Polychlorinated Biphenyls (PCBs)☆

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Background

Polychorinated biphenyls (PCBs), originally termed "chlorinated diphenyls," were first synthesized in the early 1880s by Schmidt and Schultz (1881) and were commercially produced beginning in 1929. The manufacturing levels of PCBs increased with the demand of the electrical industry for a safer cooling and insulating fluid for industrial transformers and capacitors. PCB formulations sold in the commercial market have had varied trade names; for example, Aroclor was the most common trade name in the United States and Great Britain. PCB mixture formulations were different depending on the country of origin, and were produced in Germany (Clofen), France (Phenoclor and Pyralene, Japan (Kanechlor), Italy (Fenclor), Russia (Sovol) and Czechoslovakia (Delor). The mixtures were named according to their chlorine content. For example, Aroclor 1254 contains 54% chlorine by weight while Aroclor 1260 contains 60%. PCB mixtures were produced for a variety of uses such as fluids in electrical transformers, capacitors, heat transfer fluids, hydraulic fluids, lubricating and cutting oils, and as additives in plastics, paints, copying paper, printing inks, adhesives and sealants. Millions of tons of PCBs have been produced worldwide — around 700 000 tons in the USA before they were banned following two major poisoning incidents, first in Japan in 1968 and 10 years later in Taiwan. It has been estimated that more than 1.2×10^9 kg of PCBs have been manufactured throughout the world; 3.7×10^8 kg of PCBs have already been released into the environment, and an additional 7.8×10^8 kg are still available for release from transformers or other commercial products.

PCBs are a group of hydrophobic and stable organic compounds consisting of 209 possible congeners with different positions and number of chlorines; 130 congeners are likely to be present in commercial products. The core structure and predominant PCBs that exist in the environment, especially in food, are shown in Fig. 1. The congener composition and degree of chlorination in different commercial mixtures are shown in Table 1.

Physico-chemical Properties

PCBs are mixtures of aromatic chemicals, synthesized by the chlorination of biphenyl in the presence of a suitable catalyst. The chemical formula can be represented as $C_{12}H_{10\text{-}n}Cl_n$, where n is the number of chlorine atoms between 1 and 10. Some of the key physico-chemical properties of different PCB congeners are shown in Fig. 2. PCBs are colorless to light yellow, have no smell or taste and can be either an oily liquid or a solid. They do not crystallize, even at low temperatures, but turn into solid resins. Some PCBs are volatile and may exist as a vapor in air. PCBs have very low electrical conductivity, rather high thermal conductivity, and extremely high resistance to thermal break-down. The physico-chemical properties vary widely and depend on the number and positions of chlorine atoms in the biphenyl rings. PCBs resist both acids and alkalis and are thermally stable. These characteristics led to their usefulness in a wide variety of industrial applications. In general, PCBs are relatively insoluble in water, with solubility decreasing with increasing chlorination. However, they are readily soluble in non-polar organic solvents and biological lipids. When PCBs are burned at high temperatures, the products of combustion include polychlorinated dibenzofurans (PCDFs) and polychlorinated dibenzo-p-dioxins (PCDDs) that are more hazardous than the PCB itself.

