

Polychlorinated Biphenyls: Persistent Pollutants with Immunological, Neurological, and Endocrinological Consequences

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Abstract

Polychlorinated biphenyls (PCBs) are considered “persistent organic pollutants;” fat-soluble compounds that bioaccumulate in individuals and biomagnify in the food chain. PCBs were the first industrial compounds to experience a worldwide ban on production because of their potent toxicity. These compounds are still present in our food supply (fish, dairy, hamburger, and poultry being the most contaminated) and our bodies. Once in the body, they can cause long-term problems, especially for those exposed *in utero*. PCB bioaccumulation can lead to reduced infection fighting ability, increased rates of autoimmunity, cognitive and behavioral problems, and hypothyroidism. Some research also links PCBs to increased rates of type 2 diabetes. Testing is currently available for some of the most damaging PCBs. The testing compares individual levels to national reference values and can be interpreted to determine current exposure. Dietary measures can be enacted that will reduce PCB half-lives in humans by increasing excretion.

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Background

Polychlorinated biphenyls (PCBs) are a category of industrial chemicals historically used as coolants or heat transfer agents in electrical transformers. They have also been used in microscope immersion oils, carbonless copy paper, cutting oils, and as an inert ingredient in pesticides. All PCBs have in common a biphenyl molecule (two attached benzene rings) with a minimum of 1, and no more than 10, chlorine (Cl) atoms attached. The possible positions of chlorine atoms on the two benzene rings are denoted by the numbers assigned to the carbon atoms (Figure 1).

PCBs fall into two distinct categories. One category is considered “dioxin-like” because of the structural and toxicity similarities to

polychlorinated dibenzo-p-dioxins (PCDDs). PCBs in this category contribute to overall dioxin toxicity. The other category is considered “non-dioxin-like.” While the non-dioxin-like PCB congeners do not contribute to dioxin toxicity, they can have their own toxic effects.

The possible positions of Cl atoms on the two benzene rings are denoted by the numbers assigned to the carbon atoms. Theoretically, 209 different PCB congeners are possible depending upon the placement of Cl, although only about 130 are found in commercial PCB mixtures. As an example, 2,2',3,4,4',5'-hexachlorobiphenyl (PCB congener number 138) would have a Cl attached at positions 2, 3, and 4 of the left benzene ring and positions 2', 4', and 5' of the right benzene ring.

The production of PCBs in the United States ceased in 1979 because of findings that these compounds were accumulating in the environment and were being associated with severe health problems. An international ban on production was enacted at the Stockholm Convention on Persistent Organic Pollutants in 2001. Despite these bans, it remains possible to be exposed to PCBs. Some consumer products made before 1977, including old fluorescent lighting fixtures, electrical devices, or appliances containing PCB capacitors, may still contain PCBs and can be a source of exogenous exposure. Widespread use, large-scale environmental contamination events (spills), and slow biodegradation, all combine to make PCBs a ubiquitous environmental contaminant. PCBs contaminate both ocean and fresh-water fish, are found in butter from around the globe, and have been identified in numerous other foodstuffs. PCBs have also commonly been found in breastmilk. PCBs are fat-soluble compounds that, because of their long

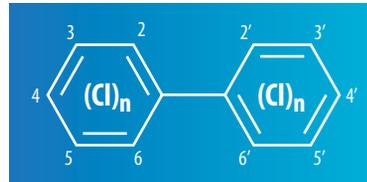
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half-lives estimated at 10-15 years in humans, can biomagnify in the body.¹

The effect of PCB contamination has been studied in different populations where it was present as a dietary contaminant. In one study group in Taiwan, over 2,000 persons became ill after exposure to PCB-contaminated rice bran cooking oil in 1979. This group developed primary symptoms of hyperpigmentation, chloracne, and peripheral neuropathy in what was termed “Yu Cheng” (Chinese for “oil disease”). Individuals used the contaminated oil for as long as nine months, consuming about 1 g of PCBs and 3.8 mg of polychlorinated benzofurans (PCDF). PCDFs are made when PCBs are repeatedly heated, as had occurred in this case. The first 39 children born to exposed mothers were all hyperpigmented and eight of those died. The exposed individuals and their surviving offspring are now followed in a registry in Taiwan.²

