displayed decreased mating indices in the second generation. Dosages using Aroclor 1254 caused the number of pups born to be reduced and also decreased the survival rate of second and third pregnancies [77]. An increased rate of stillbirths was only apparent when the dosages were of Aroclor 1260 [78]. A decrease in fetal weight and presence of neoplastic nodules in the liver were apparent [79a].

Additional experiments with minks were performed with PCP doses of 10 $\mu g/g$. At this concentration, the minks display decreased growth and reproduction [1]. Studies by Tombergs indicate that PCBs can affect the reproductive and adrenal hormones of animals by stimulating microsomal enzymes responsible for metabolizing the adrenal hormones [79b].

7. Human exposure

The lack of sufficient data concerning human exposure to PCBs is the limiting factor in determining PCB toxicity in people. Rare accidental PCB exposures have become the major source of nearly all of the acute health data. The first of these is an accident which took place in 1968 when thousands of people were orally exposed to very high concentrations of PCBs and PCDFs in Fukuoka, Japan. This exposure was caused by PCB contamination of rice oil which was subsequently used for cooking. The disease described by these symptoms was called Yusho rice oil disease. The second major accident leading

to human exposure occurred in 1978 in Taiwan. Not unlike the Yusho case, high concentrations of PCBs were ingested by humans through use of contaminated rice oil. From these two specific incidents and other less noted PCB exposure situations, the effects of PCBs on humans have been pieced together.

7.1 Physiological effects

Gross morphological or pathological effects are rarely related to PCB exposure in humans with a variety of minor impairments being reported [1]. The general symptoms of PCB ingestion are weakness, nausea, headache, impotence, insomnia, loss of appetite, loss of weight and abdominal pains. Muscle spasms and muscular pain also may be related to PCB poisoning. Ocularly, PCBs are capable of causing inflammation and burning, edema of the eyelids, cysts of the tarsal glands and conjuctiva [53]. The sebaceous gland of the eyelids, the Meibomian gland, may also become hypertrophic and result in cheese-like discharges from the eyes [54].

Autopsies of humans exposed to PCBs in the Yusho rice oil poisoning revealed typical chloracne and pigmentation of cutaneous tissue. In addition, follicular hyperkeratosis, dilation of hair follicles, and melanin increases (pigmentation) in the epidermis were observed in histological preparations of skin [80]. Other PCB effects on the skin include xerosis, nail deformity, hair loss, and hyperidiosis. In survivors of the Yusho accident, the acneiform, follicular cysts, pigmentation, and nail change all improved dramatically or returned to normal within 2–5 years [54]. It is possible that PCBs stimulate the melanocyte in some fashion, but the pathogenesis of pigmentation is unclear and any relation with PCB is merely theory [54].

Within the blood, serum triglycerides have been noted to increase due to PCB influence. A decrease in serum bilirubin is also noted. Organ system impairment such as fibrosis, hepatocellular necrosis, enlargement of the liver, and reduction of air capacity in the lungs has been observed [53]. It appears that prolonged exposure to PCBs can cause liver damage. However, the severity of such hepatic damage is not certain [44]. In addition, hypertrophia, hyperplastic gastritis, and ulcer formation have been observed in the gastrointestinal tract [75]. A group of women occupationally exposed to PCBs was studied to note effects in pregnancy. The mean birth weight of infants born to these women was 53 grams lighter ($\sim 1.5\%$) than the weight of infants born to women in a control group. The gestation period was reduced by 6.6 days in the exposed women and this decrease in the gestation period may account for the decrease in birthweight [81].

7.2 Neurological effects

The extent of the effects of PCB exposure on the nervous system are, at most, vague. Some studies indicate that both a 30% decrease in motor and a 50% decrease in sensory nerve conduction velocity occurs in PCB exposed pa-

tients [82]. In addition to nerve-conduction-velocity decreases in the central and peripheral nervous systems, other sensory disturbances may also occur. The senses of taste, hearing, smelling, and sight may be distorted as well [53].

Studies indicate that there is no correlation between neurological manifestations and PCB concentration in the blood. That is, high PCB concentrations in the blood do not always give rise to neurological effects [82]. Speculations are that these neurological symptoms are caused by some other chemical substance or that genetic factors may make certain individuals more susceptible to PCB related neurological dysfunctions.

