

NO TRESPASSING

**PCB CONTAMINATED
SEDIMENTS**

(Poly-chlorinated Biphenyls)

NÃO ENTRAR

**PCB SEDIMENTOS
CONTAMINADOS**

(Policlorinato Bifenilos)

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SEDIMENTOS**

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Polychlorinated biphenyls (PCBs): A continuing environmental health concern

What we have learned after many thought the problem of PCBs had been solved



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VETERINARY MEDICINE

Polychlorinated biphenyls (PCBs): A continuing environmental health concern

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Polychlorinated biphenyls, which are more commonly referred to as PCBs, are a structurally related family of synthetic chemicals of long-standing notoriety in the field of environmental health. PCBs were produced worldwide in large quantities from the late 1920s to the late 1970s for use in diverse industrial applications and commercial products. However, even as early as the 1930s, concerns about adverse health effects associated with occupational exposures to PCBs began to surface. In the 1960s and 1970s, it became apparent that PCBs, which are highly resistant to degradation, were accumulating in the environment, including the human food supply, and could be readily detected in human tissues. During this same time period, data began to emerge linking environmentally relevant levels of PCBs to increased risk of cancer in humans and animal models. Collectively, these studies prompted a ban on PCB production by the United States Congress in 1979, and by the Stockholm Convention on Persistent Organic Pollutants in 2001.

Over the two decades immediately following the ban on PCB production, environmental PCB levels decreased, basic research scientists identified the biological mechanisms by which PCBs cause cancer, and regulatory scientists identified "safe" levels for PCBs in the environment and in human food supplies based on cancer as the endpoint of concern. Thus, many believed that the PCB problem was largely solved, and further research on PCBs is not warranted. However, over the past 10 years, new research on PCBs has revealed a number

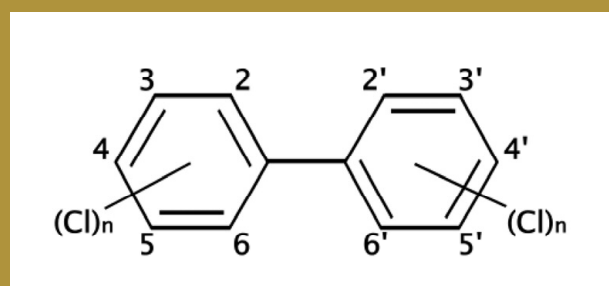


Figure 1. Structure of PCBs. The possible positions of chlorine atoms on the biphenyl are indicated by numbers assigned to each of the carbon atoms in the benzene rings.

of unexpected findings: environmental levels of PCBs are no longer decreasing, and in fact there is evidence levels may be increasing in some geographical areas; novel PCBs that were not part of the industrial mixtures synthesized in the past are being detected in the environment and in human tissues; and PCBs have been shown to cause adverse health effects via mechanisms other than those on which regulatory decisions are currently based. In the following sections I will discuss some of these new findings, and then consider future research needs and regulatory policy implications.

What are PCBs?

In the United States and United Kingdom, PCBs were synthesized and marketed primarily as Aroclor® mixtures whose degree of chlorination was identified by a four-digit designation (e.g., 1248, 1254, 1260), with the first two digits referring to the number of carbon atoms in the biphenyl backbone, and the last two digits identifying the percentage of chlorine by mass in