In the first Body Burden Study by Environmental Working Group (EWG), nine subjects were tested for 48 PCB congeners. Bill Moyers was one of the subjects and tested positive for 31 of 48 PCBs.³ The Centers for Disease Control and Prevention (CDC) has also been measuring PCB levels from some participants in the National Health and Nutrition Examination Survey (NHANES) data for their ongoing National Reports. The CDC Fourth National Report on Human Exposure to Environmental Chemicals measured levels of 38 PCB congeners (a number that is far from representing the total load of PCBs in the average U.S resident); 34 of the 38 PCBs were found in virtually all persons tested.⁴ Of these 38 PCB congeners, six have documented health effects; the levels of these six are listed in Table 1.

Figure 1. Chemical Structure of PCBs



The possible positions of chlorine (Cl) atoms on the two benzene rings are denoted by the numbers assigned to the carbon atoms. Theoretically, 209 different PCB congeners are possible depending upon the placement of Cl, although only about 130 are found in commercial PCB mixtures. As an example, 2,2',3,4,4',5'-hexachlorobiphenyl (PCB congener number 138) would have a Cl attached at positions 2, 3, and 4 of the left benzene ring and positions 2', 4', and 5' of the right benzene ring.

Key words:

polychlorinated, biphenyl, PCB, dioxin, benzofuran, pollutants, POPs, chemicals, body burden, endocrine, autoimmunity, chlorophyll, fiber, tea, detoxification, detox, toxins

Table 1. Amounts of Six PCB Congeners in the Population Studied as Part of the CDC Fourth National Report on Human Exposure to Environmental Chemicals

PCB Congener	Geometric Mean	50th Percentile	75th Percentile	90th Percentile	95th Percentile
PCB 118 (ppq)	0.037	0.032	0.066	0.143	0.216
PCB 118 (pg/g)	6	5.19	10.4	21.8	31.3
PCB 126 (ppq)	100	89.8	159	308	475
PCB 126 (pg/g)	16.3	14.7	24.8	46.7	68.7
PCB 138 (ppb)	0.092	0.095	0.206	0.359	0.477
PCB 138 (ng/g)	15.1	15.1	30.5	55.4	75.3
PCB 153 (ppb)	0.121	0.135	0.283	0.477	0.624
PCB 153 (ng/g)	19.8	20.8	43.3	71.8	97.1
PCB 170 (ppb)	0.033	0.041	0.087	0.144	0.188
PCB 170 (ng/g)	5.46	6.3	12.9	21.7	28.2
PCB 180 (ppb)	0.092	0.114	0.246	0.409	0.534
PCB 180 (ng/g)	15.1	18	37.1	63.7	81.5

Dioxin-like PCBs (PCB 118 and 126) are reported as parts per quadrillion (ppq) in the serum, and as lipid-adjusted values (pg/g). Non-dioxin-like PCBs (PCB 138, 153, 170, and 180) are reported as parts per billion (ppb) in the serum, and as lipid-adjusted values (ng/g).

Measuring PCB Levels in Patients' Blood

Quantitative and Lipid-adjusted Values

All fat-soluble toxins, including PCBs, are carried in the lipid fraction of the serum, mostly in the low density lipoprotein (LDL) cholesterol fraction. The levels of these compounds in the blood detected during testing can go up or down based solely on the blood lipid level at the time. Since serum lipid levels increase or decrease for a variety of reasons, this makes it difficult for the clinician to properly interpret the results of serum testing when results are given only as a quantity (such as parts per billion (ppb) or parts per quadrillion (ppq)). This recognition has led to adjustments to take into account the amount of lipid present at the time of testing. Using this lipid-adjusted value, one can more easily discern the approximate body burden of the individual being tested.

Levels reported in ppb (or ppq) are reflective of the amount of PCBs present in the serum, mostly found in the cholesterol and albumin fractions.⁵ This serum value should be considered a “current exposure level” from both endogenous and exogenous sources. Endogenous exposure occurs when PCBs are mobilized from adipose tissue stores. If the individual happens to be experiencing increased lipolysis due to stress, rigorous exercise, or weight loss, more PCBs are mobilized from adipose tissue and endogenous exposure increases. Although in most people serum PCB levels are primarily influenced by PCBs released from their own adipose tissue stores, serum levels of PCBs also reflect recent exogenous exposure, with recent dietary choices being a major source of exogenous exposure.