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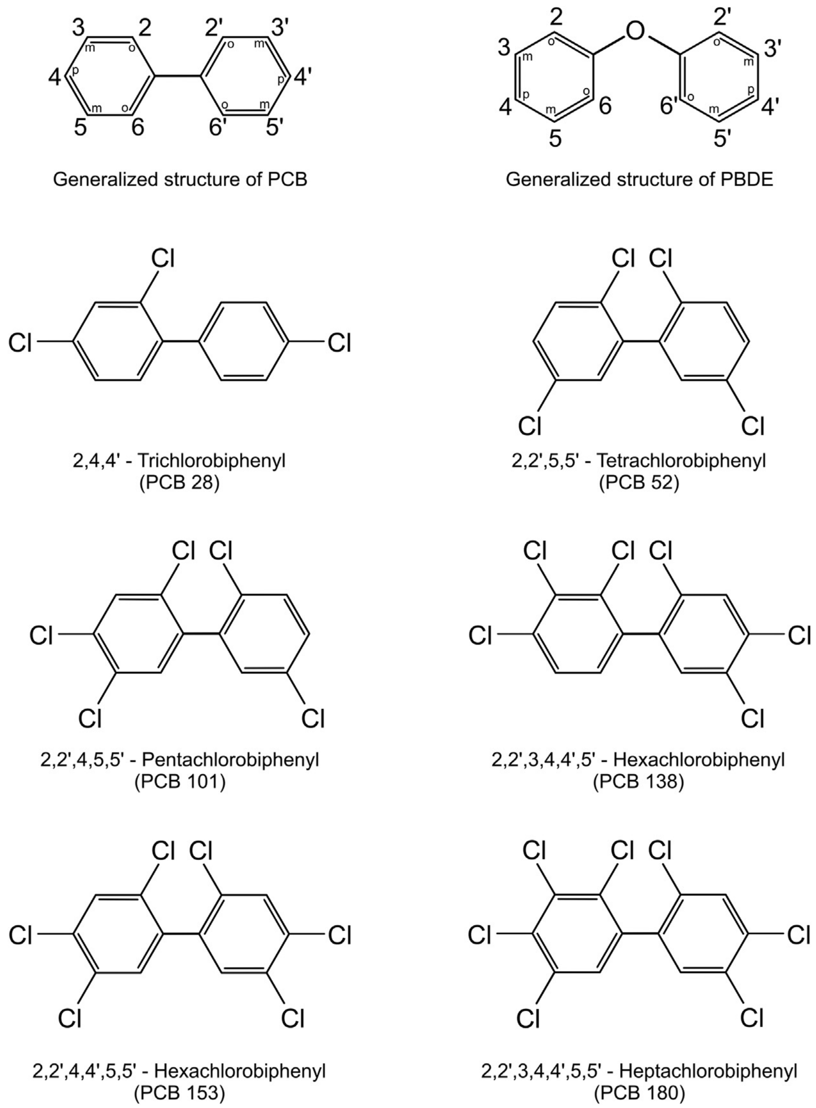

Figure 1 Core chemical structure of polychlorinated biphenyls and some prevalent congeners with highest percentage in the environments, especially in food.

Table 1 Composition and degree of chlorination in selected commercial PCB mixtures

		% of congeners with different number of chlorines								
Commercial mixture	*% Chlorine*	*Mono*	*Di*	*Tri*	*Tetra*	*Penta*	*Hexa*	*Hepta*	*Octa*	*Nona*
Aroclor 1016	41	2	19	57	22					
Aroclor 1242	42	3	13	28	30	22	4			
Aroclor 1248	48		2	18	40	36	4			
Aroclor 1254	54				11	49	34	6		
Aroclor 1260	60					12	38	41	8	1

Environmental Contamination and Human Exposure

PCBs entered the air, water and soil during their manufacture, storage, disposal and use in a variety of applications. For instance, PCB wastes were stored in landfills. PCBs also entered the environment from accidental spills and leaks during the transport of PCB containing materials. Once in the environment, PCBs do not readily breakdown, therefore, they remain in the ecosystem for a very long period of time. They can easily cycle between air, water, and soil. For example, PCBs can enter

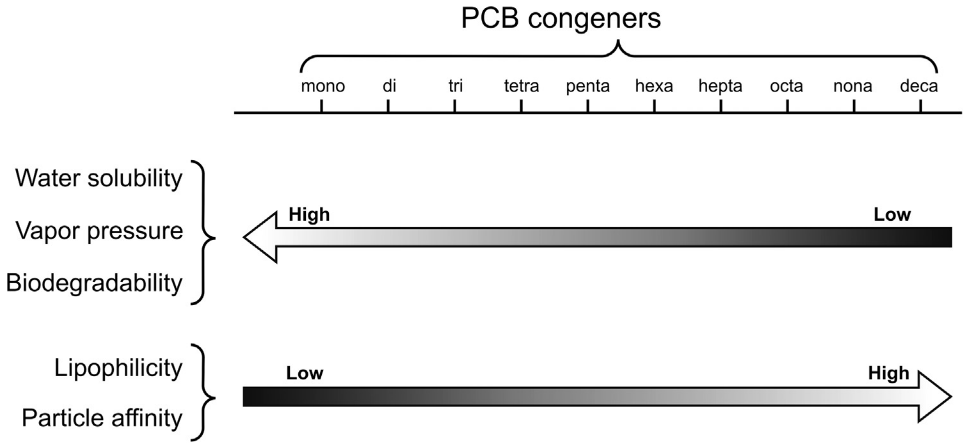

Figure 2 Physico-chemical properties of PCB congeners with chlorination ranging from Mono to Deca.