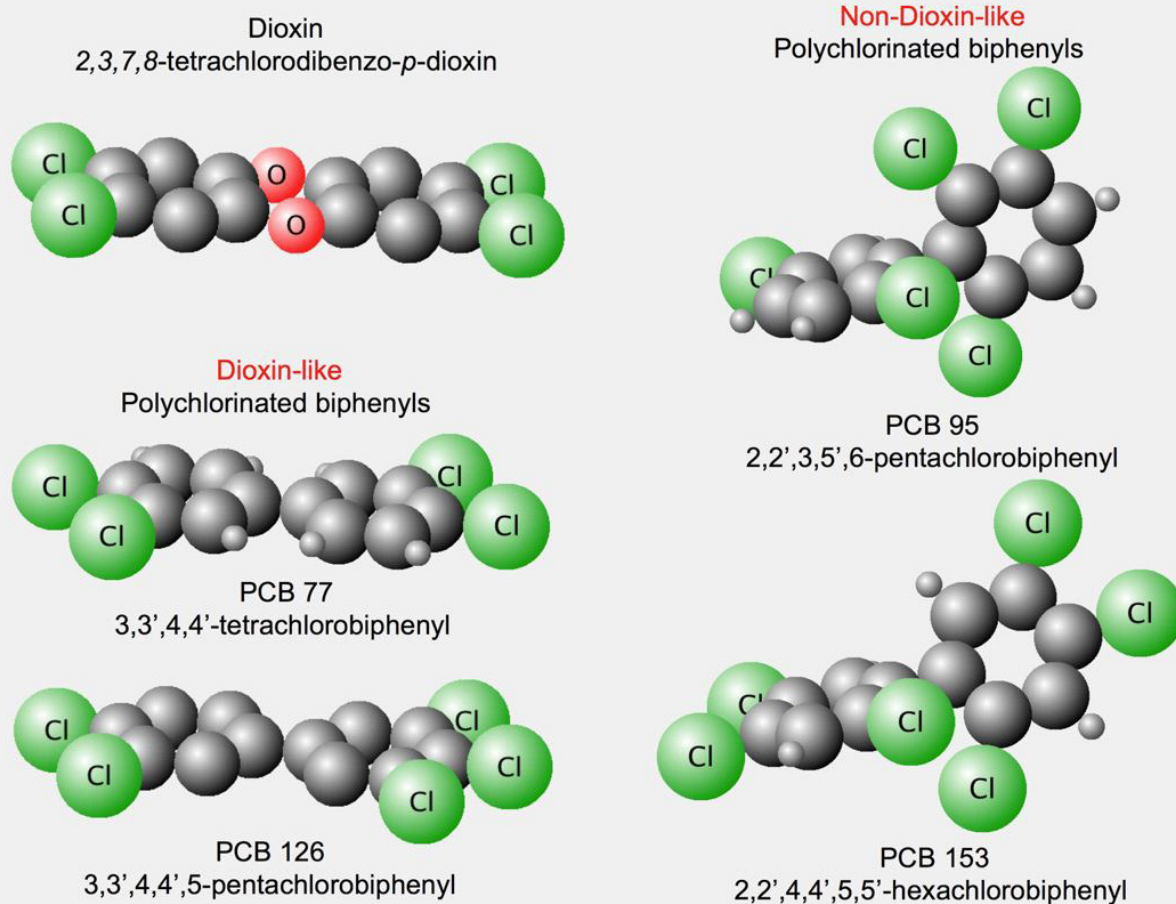


Figure 2. Structures of dioxin, dioxin-like (DL) PCBs and non-dioxin-like (NDL) PCBs.

the mixture. Similar PCB mixtures were synthesized worldwide and identified under several trade names such as Clophen® (Germany), Phenclor® (France) and Kanechlor® (Japan). Because of their low flammability, chemical stability and electrical insulating properties, PCB mixtures were widely used as coolants and lubricants in electrical transformers, capacitors, fluorescent light ballasts and hydraulic equipment. PCBs were also broadly incorporated into a variety of common products such as thermal insulation material, paints, cements, caulking compounds, pesticides, varnishes, adhesives, carbonless copy paper and newsprint.

Chemically, PCBs are biphenyls with variable chlorine substitutions for the hydrogen atoms in the benzene rings (Fig. 1). There are 209 possible PCB compounds – each of which is referred to as a congener – that vary according

to the number and position of chlorine substitutions. PCBs are broadly divided into two categories – dioxin-like or non-dioxin-like – based on their structure (Fig. 2). The dioxin-like (DL) PCB congeners typically have fewer than two chlorines at the ortho positions of the biphenyl (which correspond to the 2, 2', 6 and 6' carbons). As a result, these congeners tend to have a fairly rigid coplanar structure, like dioxin. In contrast, the non-dioxin-like (NDL) PCBs have more than one ortho-substituted chlorine, and are typically non-coplanar with a more flexible structure. As discussed below, these structural differences are associated with different toxicity profiles.

Human Exposures to PCBs

During the time they were being actively produced for commercial applications, PCBs entered the air, water and soil during their

Golgi analyses of brains of weanling rats exposed developmentally to PCBs in the maternal diet throughout gestation and lactation