In 1980, a neurological study was performed with 35 of the 2000 people exposed to PCBs in the 1978 accident in Taiwan [82]. Neurological symptoms of some type were observed in 31 patients (89%). Thirteen patients (37%) suffered from a dull, non-pulsating headache. Dizziness or light-headedness was experienced by 12 patients (34%). Nausea and vomiting sometimes accompanied these symptoms, but no vertigo or tinnitis was observed. Both paresthesia and hypoesthesia were experienced, and some patients demonstrated sluggish or absent deep tendon reflexes. Blood testing revealed no correlation between these effects and PCB concentrations in blood.

7.3 Carcinogenicity

It has been determined that large doses of highly chlorinated compounds have the ability to induce tumor growth in both rats and mice, but the specific role of less than extremely high levels of PCBs in promotion of tumor growth is unclear [1]. Oxidation of PCBs may produce arene oxides [27] which potentially could act as a tumor promoter. In mice, PCBs induced the development of liver tumors [83] and mice exposed to high levels of PCBs (500 μg/g) for prolonged time spans have displayed hepatocellular carcinomas and nodular hyperplasia [84, 85]. Although few PCBs have been tested for carcinogenic effects, Aroclor 1254 and 500 have been determined to produce both benign and malignant tumors in the livers of mice [86]. In a study of Kaneclor 500, 7 of 12 mice fed 500 ppm PCBs over a 32 week period developed liver nodules. Five of the mice had hepatocellular carcinomas whereas other organs displayed no trace of metastases or tumors [87].

There have been extensive data collected on the carcinogenic effects of PCBs in laboratory animals, but few concerning humans [88]. Limited accidental and prolonged occupational exposures are the only source of such data. Of the thousands of individuals exposed in the Yusho, Japan incident of 1968, four deaths were examined to determine the absence or presence of PCB related effects. The four autopsies which were conducted, included three adults and one stillborn infant [89]. All four individuals displayed skin lesions that we now know are characteristic of PCB exposure. Additionally, mesenteric fatty tissue and skin contained high levels of PCBs. This again is to be expected since PCBs tend to bioaccumulate in adipose tissue [90, 91]. The stillborn was

heavily pigmented, being in a state referred to as "Brown Baby (or Cola-colored)". This pigmentation indicated transported passage of PCBs to the developing fetus [90]. Only one of the four autopsies revealed any hepatic damage. This victim, a 48-year-old Japanese woman, was diagnosed as having liver cirrhosis with multilobular cirrhotic changes being accompanied by many hepatic-cell carcinoma nodules [89], however, this was not considered significant.

Although the dermatitis of these four individuals has been associated with PCB exposure, the stillbirth and liver damage is not conclusive enough to establish a causal relationship between PCB exposure and these given effects. Furthermore, reevaluation of mixtures of the contaminated rice oil from Yusho indicate that other compounds, such as hazardous polychlorinated dibenzofurans (PCDFs) [92] and polychlorinated quaterphenyls (PCQs) were present in the PCB mixture [10].

The major PCB-related effects in humans are subtle even when the PCBs are present in large concentrations. Although, acute exposure is rare for humans and wild life [1], an exception to this is the direct and cumulative occupational exposure to PCBs. Some workers in capacitor plants have been exposed for decades to PCBs [93]. Lower levels of PCBs may be linked to minor transient effects such as headaches, abnormal fatigue, and possible joint soreness. Higher levels may result in dermatological effects such as hyperpigmentation and chloracne [94, 95].

One occupational exposure study used 14 capacitor plant workers who were breathing 0.1 mg/m^3 of PCBs. Seven of the 14 workers acquired chloracne which disappeared after exposure to PCBs was discontinued. Of these 7, 6 possessed normal liver function. The remaining individual with chloracne, had only borderline liver abnormalities. Within 13 months after termination of exposure, liver function returned to normal. Although chloracne appears to be related to PCB exposure, the data do not show with certainty that the liver problems were caused by PCBs. Lack of controls and only a single liver abnormality make its occurrence not statistically significant [96].

The South Carolina Department of Health conducted a study with 32 capacitor plant workers [97]. Ten of these individuals were regularly exposed to PCBs. The findings revealed that there was "no evidence of physical harm resulting from working with PCBs" [98].

The carcinogenicity of PCBs was tested in three additional epidemiological studies. The first one used 92 refinery workers. Of these 92 people, three had melanomas. However, sunlight could not be ruled out as a cause for the melanomas. Additionally, these employees may have been exposed previously and simultaneously to other known carcinogens [99, 100].

The second study covered a time span from 1945 to 1965. In this study, 89 Monsanto workers with at least 6 months exposure were monitored. Neither liver cirrhosis nor liver dysfunction was noted in any of the employees. Four respiratory cancer cases occurred, but were not statistically significant from

controls. Furthermore, there were additional exposures to known carcinogens, particularly through cigarette smoking [101].