the air by evaporation from either water or soil. In air, PCBs can be carried long distances and have been found in snow and seawater in areas far removed from where they were released. This has resulted in extended contamination and global distribution. PCB contamination has been found in the Arctic and Antarctic atmosphere, hydrosphere, and biosphere. Due to their environmental persistence and lipophilic properties, PCBs have bioaccumulated in various lower trophic organisms (plankton), bivalve mollusks, fish, reptiles, marine mammals, birds, terrestrial mammals. In concurrence with these findings, these compounds have been detected in fish and other food products. The primary route of human exposure of PCBs is through consumption of contaminated foods such as dairy products, meat and freshwater fish, leading to unexpectedly high levels of these compounds being found in human adipose tissues, blood and milk.

PCB Contamination in Schools and Other Buildings

PCBs were used as a plasticizer in caulk either during manufacture or mixed on site prior to installation in some buildings including schools in the 1950's through 1970's. Another source of PCBs in schools is from ballast capacitors in fluorescent lights. There have been several studies in Germany, Sweden, and Finland demonstrating the relationship between PCBs in caulking and levels in indoor air and settled dust, as well as in soil around the foundation buildings containing these materials. Studies from schools in Boston and New York City indicated that PCB-containing caulk and fluorescent light ballasts which remain in use are the primary source of PCBs in and around school buildings. PCB concentration in indoor air ranged from 70 to 600 ng/m3 depending on age and location within these schools. Inhalation was estimated to be responsible for over 80% of the exposure with the remainder from ingestion of dust/soil and dermal contact in these school buildings. Hence, mitigation efforts that focus on reducing indoor air PCB concentrations were undertaken to reduce the exposure particularly to children. The mitigation efforts included removal of window components from the building, abatement of caulking residues from window openings, removal of PCB-containing caulking, removal and replacement of unit ventilators etc. These efforts were necessary to avoid exposure to these chemicals and to prevent adverse health effects related to PCB exposure.

Effects on Human Health

There is ample evidence that PCBs cause neurotoxicity in humans (see Table 2). It is believed that in utero exposure is more important than lactational exposure in causing the neurotoxic effects. As the developing nervous system is very sensitive to PCB exposure, this chapter focuses on the known epidemiology and behavioral effects of PCB-induced developmental neurotoxicity. The toxicological properties of PCBs became evident after two well documented episodes of accidental exposure. These were "Yusho," which occurred in 1968 in Japan and "YuCheng," which occurred 10 years later in Taiwan. These incidents resulted in multiple health problems including chloracne, numbness, limb weakness, decreased peripheral nerve conduction velocities, developmental delays, and speech problems. The offspring of women who had ingested PCB-contaminated rice-bran cooking oil in Taiwan and Japan were perinatally exposed to PCBs or related chemicals. The Japanese children were intellectually impaired while the Taiwanese children had more behavior problems compared with unexposed controls. When the children were tested between the ages of 7 and 12, the exposed Taiwanese children also had significantly lower verbal and full-scale IQs. They also showed prolongation of, and a significant reduction in the amplitude of auditory evoked potentials. The YuCheng and Yusho incidents were also attributed to PCDF exposure, since rice oils were cross-contaminated with PCDFs and PCBs.