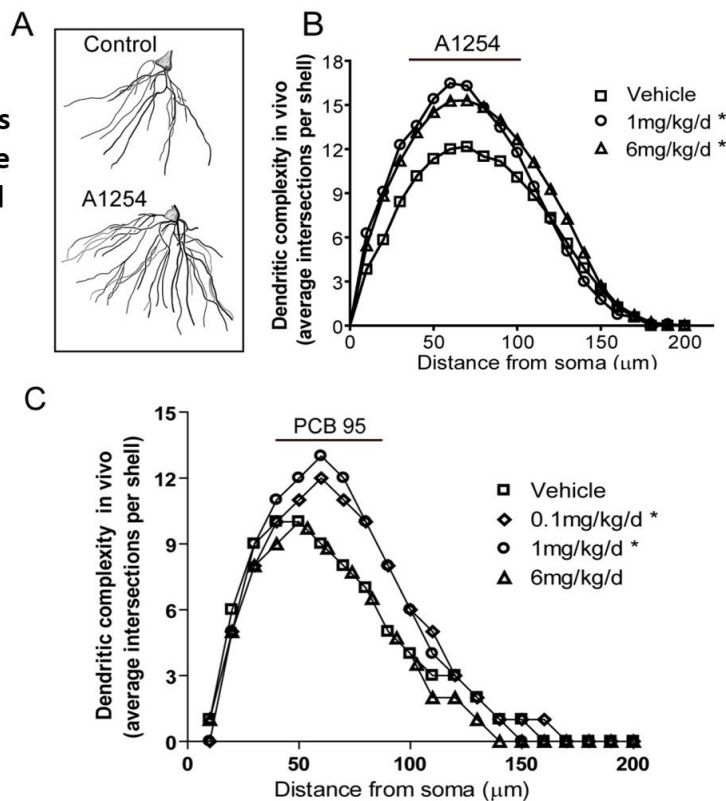


Figure 3. Developmental PCB exposure increases dendritic arborization in vivo. Rat pups were exposed to vehicle or varying concentrations of the commercial PCB mixture Aroclor 1254 (A1254) or the NDL congener, PCB 95, in the maternal diet throughout gestation and lactation. Dendritic arborization was analyzed in the CA1 pyramidal neurons in the hippocampus of male pups at postnatal day 31 (10 days after weaning). Brains were Golgi stained to visualize the dendritic arbor of individual neurons (A) by Sholl analysis, which involves counting the number of intersections between dendrites and concentric circles centered on the cell's nucleus. An upwards shift of the Sholl plot (panels B and C) indicates increased dendritic growth. Figure adapted from Wayman et al., 2012.

manufacture, use and disposal. Today, these legacy PCBs are still being released into the environment from hazardous waste sites, illegal or improper disposal of industrial wastes and consumer products, leaks from old electrical transformers that contain PCBs or burning of PCB-containing products. PCBs persist in the environment, cycling between air, water and soil. Many PCBs are readily soluble in fats, and tend to accumulate in fatty tissues. These lipophilic PCBs have long biological half-lives (months to years), and they bioaccumulate up the food chain. As a result, tissue levels in top predators, including humans, can be significantly greater than levels found in the air, water and soil. Conventional thinking has been that the primary route of human exposure to PCBs is via the diet, with fish (especially sportfish caught in contaminated lakes), meat

and dairy products constituting the main dietary sources of PCBs.

While the average PCB levels in the environment and in human tissues steadily declined in the United States during the first two decades after the 1979 ban on production, data published over the past 10 years suggest that environmental levels stabilized after the late 1990s, and, more recently, levels may be increasing, at least in some areas. One possible explanation for the observation that environmental levels are no longer decreasing is the accelerated release of legacy PCBs from aging products. For example, higher than expected levels of PCBs in the air over the city of Chicago are thought to be due in part to the release of PCBs from aging paints and caulking materials used to construct municipal buildings

during the era when PCBs were intentionally added to these construction materials. Similarly, release of legacy PCBs from paints and caulking materials was invoked in a 2012 report to explain the observation that PCB levels in the indoor air of elementary schools in the United States exceeded the 2009 public health guidelines set by the United States Environmental Protection Agency (U.S.E.P.A.).

Research over the past decade also suggests that the congener profile of PCBs in various environmental matrices, including human tissues, appears to have shifted: earlier studies identified predominantly DL PCBs, whereas more recent data suggests that NDL PCBs predominate. Moreover, PCB congeners not found in the commercial mixtures synthesized prior to the 1979 ban have recently been identified in the human chemosphere. In contrast to the heavily chlorinated PCB congeners associated with the commercial mixtures, most of these “contemporary” PCBs are lightly chlorinated. These are unintentional byproducts of modern pigment manufacturing processes that have now been documented in air and water worldwide. Of concern, one of these contemporary PCBs, PCB 11, has recently been detected in commercial cow’s milk in California, and in serum from pregnant women living in northern California, and from women and adolescent children living in not only the greater Chicago area, but also in rural Iowa.

Human Health Effects of Concern: Beyond Cancer

Until recently, most research on the adverse human health effects associated with PCBs has focused on the DL PCBs. Not only do these PCBs resemble dioxin structurally, but, like dioxin, they bind to the arylhydrocarbon receptor (AhR). As a result, the toxicity profiles of DL PCBs are similar to that of dioxin. Exposure to high levels of dioxin or DL PCBs can cause chloracne and liver damage, while chronic exposures to lower levels are associated with immune dysfunction and cancer. Mechanistic studies have linked these adverse health effects to AhR activation. Based

on epidemiological evidence and data from animal and mechanistic studies, PCBs have been classified as human carcinogens (group 1) and probable human carcinogens by the International Agency for Research on Cancer (IARC) and the U.S.E.P.A., respectively. Current regulatory policies for PCBs are largely based on its carcinogenic risk.

The NDL PCB congeners have negligible AhR binding activity. Thus, it was largely believed that NDL PCBs were toxicologically inert. However, in the late 1980s and early 1990s, pioneering work by research scientists at the Wadsworth Center in the New York State Department of Health and at the U.S.E.P.A. revealed that at least some NDL PCBs are biologically active. Specifically, NDL PCBs, but not DL PCBs, interfere with signaling by dopamine, one of the major neurotransmitters in the brain, and alter calcium-dependent signaling in neurons grown in tissue culture. These data, which were among the first experimental evidence to suggest that NDL PCBs may be neurotoxic, coincided with early epidemiological and preclinical studies in non-human primate and rodent models suggesting that PCBs are neurotoxic, and that the developing nervous system is much more sensitive than the mature nervous system to the neurotoxic effects of PCBs. These reports raised significant concern in light of NHANES (National Health and Nutrition Examination Survey) data from the United States Centers for Disease Control (CDC) confirming widespread exposure to PCBs among women of childbearing age living in the United States, and experimental evidence demonstrating that PCBs can cross the placenta, and accumulate in breast milk.