The last study used 2,567 capacitor plant employees in whom there appears to be an increased rate of death due to liver cancer [102]. However, the incidence of cancer was "inversely related to duration and latency of exposure" [103], which does not suggest occupational exposure to PCBs as the causative mechanism. Additionally, there was an increased rate of rectal cancer. The plant was, however, located in an area where there is a higher than average rectal cancer mortality rate for all inhabitants [104].

From these occupational studies, high levels of exposure to PCBs have demonstrated the ability to cause dermatitis, but other clinical effects, including cancer, have not been observed. Studies of individuals who were environmentally exposed to PCBs, not occupationally, demonstrated no clinical effects, including dermatitis [105, 98].

The small sample size and simultaneous exposure to additional toxic compounds makes the cancer evaluation in these studies difficult. These studies demonstrate an excessive mortality rate pattern that is inconsistent with the probable carcinogenic effects of PCBs [106, 98].

8. Case studies of accidental exposures

The best insight into the effects of PCB exposure has come from case studies of accidental and occupational exposures.

In 1983 in Simcoe County, Ontario, a material dripping from a fluorescent light fixture in a school room was found to contain 200,000 ppm of PCBs (20% PCB by weight) which was later identified as Aroclor 1254. The ballast of the light had originally contained 1.5 ounces (42 g) of PCBs and 1/3 of an ounce was lost in the leak. Among all the students and teachers exposed to these PCBs, there were no noted symptoms except several headaches which were attributed to the pungent odor that was present.

The Yusho exposure of 1968 was caused by a leak in a heat-exchanger used in rice oil manufacturing. Kaneclor 400 was the PCB present and the contamination level was determined to be between 1500 to 2000 ppm of PCBs. Of 12 Yusho patients studied, 10 subsequently died. Four of these patients (ages 13, 25, 46, and 73) died from heart failure. It was never determined if any of these four victims had a family history of heart disease. Three other patients died from respiratory failure. Rupture of liver carcinomas resulted in the deaths of two patients and a tenth patient died as a result of aspiration pneumonia.

Analytical methods for the determination of PCBs were not developed until 5 years after the Yusho incident. In 1973, gas chromatography was used to determine PCB concentration in whole blood. By this time, the Yusho patients had a mean PCB level in blood of only 7 ppb [10]. Later testing verified that the rice oil was also contaminated with PCDFs [92]. Almost all Yusho patients

displayed PCQ blood levels greater than 0.02 ppb [10]. Elevated concentrations of PCQs and PCDFs in the rice oil indicated that the oil was heated first [107]. Recent data concerning the Yusho incident seem to indicate that adverse health effects originally blamed on PCBs were really due to exposure to these toxic contaminants of the PCB mixture [11].

The source of PCB in the 1978 Taiwan incident has not been determined. However, just as in the Yusho case there was more than one chemical in the contaminated rice oil. In addition to a PCB concentration of 53 to 99 ppm in rice oil samples, there were also PCDFs and PCQs present in concentrations of 0.18 to 0.40 ppm and 25 to 53 ppm, respectively. One of the most hazardous PCBs, 3,4,3′,4′-tetra-chlorobiphenyl, was present in rice oil samples as well as adipose tissue of patients. Furthermore, a highly toxic PCDF — 2,3,4,7,8-pentachlorodibenzofuran — was also present in the oil sample and in liver tissue of a patient who had died [107].

Most extended exposures to PCBs have been associated with industrial accidents with workers who manufactured PCB-containing goods. In 1975, approximately 12,000 people were occupationally exposed to PCBs. The majority of these exposures occurred in the manufacturing of capacitors [108]. In industry, most of these exposures were dermal, not oral, so the common effect was chloracne. There are reports of several deaths involving dermal exposure to very high concentrations of PCBs, but evidence suggests the presence of chlorinated naphthalenes in these substances [6].

The General Electric Corporation conducted studies on almost 200 workers at their capacitor plant in Hudson Falls, New York. These workers had direct contact with PCB mixtures and vapors for several decades. The results of these studies revealed that no confirmed cases of chloracne or other PCB-related effects were present in workers exposed to ordinary, unpyrolyzed American-made PCBs [93].