Table 2 Evidence of neurotoxicity in humans and laboratory animals following exposure to PCBs

PCB mixtures/congeners (exposure)	*Effect*
Neurotoxicity in humans:	
Mixture of PCBs and PCDFs (Adult and developmental)	Decreased peripheral nerve conduction velocities, developmental delays, speech problems, hypoactive, hyperactive
Mixture of PCBs (developmental)	Learning and memory deficits poor performance in psychomotor performance
Neurotoxicity in monkeys:	
PCB mixture (developmental)	Locomotor hyperactivity, long-term changes in cognitive function
Neurotoxicity in rats:	
PCB mixture (adult)	Decreased motor activity, transient changes in functional
PCB mixture (developmental)	Observation battery, impaired radial arm maze, Affected long term potentiation, low frequency hearing Deficits; deficits in hearing
Ortho congeners (developmental)	Hyperactive and impulsive
Neurotoxicity in mice:	
PCB mixture (developmental)	Increased motor activity, impaired learning
Non-ortho congener (developmental)	Hyperactivity and reduced visual discrimination learning
Ortho congener	Persistent aberrations in (developmental) spontaneous behavior

In addition to these accidental poisoning incidents, several epidemiological studies have been conducted. Recently, PCB levels across 10 epidemiological studies were compared for effects on human neurodevelopment. These investigators found low levels of exposure consistently resulted in measurable changes in learning and behavior regardless of the PCB mixtures/congeners. Scientists from Michigan reported learning and memory deficits in children born to mothers who had ingested fish thought to be contaminated with PCBs. It has been reported that prenatal PCB exposure is associated with poorer performance on the Psychomotor Index from Bayley Scales of Infant Development in children from the general population in North Carolina. Studies from The Netherlands indicated that in utero exposure to "background" PCB concentrations is associated with poorer cognitive functioning in preschool children. Studies from Germany also indicated that PCB exposure is associated with deficits in mental and motor scores in children up to 7 months of age. Studies from the Faroese birth cohort in Denmark indicated that cord PCB concentration was associated with deficits in learning; however, these results may have been confounded by mercury, suggesting a possible interaction between these two neurotoxicants. The accidental poisoning incidents and epidemiological studies both suggest that the nervous system, especially during development, is sensitive to exposure to PCBs and related chemicals.

Effects in Laboratory Animals

Several studies using experimental animals support the results observed in humans. Behavioral changes and learning deficits have been observed in monkeys, rats, and mice (Table 2). Neurobehavioral changes were observed in adult animals following acute exposure as well as in animals exposed perinatally. In many of these animal studies, functional deficits were observed in the absence of reduced body weight or overt signs of toxicity. Animals that were prenatally, postnatally or perinatally exposed to PCBs showed many of the behavioral characteristics indicative of Attention Deficit Hyperactivity Disorder (AD/HD). For example, in utero exposure of mice led to increased motor activity and impaired learning. Similarly, pre- and/or post-natal exposures of rats lead to higher activity levels and poorer visual discrimination learning. Male rats exposed to PCB 153 during lactation became hyperactive and impulsive. Rhesus monkeys exposed throughout gestation and lactation showed locomotor hyperactivity during their first year of life.

Apart from effects on motor activity, PCBs have been shown to decrease cognitive function in rats, non-human primates, and mice. Developmental exposure to 3,3′,4,4′,5-pentachlorobiphenyl (PCB 126) and 2,3′,4,4′,5-pentachlorobiphenyl (PCB 118), at doses that did not produce maternal or fetal toxicity, interfered with visual discrimination learning of rats in an operant task. Gender differences have been reported in a study where developmental exposure to PCBs significantly interfered with acquisition of the spatial alternation task in females, but not in males. Studies also indicated that gestational and lactational exposure to a commercial PCB mixture, Aroclor 1254, impaired radial arm maze performance in male rats and affected long-term potentiation in the dentate gyrus of the hippocampus. In non-human primates, developmental exposure to commercial PCB mixtures (Aroclor 1016 or Aroclor 1248) resulted in long-term changes in cognitive function. Some differences in PCB congener effects have been reported. For instance, mice exposed during brain "growth spurt" on postnatal day 10 to 2,2′,5,5′-tetrachlorobiphenyl exhibited deficits in learning and memory function while 2,3′,4,4′,5-penta – and 2,3,3′,4,4′,5-hexa-chlorobiphenyls did not.