The amount of PCBs stored in adipose tissue (body burden) occurs as a result of bioaccumulation of these toxins over a lifetime of exposure. The advantage of reporting lipid-adjusted value is that it gives a more accurate picture of the total burden of PCBs that are residing in adipose tissue throughout the body.⁶ When lipolysis occurs due to normal thermogenesis, or with fasting, exercise, stress, weight loss, or saunas, a portion of these stored toxins are dumped into the bloodstream along with cholesterol and triglycerides. By measuring the amount of lipids present in the blood and adjusting the amount of detected PCBs to that lipid burden, one is able to get an accurate idea of the amount of stored toxins. If the lipid-adjusted values are increasing, it generally means body burden of the particular PCB is increasing. If the value is decreasing, body burden is decreasing. Attention to changes in the lipid-adjusted values allows individuals who are following a cleansing protocol to actually monitor progress in toxin reduction.

Identifying Current Exposures

By utilizing the CDC percentile values for PCBs and comparing the serum level (in ppb or ppq) and lipid-adjusted values, one can determine the extent of current exogenous exposure, which is critical to treatment. The laboratory results listed in Table 2 illustrate how to use lab findings to interpret the extent of exogenous exposure.

Table 2 lists the levels of three PCB congeners found in a female patient in both ppb and as lipid-adjusted values (ng/g). Reference ranges, expressed as 75th, 90th, and 95th percentile, are taken from the CDC Fourth National Report on

Table 2. Results of PCB Testing for Three Non-dioxin-like Congeners in a Female Patient

PCB Congener	Serum Levels (ppb)	75th Percentile	90th Percentile	95th Percentile	Lipid-Adjusted Levels (ng/g)	75th Percentile	90th Percentile	95th Percentile
138	0.30	0.206	0.359	0.477	31.5	30.5	55.4	75.3
153	0.42	0.283	0.477	0.624	44.1	43.3	71.8	97.1
180	0.42	0.246	0.409	0.534	44.1	37.1	63.7	81.5

Results are reported in quantity (ppb) and lipid-adjusted values (ng/g) for each of the three PCB congeners assessed. Serum levels for PCB 138, 153, and 180 are in higher percentile categories than are the corresponding lipid-adjusted levels, which suggest the patient has some source of ongoing exogenous exposure to these specific PCB congeners.

Human Exposure to Environmental Chemicals. The patient's PCB 138 appears to be in about the 85th percentile for serum and the 75th percentile for lipid-adjusted levels. Her PCB 153 serum value falls just below the 90th percentile, while her lipid-adjusted value is slightly above the 75th percentile. Her serum level of PCB 180 is just above the 90th percentile, while the lipid-adjusted value is just over the 75th percentile. The general rule of thumb is that current exogenous exposure to a PCB congener is occurring whenever the serum value of that PCB expressed in ppb is in a higher relative percentile than the lipid-adjusted level. If there is no current exogenous exposure, and all the circulating PCBs are coming from adipose stores, the serum levels will always be found in a percentile less than (or equal to) the percentile of the lipid-adjusted value. In this case, her percentile of exposure for serum levels for all three PCB congeners is higher than her lipid-adjusted exposure. The interpretation is that she has some source of ongoing exogenous exposure. After conducting an investigation into potential sources of exposure, it was determined that consumption of farmed salmon was a significant source of this exogenous exposure; a finding that has been common in most of this author's patients with similar lab findings.

Potential Adverse Effects of Polychlorinated Biphenyls in Humans

Potential adverse effects occurring from PCB exposure are described in this section. These effects are summarized in Table 3.