Another study involving occupational exposures divided exposed workers into two main groups. The first group included silk workers from Kyoto exposed to PCBs by the oil used on the machines. Levels of 50 ppb were found in some members of this group but no clinical symptoms were displayed as in the Yusho case. The PCBs present were identified as Kaneclor 500. Furthermore, PCQ levels were lower than 0.02 ppb in blood. The second group in the study included paint manufacturers who were exposed to paints containing PCBs. As in the first group, concentrations were found to be higher than in the Yusho patients, but no clinical symptoms were observed. The PCB present in these workers was identified as Kaneclor 600. Again, PCQ concentrations in blood were less than 0.02 ppb [109].

9. Regulation of PCBs

In 1976, the manufacturing process and use of PCBs in the United States were banned by the U.S. EPA in spite of clear evidence indicating that long

term exposure to PCBs by numerous electrical equipment workers was not a serious adverse health problem [110]. The stringent regulations placed upon PCB use were based upon the assumption that any level of exposure to PCBs is hazardous. The regulations banning PCBs which were instituted in 1976 were based upon only one human exposure incident [58] even though approximately 2500 scientific articles had been published prior to that date. Moreover, recent research shows that lower-level exposures to PCBs have not been shown to be hazardous to man [11].

In the 5 years following the issue of these ban regulations, over 5000 additional scientific publications detailing PCB toxicity have been published indicating that PCBs have not been shown to be significantly hazardous to man [27, 28]. It seems apparent that all scientific resources and studies were not used in establishing regulatory bans on PCBs. The last several years have provided many additional human exposure cases which need to be considered in updating the alleged toxicity of PCBs [11].

A committee established by the National Research Council of the National Academy of Sciences to reevaluate PCBs in 1979 concluded:

> "An analysis of PCB data compiled following the criteria of FIFRA and TSCA proposed guidelines, leads to the conclusion that PCBs are persistent, and are likely to accumulate. PCBs do not appear particularly toxic for short-term exposure, but results are subject to interpretation". [11].

A reevaluation of PCB toxicity, especially in humans, revealed that human health is generally not seriously jeopardized by PCB exposure. PCBs have not been shown to be carcinogenic in humans, and there is no proof that leads us to believe that PCBs are mutagenic, teratogenic, indicative of birth defects, or deterimental to human reproduction. Only dermatitis and chloracne have been conclusively proven to be caused by PCB exposure. Both of these adverse effects are completely reversible and disappear if PCB exposure is terminated. Data compiled in the last decade have introduced additional human exposure cases upon which to base these conclusions [11].

In May of 1982, the U.S. EPA sponsored a symposium on the effects of PCBs. It was concluded that PCBs themselves do not promote unreasonable risks to the environment or human health.

10. Elimination of PCBs from the environment

There are several means by which PCBs can be eliminated from the environment. Hydrolysis can be used under extreme conditions although PCBs are usually inert to this reaction [111, 112]. Chemical degradation is another method that can be used to eliminate PCBs [113]. The stability of PCBs is so great that environmental conditions are not likely to promote chemical reactions with them. However, under controlled conditions, oxidation, reduction,

nitration, isomerization, and nucleophilic reactions can occur with PCBs [111]. For example, PCBs have recently been shown to be degraded to polyphenylene and sodium chloride by treatment with metallic sodium [44].

Photodegradation is another method for destruction of PCBs. Dechlorination of PCBs as well as the production of polymerized materials occur in hexane when exposed to irradiation in sunlight [114]. Chlorine can be replaced by hydrogen or hydroxyl groups, a condensation or rearrangement may occur, or even the production of polar products can result from such a reaction. Specifically, Aroclor 1254 can be degraded to hydroxylated and carboxylated species by irradiating it in the presence of hydroxylic solvent at pH 9 [114]. Very little photodegradation of PCBs occurs naturally because they are usually subterrestrially stored and not readily accessible to sunlight.

Another natural process that can eliminate PCBs from the environment is biodegradation. A recent report indicates that natural soil processes will degrade PCBs [115]. In this process, both position and degree of chlorination of PCBs play crucial roles in determining whether or not microbial degradation will occur. Bacteria can transform biphenyls of lower chlorination, but encounter difficulty with more highly chlorinated biphenyls [8]. Many PCBs are oxidized to their corresponding chlorobenzoic acids, but other mixtures of dihydroxy compounds, meta-cleavage compounds and other unknown products are possible based upon the degree of chlorine substitution [86]. Conversion