To date, numerous epidemiological studies have been conducted to examine the developmental neurotoxicity of PCBs in humans, with the majority reporting a significant association between prenatal exposure to PCBs and neuropsychological deficits in children. These findings have been corroborated in non-human primate and rodent animal models. A meta-analysis of the human data published in 2009, which reviewed

longitudinal birth cohort studies published in the peer-reviewed literature, concluded that impairment of executive functions – higher order brain processes responsible for planning, flexible thinking, abstract reasoning, problem solving, and inhibition of inappropriate actions – was the neuropsychological deficit most consistently associated with prenatal PCB exposure. More recent epidemiological studies have linked developmental PCB exposures to not only intellectual deficits, but also attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).

Mechanisms of PCB Developmental Neurotoxicity: Not Just Thyroid Hormone Disruption

How PCBs interfere with neurodevelopment, and whether all or only a subset of PCB congeners act as developmental neurotoxicants, remain key questions in the field. Early experimental data implicating NDL congeners in PCB disruption of dopamine and calcium signaling suggested mechanism(s) other than AhR activation. Prevailing mechanistic hypotheses include not only decreased dopamine content or altered neuronal calcium signaling, but also interference with thyroid hormone signaling. The dopamine hypothesis is strongly relevant to potential effects of PCBs on ADHD, but whether NDL PCBs decrease dopamine content in vivo at environmentally relevant concentrations, the mechanisms underlying this effect, and a causal relationship between PCB-induced changes in dopamine to relevant behavioral deficits have yet to be determined.

PCB disruption of thyroid hormone signaling has been more widely posited as a mechanism of PCB developmental neurotoxicity. Thyroid hormone is critically important for normal neurodevelopment, and thyroid hormone imbalance is linked to significant neurodevelopmental defects. PCB exposures have been associated with decreased serum levels of thyroid hormone in humans, and studies in experimental animal models corroborate this association. Moreover, auditory

deficits induced by developmental PCB exposure in a developing rodent model were shown to not only correlate with decreased thyroid hormone levels, but also to be prevented by supplementation with thyroid hormone. However, studies with individual PCB congeners do not provide strong support for the hypothesis that decreased thyroid hormone mediates PCB-induced cognitive deficits. The NDL PCBs 28, 118 and 153 produce similar deficits in spatial learning and memory in rodent models, but have variable effects on serum thyroid hormone levels ranging from a marked reduction to no effect. In contrast, DL PCBs 77 and 126 significantly reduce serum thyroid hormone levels, but have few, if any, adverse effects on cognitive behavior.

Our studies of the effects of PCBs on the morphological maturation of neurons also do not strongly support the thyroid hormone hypothesis. Neurons have a very unique cell shape, characterized by the extension of processes from the cell body that connect with other cells to form neural circuits. Most neurons extend two types of processes: axons, which typically conduct signals from the neuronal cell body to the downstream cell in the circuit, and dendrites, which form the major receptive surface of the neuron for signals from cells upstream in the circuit. Perturbations of the rate of growth of axons and dendrites, or in their number and branching patterns (referred to as the axonal plexus and dendritic arbor) are implicated in a number of neurodevelopmental disorders, including ASD. Thyroid hormone promotes dendritic arborization in cerebellar Purkinje cells. However, using a rat model, we found that exposure throughout gestation and lactation to a commercial PCB mixture in the maternal diet at a dose that significantly decreased serum thyroid hormone levels in weanlings, did not decrease dendritic arborization in cerebellar Purkinje cells, but rather significantly increased dendritic arborization in these neurons. Moreover, PCB effects on dendritic growth were replicated in primary neuronal cell cultures, which are removed from systemic thyroid hormone