Immune System Effects

In vitro testing indicates that PCBs are potent inducers of apoptosis for monocytes⁷ and thymocytes.⁸ Apoptosis of thymocytes appears to be secondary to mitochondrial damage by PCBs. Increased apoptosis of monocytes and thymocytes results in lower numbers of white blood cells (WBCs) to initiate an immunological defense. In order to determine if dietary intake of PCBs leads to immunological problems, mice were fed diets with either PCB-contaminated whale blubber or beef fat that was not contaminated with PCBs. The WBCs of the blubber-fed mice exhibited diminished mitogen response, decreased phagocytosis, and diminished numbers of CD8+ cells, indicating immunosuppression, while the mice fed PCB-free beef fat showed no such problems.⁹ Animals exposed to dioxin-like PCBs also developed thymic atrophy and immunosuppression.¹⁰ PCBs reduce

available superoxide dismutase (SOD), resulting in a pro-oxidative state that diminished the number of neutrophils and reduced cellular immunity.¹¹ Both pre- and postnatal exposures to PCBs in the Netherlands, resulting in elevated serum PCB levels at adolescence, have been associated with a reduced number of circulating polymorphonuclear neutrophils.¹² In another report, when children who had been exposed *in utero* to PCBs reached age 15, they showed a significantly higher incidence of middle ear disease and exhibited higher serum levels of dibenzofurans than children of non-exposed mothers,¹³ indicating that prenatal exposure to PCBs has a lasting effect on cell-mediated immunity. Dutch preschoolers with higher serum PCB levels were also found to be more likely to have recurrent middle ear infections.¹⁴

PCBs have also been linked to the development

Table 3. Potential Health Consequences from PBC Exposure

- In Utero* Exposures to PCBs can result in:**
- ▶ Long-term cell-mediated immune deficiency
 - ▶ Increased incidence of recurrent middle-ear infection
 - ▶ Reduced numbers of white cells
 - ▶ Persistent neurological deficits (cognition, mood and behavior problems).
- PCB dietary exposures can result in:**
- ▶ Increased rates of anti-thyroid and anti-nuclear antibodies present
 - ▶ Possible increases in the incidence of lung and liver cancers
 - ▶ Problems with learning, memory and vision
 - ▶ Endometriosis, menstrual disorders and reproductive problems (women)
 - ▶ Hypothyroidism
 - ▶ Increased risk of type 2 diabetes

of autoimmunity. Chlorinated compounds were studied in a German clinic for association with reproductive difficulties. Not only were serum levels of chlorinated compounds significantly associated with miscarriage history and uterine fibroid presence, but high levels of PCBs were associated with the presence of antithyroid and antinuclear antibodies.¹⁵ PCB exposure and elevated antithyroid antibodies have also been linked in persons living close to industry.¹⁶

Individuals with short-term toxic dietary PCB exposure died from cancer at higher rates than others in the same area who were not exposed. Increased rates of lung and liver cancers occurred

at the highest rates in those who were inadvertently poisoned with PCBs from contaminated cooking oil.¹⁷

Neurologic Effects

The greatest neurological consequences from PCB exposure appear to happen when exposure occurs *in utero*, during the time of initial neurologic development. This contrasts with PCB exposure from breast milk, which does not appear to cause the same type or degree of developmental deficit, a phenomenon that has been seen in both animals and humans. Neonatal PCB exposure of mice results in long-term neurologic deficits, including persistent problems with spontaneous behavior that worsens as they age. *In utero* PCB exposure also adversely affected learning and memory function when the exposed mice reached adulthood.¹⁸

Several studies examining the effect of *in utero* exposure in humans have demonstrated similar problems. Children exposed *in utero* to PCBs via fish consumption exhibited problems with intellectual functioning.¹⁹ Studying mother-infant pairs in Germany revealed that *in utero* exposures to PCBs affected the mental and motor neurological development of children.²⁰ Studies in Michigan, North Carolina, and Taiwan show that children exposed to PCBs have increased cognitive defects, poorer gross motor function, and decreased visual recognition memory.^{21,22} By age 11, the Michigan children with prenatal PCB exposure continued to show greater rates of impulsivity, poorer concentration, and poorer verbal, pictorial, and auditory working memory.²² Exposed children also have lower IQ levels than children who are not exposed *in utero*, and have increased rates of hyperactivity, with both problems persisting as they grow.²³⁻²⁵ A study of Inuit preschoolers with both prenatal and postnatal PCB exposures revealed that prenatal exposure to PCB 153 was associated with increased states of unhappiness and anxiety.²⁶