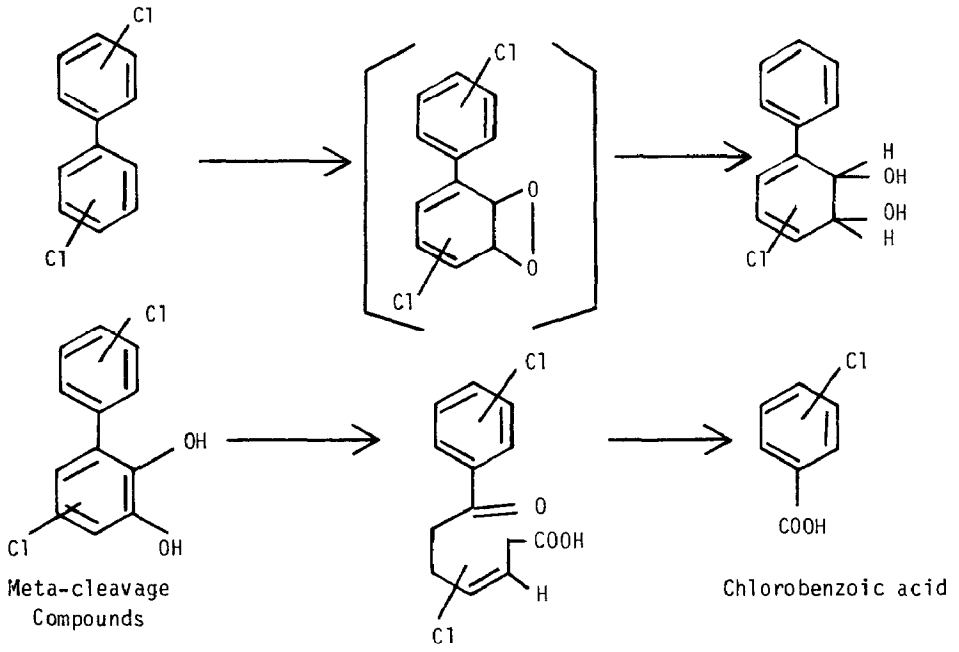


Fig. 4. Most probable reaction in biodegradation of PCBs.

of PCBs to chlorobenzoic acids is the main process of biodegradation (Fig. 4). Not only do Acinetobacter bacteria follow this pathway, but so do other genera of bacteria such as *Alcaligenes*, *Arthrobacter*, *Achromobacter*, *Nocardia*, and *Pseudomonas* [88]. All pathways and products must be considered in biodegradation because it is possible that metabolites generated during this process are even more toxic than are the PCBs [88].

The final method for the destruction of PCBs, as previously mentioned, is incineration. As PCBs are incinerated, hexachlorobenzene is formed. Both PCBs and hexachlorobenzene can be destroyed thermally at a temperature of 950 °C with a residue of 100 mg of hexachlorobezene per kg remaining [116]. Heating may cause PCBs to form different polymeric compounds incorporating oxygen [117]. Heating PCBs to 500–600 °C will cause formation of degradative products such as chlorinated dibenzofurans [118].

Despite these methods for eliminating them, PCBs remain a persistent problem in the environment. Of the 570×10^6 kg of PCBs produced in the U.S. since 1930, more than half (60%) are still in service and twelve percent is mobile in the environment. Twenty-eight percent of these PCBs have been eliminated, 5% by incineration or chemical degradation and 23% by being placed in landfills [1].

11. Permissible human exposure

It is difficult to ascertain the quantity of PCBs, if any, that would be a permissible exposure limit for humans. Generally, the concentration of 200 μg/kg of body weight per day has been determined to be minimum oral intake of PCBs shown to produce toxicity in humans [116]. As with all compounds, toxicity is a function of dose or extent of exposure and adverse effects of PCBs would be expected to be expressed to a greater extent as the level of exposure is increased. Signs and symptoms of toxicity to PCBs begin to occur in humans after an oral intake of 0.5 g [119].

This quantity represents a fairly large dosage and would indicate that there has been an over-reaction to the perceived toxicity of PCBs. In humans, acute poisoning outbreaks have only occurred following exposure to a combination of PCBs and PCDFs. When humans were exposed only to PCBs, the only observed acute effects have generally been minor and no significant chronic health effects have been causally associated with exposure to PCBs [120]. Therefore, the effects of PCBs on human health still have not been conclusively determined. Problems arise concerning this determination because accidental exposure to PCBs cannot be clearly identified as pure PCB exposures or as exposures to mixtures of several hydrocarbons. Additionally, interactions between chemicals can occur within the body following ingestion of food, breathing air contaminants, as well as simultaneous or later exposures to other

chemicals. Such interactions can produce additive effects making the study of PCB effects very difficult.

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