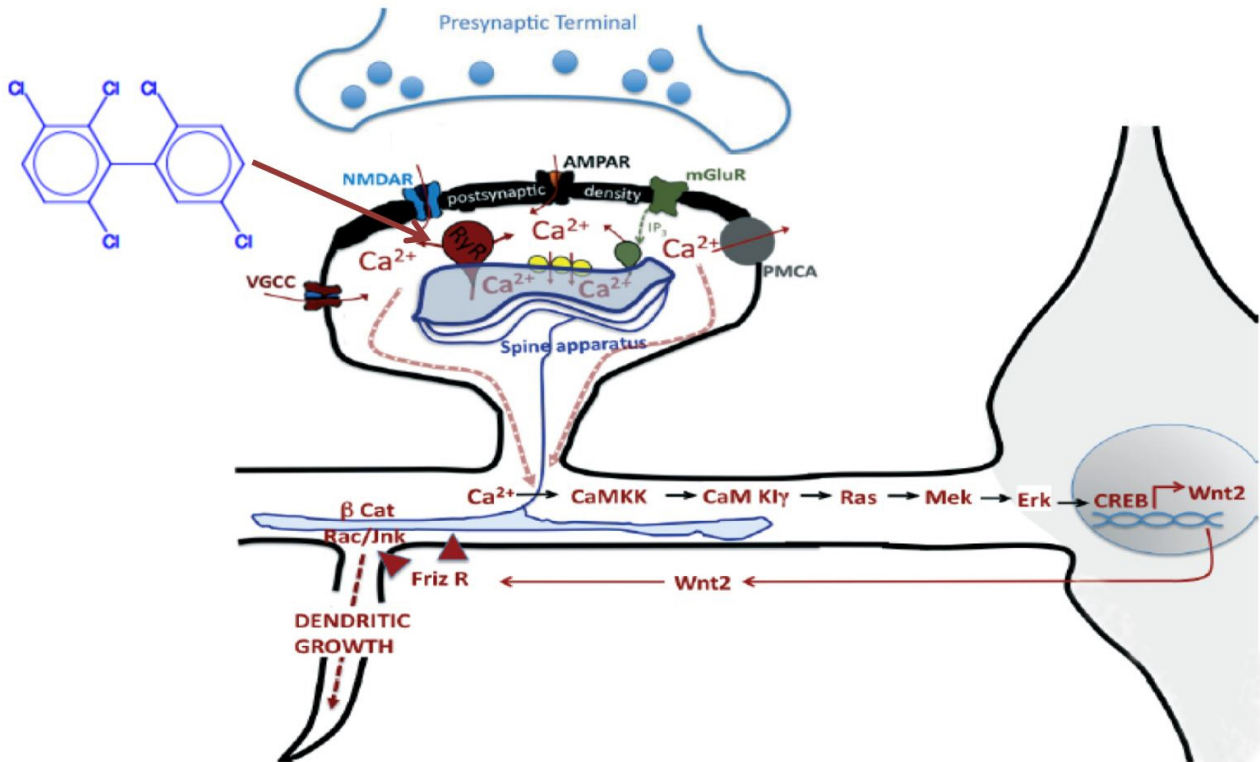


Figure 4. Non-dioxin-like (NDL) PCBs “high-jack” calcium (Ca^{2+})-dependent signaling pathways that control dendritic growth. In the context of activity-dependent dendritic growth, RyRs in the endoplasmic reticulum of the dendrite functionally link Ca^{2+} influx via NMDA and AMPA receptors to Ca^{2+} release from intracellular stores. Increased intracellular Ca^{2+} as a consequence of RyR activation sequentially activates the CaMKK-CaMK-MEK/ERK-CREB-Wnt2 signaling pathway to promote dendritic growth. (Abbreviations: β Cat = β -catenin; Friz = frizzled, the cognate receptor for Wnt2; PMCA = plasma membrane calcium ATPase; R = receptor). Figure adapted from Wayman et al., 2012.

influence. Collectively, these data strongly suggest that thyroid hormone deficits are not involved in all aspects of PCB developmental neurotoxicity.

Our research has, however, pointed to a critical role for calcium signaling in the effects of PCBs on dendritic arborization. Earlier studies had demonstrated that NDL, but not DL, PCBs increase intracellular calcium levels in cultured neurons. The most sensitive mechanism by which NDL PCBs increase intracellular calcium involves the ryanodine receptor (RyR). RyRs are ion channels in the endoplasmic reticulum (ER) that regulate calcium release from the ER into the cytoplasm. RyR activity determines the amplitude and spatiotemporal patterns of intracellular calcium fluxes, which determine cell function. NDL PCBs interact with RyRs to stabilize them in their open conformation,

which increases calcium release from the ER. Calcium signaling is critically involved in the dynamic structural remodeling of the dendritic arbor that occurs during development as neural circuits form. Experiments in experimental animal models demonstrated that gestational and lactational exposure to a commercial mixture of PCBs comprised predominantly of NDL PCBs or to a single NDL congener, PCB 95, in the maternal diet increased dendritic arborization in the brains of weanling rats (Fig. 3), coincident with deficits in learning and memory. The dendritic effects were replicated in neuronal cell cultures exposed to NDL, but not DL, PCBs. Moreover, the dendrite promoting activity of PCBs required RyR activity, and PCB interactions with RyRs trigger a calcium-dependent signaling pathway implicated in normal activity-dependent dendritic growth (Fig. 4).