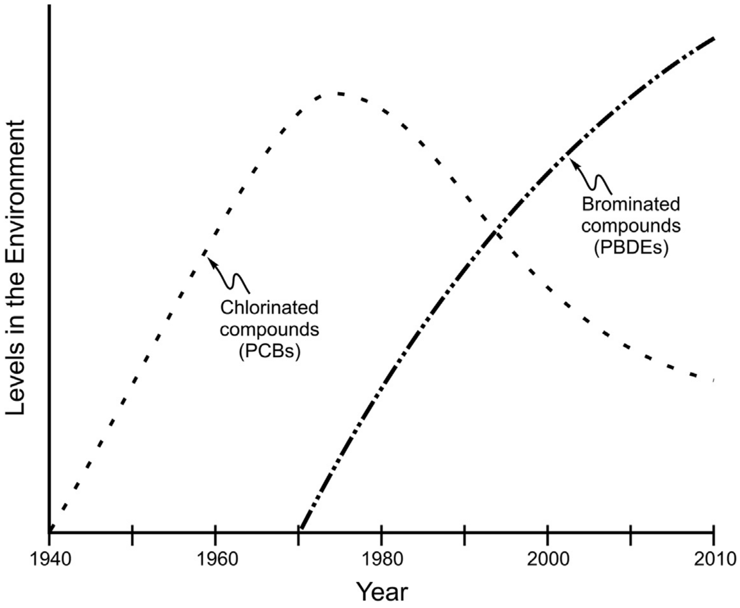

Figure 3 Schematic showing the trend of environmental levels of PCBs and its structurally related compounds, PBDEs. Adapted from Kodavanti, P.R.S., Senthil Kumar, K., Loganathan, B., 2008. Organohalogen pollutants and human health. Intl Encycl. Public Health 4, 686–693.

Other effects seen with developmental exposure to PCBs include sensory deficits. The most significant effect seen with developmental exposure to PCBs was deficits in hearing; the auditory threshold at low frequency (1 kHz) was significantly increased. Developmental PCB exposure has no significant effect on visual-, somatosensory- or peripheral nerve-evoked potentials. Scientists also reported gender-specific effects of PCBs on neurobehavioral development to measures of acquisition and sensory function, as seen with some behavioral endpoints. These animal studies clearly indicated that developmental exposure to PCBs resulted in cognitive dysfunction, motor deficits, and hearing loss.

Summary and Conclusions

Chlorinated persistent organic compounds continue to be a cause of human health and ecological concern because of their presence in the environmental media (air, water, soil, sediment) and in human tissues (adipose tissue, breast milk, and placenta). In humans, consumption of contaminated fish and other food materials has been the main route of exposure to PCBs. In some incidences such as school buildings, inhalation seems to play a key role as a primary source of exposure. Since PCBs are highly persistent in the environment and bioaccumulate in the food chain, it is nearly impossible to avoid human exposure. As a result, human health effects of these compounds will continue long after the ban on their production. Following the rapid contamination of the environment and biota during the periods of high PCB use for industrial purposes, levels declined after the ban/severe restrictions were placed on the production and use of these compounds in most of the developed countries. However, several tons of PCBs are still available for release in to the environment from industrial products. Therefore, future toxic effects in humans and wildlife by PCBs cannot be ruled out. In contrast, structurally related chemicals such as polybrominated diphenyl ethers (PBDEs) are currently being produced in large quantities and used globally. These compounds are widely used in indoors appliances and materials as flame retardants. Because of their use in household items, human exposure pathways for PBDEs are direct and intimate. Considerable data have been amassed on the presence of PBDEs in indoor environmental media (air, water, dust, lint, clothing, food packaging materials etc.) and human tissues (blood, breast milk, liver, fetus etc.). Like PCBs they are persistent in the environment and bioaccumulate in the food chain. In addition, data are beginning to accumulate on the potential neurotoxic effects of PBDEs. Therefore, it can be predicted that the environmental contamination as well as human exposure and health effects by these halogenated compounds will continue to increase for several decades in both developed and developing countries (Fig. 3). The prevalence, persistence and biomagnification in the environment, the multiple routes of exposure and the potential for adverse toxic outcomes emphasize the need to minimize exposure to PCBs and other structurally related chemicals in order to protect humans from possible long-term health effects.

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