Postnatal exposures can also cause neurological problems. Adults who consumed Great Lakes fish with high PCB levels exhibited neurotoxicity symptoms. Sport anglers who annually consumed at least 24 lbs of fish caught in Lake Michigan had much higher serum levels of PCBs and DDE than non-fish eaters (<6 lbs yearly); the higher the PCB levels, the more memory and learning problems were experienced.²⁷ Hundreds of residents in Perry County, Tennessee were exposed to PCBs from a gas pipeline. On examination for neurological

problems, they were found to have significantly slower reaction time (for both simple and choice reactions), faster sway speeds, diminished color discrimination and visual performances, and constricted visual fields. They also had diminished scores on digit symbols, vocabulary, verbal recall, and embedded memory.²⁸

Endocrine Effects

Exposure to PCBs has reproductive effect on males. Taiwanese men who were exposed to PCBs before age 20 had significantly fewer male children than age- and neighborhood- matched Taiwanese controls. Men who were exposed after age 20 had a nonsignificant 10-percent fewer daughters than controls.²⁹ This finding is similar to what was noted in Seveso, Italy in individuals exposed to 2,3,7,8-TCDD, the most toxic dioxin known.³⁰ Although no such difference was found with Taiwanese mothers exposed to PCBs at any age, they experience a higher incidence of stillbirth and more abnormal menstrual bleeding than nonexposed women.³¹ An exposed population also demonstrated substantially elevated mortality rates from chronic liver disease and cirrhosis.³²

Chlorinated compounds were studied for association with reproductive difficulties in a German clinic. PCB serum levels were significantly associated with endometriosis and DDT levels with reduced conception.¹⁵ When Italian women, who had experienced miscarriage, were compared to controls with successful births, higher serum PCB levels were found.³³ An uncontrolled Canadian study looked for the presence of xenobiotics in the serum and follicular fluid from infertile females and seminal plasma from male partners in 18 couples attending an *in vitro* fertilization (IVF) program. DDE, mirex, hexachloroethane, trichlorobenzene, and three PCBs were detected in more than 50 percent of all follicular fluid samples. Four PCBs, DDE, and endosulfan were also found in over 50 percent of all serum samples. Of the couples tested, those who failed to achieve pregnancy with IVF methods generally had higher toxic levels than successful couples.³⁴ The researchers did not use a matched control group of fertile couples to determine if fertile couples had similar toxic burden.

The effect of PCBs on thyroid hormonal status and function has been studied. *In vitro*, PCBs bind transthyretin, a transport protein mechanism for thyroxine (an effect shared by dioxins and furans).³⁵ PCBs also appear to adversely affect

thyroid hormone metabolizing enzymes (uridine-diphosphate-glucuronyl transferases, iodothyronine deiodinases, and sulfotransferases) found in the liver and brain.³⁶

A recent Swedish study examined women who became exposed to PCBs from consuming at least two meals of fish from the Baltic Sea each month. PCB serum levels were measured along with free and total triiodothyronine (FT3 and TT3) and free and total thyroxine (FT4 and TT4). A significant inverse correlation between PCB levels and TT3 was revealed, and an insignificant inverse correlation with TT4.³⁷ German children showed a significant positive correlation between PCB serum levels and elevation of thyroid stimulating hormone (TSH) and a significant inverse correlation between serum PCB levels and FT4 (as one would expect with increasing TSH levels).³⁸ PCBs and other chlorinated compounds have also been linked to increased risk for type 2 diabetes.^{39,40}