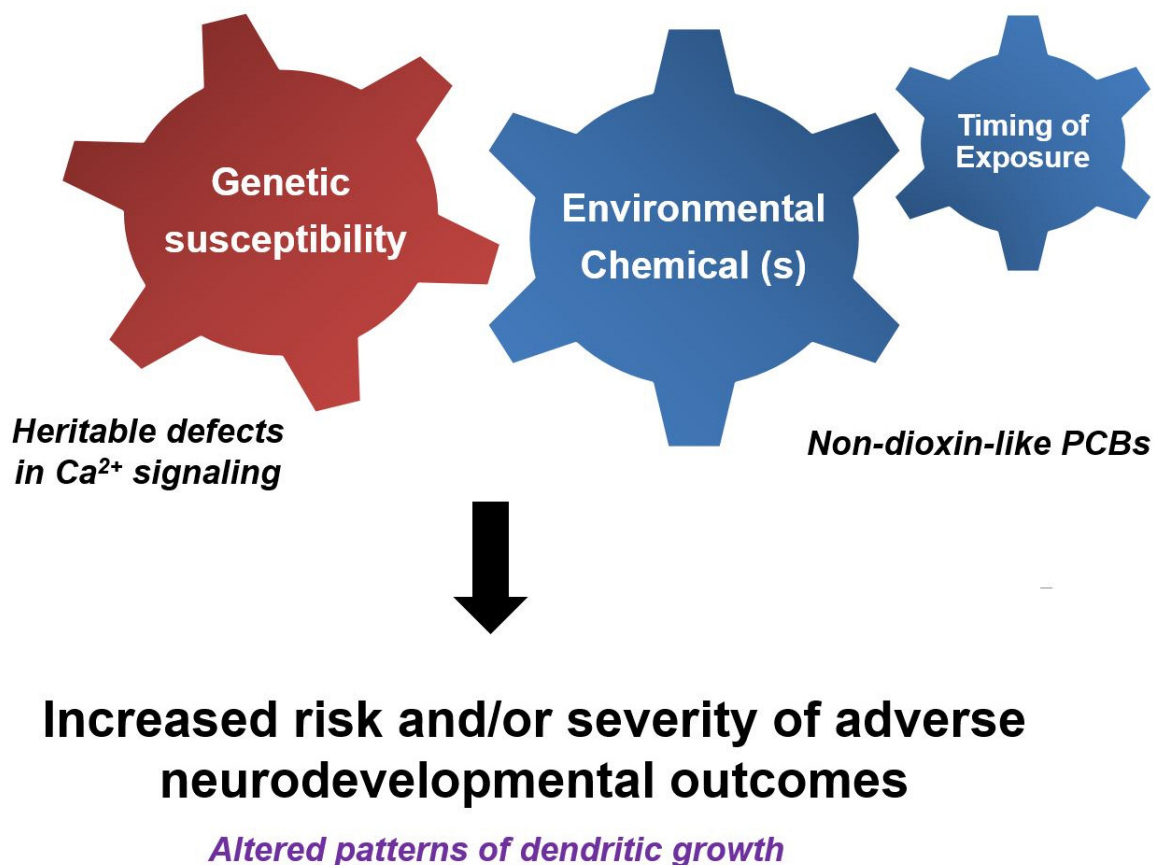


Figure 5. Non-dioxin-like PCBs may increase risk for neurodevelopmental disorders by converging on calcium-dependent signaling pathways impacted by genetic susceptibilities.

The human health relevance of these observations is suggested by reports of increased dendritic arborization in the brains of autistic individuals relative to neurotypical controls. Even more intriguing, the calcium-dependent signaling pathway activated by NDL PCBs to trigger dendritic growth maps onto genes implicated in autism. Collectively, these studies support the hypothesis that NDL PCBs amplify the risk and/or severity of neurodevelopmental disorders such as ASD, or even possibly ADHD, by converging on signaling pathways targeted by heritable defects in calcium-dependent signaling pathways that regulate the formation of neural circuits in the developing brain (Fig. 5).

But that is not the end of the PCB developmental neurotoxicity story. More recent research in our

laboratory has revealed that PCB 11, one of the contemporary PCB congeners not found in the synthesized commercial mixtures, also increases dendritic arborization in neuronal cell cultures. However, the dendritic effects of PCB 11 do not seem to require RyR activity. Nor are they dependent on AhR- or thyroid hormone. While further work is required to identify how PCB 11 promotes dendritic growth, these observations suggest that there are multiple mechanisms by which PCBs cause similar neurodevelopmental outcomes, e.g., increased dendritic arborization.

Conclusions

In summary, the cumulative evidence from the past 10 years of PCB research suggests that we need to revise the conventional understanding of the environmental health risks associated

with PCBs. The recent data indicate that environmental levels of PCBs, and thus potentially human exposures, are no longer decreasing, and the congener profile of PCBs in the environment is changing. The presumption of diet as the primary route of exposure to PCBs may also need to be reconfigured to consider inhalation as a second important route of exposure. Understanding how these shifts in human exposures to PCBs impact toxic outcomes are a critically important research need.

Evidence from the past 10 years has also built a convincing case for NDL PCB congeners as significant environmental health risks, and for developmental neurotoxicity as a significant endpoint of concern. With regards to the latter, epidemiological evidence of an association between developmental PCB exposure and adverse neurodevelopmental outcomes has been corroborated in preclinical studies. However, discrepant or inconsistent findings in the epidemiological literature have raised questions as to whether PCBs are developmental neurotoxicants in humans. There is an urgent need to conduct a systematic review of the human, animal and mechanistic literature to determine whether current regulatory guidelines should be reconsidered to address developmental neurotoxicity as an endpoint of concern. A significant effort along these lines has been undertaken by the U.S.E.P.A., which is currently conducting an Integrated Risk Information System (IRIS) toxicological evaluation of non-carcinogenic endpoints associated with PCBs. Another pressing research need is to identify which PCB congeners are developmental neurotoxicants, and to elucidate the mechanism(s) by which they interfere with neurodevelopment. Answers to these questions will inform rigorous approaches for assessing risks to the developing brain associated with exposures to complex PCB mixtures.

Further Reading

Berghuis SA, Bos AF, Sauer PJ, Roze E (2015) Developmental neurotoxicity of persistent organic pollutants: an update on childhood outcome. *Arch Toxicol* 89: 687-709.

- Boucher O, Muckle G, Bastien CH (2009) Prenatal exposure to polychlorinated biphenyls: a neuropsychologic analysis. *Environ Health Perspect* 117(1):7-16.
- Eubig PA, Aguiar A, Schantz SL (2010) Lead and PCBs as risk factors for attention deficit/hyperactivity disorder. *Environ Health Perspect* 118: 1654-67.
- Hu D, Hornbuckle KC (2010) Inadvertent polychlorinated biphenyls in commercial paint pigments. *Environ Sci Technol* 44: 2822-7.
- Koh WX, Hornbuckle KC, Thorne PS (2015) Human serum from urban and rural adolescents and their mothers shows exposure to polychlorinated biphenyls not found in commercial mixtures. *Environ Sci Technol* 49(13): 8105-12.
- Lyall K, Croen LA, Sjodin A, Yoshida CK, Zerbo O, Kharrazi M, Windham GC (2016) Polychlorinated biphenyl and organochlorine pesticide concentrations in maternal mid-pregnancy serum samples: association with Autism Spectrum Disorder and Intellectual Disability. *Environ Health Perspect* doi: 10.1289/EHP277.
- Pessah IN, Cherednichenko G, Lein PJ (2010) Minding the calcium store: Ryanodine receptor activation as a convergent mechanism of PCB toxicity. *Pharmacol Therap* 125(2):260-285.
- Sethi S, Keil KP, Chen H, Hayakawa K, Li X, Lin Y, Lehmler HJ, Puschner B, Lein PJ (2017) Detection of 3,3'-dichlorobiphenyl in human maternal plasma and its effects on axonal and dendritic growth in primary rat neurons. *Toxicol Sci* 158(2): 401-411.
- Stamou M, Streifel KM, Goines PE, Lein PJ (2013) Neuronal connectivity as a convergent target of gene x environment interactions that confer risk for Autism Spectrum Disorders. *Neurotoxicol Teratol* 36: 3-16.
- Thomas K, Xue J, Williams R, Jones P, Whitaker D (2012) Polychlorinated Biphenyls (PCBs) in School Buildings: Sources, Environmental Levels, and Exposures. United States Environmental Protection Agency.
- Wayman GA, Yang D, Bose DD, Lesiak A, Ledoux V, Bruun D, Pessah IN, Lein PJ (2012) PCB 95 promotes dendritic growth via ryanodine receptor-dependent mechanisms. *Environ Health Perspect* 120(7): 997-1002.
- Wayman GA, Bose DD, Yang D, Lesiak A, Bruun D, Impey S, Ledoux V, Pessah IN, Lein PJ (2012) PCB 95 modulates calcium-dependent signaling pathway responsible for activity-dependent dendritic growth. *Environ Health Perspect* 120(7):1003-9.
- Yang D, Kim KH, Phimister A, Bachstetter AD, Ward TR, Stackman RW, Mervis RF, Wisniewski AB, Klein SL, Kodavanti PRS, Anderson KA, Wayman G, Pessah IN, Lein PJ (2009) Developmental exposure to PCBs interferes with experience-dependent dendritic plasticity and ryanodine receptor expression in weanling rats. *Environ Health Perspect* 117:426-435.

Environmental health science: reducing the risk

Virginia Guidry and Kimberly Gray from the NIEHS outline how environmental health science can help to identify potential hazards in a child's environment

Now able to crawl and curious to discover all that's around her, little Emma reaches for a dusty toy under the table and, just like any infant would, immediately puts it into her mouth.

What chemicals are in the toy, and is there lead in its worn paint? Do the baby's pyjamas, or perhaps her crib mattress, contain flame retardant chemicals? Has the home been treated with pesticides, now lingering as residue in the dust? Does it matter?

These are the questions that drive environmental health science.

Parents, grandparents, and caregivers have enough to focus on regarding the needs and well-being of their children - making sure they are nourished, clean, and sleeping soundly. The National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health (NIH), funds scientists to methodologically study the silent factors that we often cannot see or smell in a child's environment.

These environmental toxicants can be in the water, food, dust, or air in children's homes, schools, and neighbourhoods. NIEHS-funded scientists determine the likelihood of harm, the sources if unknown, and how to reduce exposure or mitigate potential damage.

Why focus on children?