Exposure Sources

The greatest sources of exposure to PCBs are from food (especially fish from contaminated waters) and polluted air. The highest content of PCBs in one dietary study was found in dairy products, meat, and fish.⁴¹ Another study reported dairy, chicken eggs, and fish as having the highest amounts of PCBs.⁴² For Canadians, the greatest food sources of PCB exposure are from butter and fish, with the average intake of PCBs for Canadians reported as being 5.7 ng/kg/day.⁴³ Spanish butter has also been shown to have high levels of PCBs (5.4 ng/g wet weight (ww)), along with elevated levels of hexachlorobenzene (HCB), beta-hexachlorocyclohexane, and Lindane.⁴⁴ Levels of PCBs and other pollutants were examined in a small number of foods in Dallas, Texas grocery stores. Farmed (Atlantic) salmon had the highest total number of toxins, with 23 of 25 measured compounds detected. The average amount of PCB 153 in the salmon was 1.21 ng/g ww. Canned sardines had even higher levels of PCB 153 at 1.83 ng/g ww. The sardines also had the highest levels of another PCB congener (PCB 130) with 1.80 ng/g ww. Hamburger had PCB 153 levels similar to farmed salmon (1.2 ng/g ww).⁴⁵ Several studies have measured the levels of PCBs, dioxins, and other persistent chlorinated contaminants in farmed salmon. A study conducted by the Food Safety Authority of Ireland found that farmed salmon had an average of four times the amount of PCBs and dioxins as wild salmon.⁴⁶ In the United States, the EWG

studied farmed salmon purchased at stores in Washington, DC, San Francisco, CA, and Portland, OR, and found an average PCB level of 27.3 ppb in the 10 fish studied, with highest levels in farm-raised salmon from Scotland.⁴⁷ This amount was over five times higher than the level of PCBs found in a sampling of wild salmon.⁴⁸ Persons who fish in the Great Lakes and consume their catch can also have elevated PCB blood levels.⁴⁹ Regarding fish caught in Alaskan waters, rock sole contained the highest PCB levels.⁵⁰ Samples of fish oil supplements were collected from markets in Vancouver, BC. All samples had detectable amounts of PCBs and organochlorine pesticide residues. Levels of PCBs found in the samples of shark (5,260 ng/g), menhaden (321 ng/g), and seal oil (519 ng/g) were alarmingly high in this study.⁵¹

PCBs concentrate in breast milk, resulting in daily exposure by breast-fed infants.⁵² Numerous global studies consistently document PCBs in breast milk samples.⁵³ PCB exposure has also been attributed to inhalation of indoor air in buildings with old electrical fixtures.⁵⁴

Treatment Options

In the author's clinical experience, the first step in dealing with potential PCB toxicity is to identify and remediate sources of exogenous exposure. As detailed above, food is often a significant source of exogenous exposure. Identification and avoidance of potential contributing foods is an important first step. As general recommendations, patients are advised to avoid consuming Atlantic (farmed) salmon and to use only organic butter.

Cleansing protocols can enhance the clearance of persistent toxins, including PCBs. The use of sauna therapy along with colonic irrigations can reduce levels of PCBs and chlorinated pesticides.⁵⁵ Various dietary measures can increase the bowel excretion of fat-soluble toxins like PCBs. The daily use of rice bran fiber has been documented in several Japanese studies to increase the clearance of PCBs.⁵⁶⁻⁵⁸ Chlorophyll and all chlorophyll-containing foods are effective for increasing fecal excretion of fat-soluble persistent toxins.⁵⁹⁻⁶¹ In the author's experience, supplementation and increasing these foods in the diet can slowly increase the excretion of PCBs and other persistent pollutants. In addition to chlorophyll-containing agents, green and white tea polyphenols have also been shown to increase excretion of fat-soluble toxins.⁶²

In addition to strategies aimed at increasing the excretion of these toxins from the body, the author recommends that persons dealing with PCB-related toxicity also take high amounts of nutrient and botanical antioxidants to protect the tissues and cells that are under toxic assault.

Summary

PCBs are fat-soluble, biologically persistent compounds that are currently present in common food items. Because of their fat-soluble nature, they have very long half-lives (10-15 years in humans). They can cause long-term immune, neurological, and hormonal consequences in individuals exposed *in utero* or from exposure via diet or dust. Fortunately, current testing methods can detect body burden and likelihood of high exogenous exposure. Information gleaned from these lab tests can be used to determine whether further exposure investigation is required and to track progress in reducing exposure and lowering body burden. Exogenous exposure can be reduced by avoidance of the foods most likely to have high PCB levels. Several readily available dietary foodstuffs, including chlorophyll, rice bran fiber, and white and green teas, can be used to increase toxin excretion. Because PCBs can cause more serious health problems in the case of *in utero* exposure, it is highly recommended women be tested for these compounds before trying to conceive. If levels are high, exposure reduction and toxin elimination can commence prior to conception.

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