One thing is clear from NIEHS-funded research - children are more vulnerable to environmental toxicants than adults, particularly while in the womb¹. External substances can interfere with the complex processes of growth and development, which involve rapid cell division

and intricate hormonal signals. Additionally, children don't have the mature defense systems that adults do, such as fully functional liver detoxification¹. Sometimes changes that occur during childhood can have permanent effects².

For example, NIEHS-funded research shows the potential for environmental toxicants to harm brain development. Lead is the best-known example, but there are many others. When pregnant mothers are exposed to high levels of flame retardant chemicals, such as polybrominated diphenyl ethers (PBDEs), their offspring may be more likely to have decreases in IQ, problems with fine motor skills, and symptoms of ADHD³.

Environmental scientists are using MRIs and related technologies to study the brain regions of children exposed to common air pollutants called polycyclic aromatic hydrocarbons (PAHs), which come from fossil fuel combustion⁴. The structural and functional changes they have observed in the brain may explain why exposure to PAHs while in the womb has been linked to lower IQ and symptoms of anxiety, depression, or ADHD^{5,6}.

Technologies help identify hazards

However, it can be difficult to know what toxicants a child has been exposed to in the womb or as a baby. Some scientists are analysing naturally shed baby teeth to reconstruct early-life exposure to lead and other metals that are incorporated into teeth as a child grows⁷. By comparing exposure information with later diagnoses, the scientists have shown that increased lead uptake, and decreased uptake of the essential nutrients zinc and manganese, may be related to autism⁸.



NIEHS-funded researchers also are developing wearable or mobile technologies to help caregivers recognise hazards in a child's environment. Scientists have designed wearable wristbands that can detect exposure to organic chemicals, such as flame retardants or pesticides, over the course of a few hours or days⁹. Others are collaborating on an **app** that will help children, their parents, or healthcare providers track real-time air quality conditions so that asthma triggers can be avoided.

New programme to study children's health

Fortunately, there is a new, national effort that will allow scientists to study a variety of environmental influences on children's health. In 2016, NIH launched the 7 year Environmental influences on Child Health Outcomes (**ECHO**) programme. ECHO is focused on 4 important children's health outcomes: illnesses like asthma in the upper and lower airways, obesity, neurodevelopment, and health around the time of birth. ECHO is pooling resources from many NIH-funded studies to increase researchers' ability to study how a child's environment, from pregnancy through adolescence, may affect the immediate or long term health of our children.

ECHO and NIEHS-funded research will continue to point to ways that we can advance lifelong health by improving the environmental conditions around pregnant women and children. We already know that when air quality improves, children have better lung growth¹⁰ and decreased bronchitis-like symptoms¹¹. Similarly, women at the end of their pregnancies during the 2008 Beijing Olympics had babies with healthier birth weights than women

exposed to higher, typical air pollution levels during the same dates in 2007 and 2009¹².

These studies show the potential health benefits of reducing environmental toxicants. These improvements matter - especially for children.

References

- 1 Selevan, S.G., C.A. Kimmel, and P. Mendola, Identifying critical windows of exposure for children's health. *Environ Health Perspect*, 2000. 108 Suppl 3: p. 451-5.
- 2 Cohn, B.A., et al., DDT Exposure in Utero and Breast Cancer. *J Clin Endocrinol Metab*, 2015. 100(8): p. 2865-72.
- 3 Ehrlich, S.F., et al., Pregnancy glucose levels in women without diabetes or gestational diabetes and childhood cardiometabolic risk at 7 years of age. *The Journal of pediatrics*, 2012. 161(6): p. 1016-21.
- 4 Peterson, B.S., et al., Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood. *JAMA Psychiatry*, 2015. 72(6): p. 531-40.
- 5 Perera, F.P., et al., Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. *Pediatrics*, 2009. 124(2): p. e195-202.
- 6 Perera, F.P., et al., Prenatal polycyclic aromatic hydrocarbon (PAH) exposure and child behavior at age 6-7 years. *Environ Health Perspect*, 2012. 120(6): p. 921-6.
- 7 Arora, M., et al., Determining prenatal, early childhood and cumulative long-term lead exposure using micro-spatial deciduous dentine levels. *PLoS One*, 2014. 9(5): p. e97805.
- 8 Arora, M., et al., Fetal and postnatal metal dysregulation in autism. *Nat Commun*, 2017. 8: p. 15493.
- 9 Kile, M.L., et al., Using silicone wristbands to evaluate preschool children's exposure to flame retardants. *Environ Res*, 2016. 147: p. 365-72.
- 10 Gauderman, W.J., et al., Association of improved air quality with lung development in children. *N Engl J Med*, 2015. 372(10): p. 905-13.
- 11 Berhane, K., et al., Association of Changes in Air Quality With Bronchitic Symptoms in Children in California, 1993-2012. *Jama*, 2016. 315(14): p. 1491-501.
- 12 Rich, D.Q., et al., Differences in Birth Weight Associated with the 2008 Beijing Olympic Air Pollution Reduction: Results from a Natural Experiment. *Environ Health Perspect*, 2015.

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