ARTICLE

Persistent Organic Contaminants in Human Milk

Les polluants organiques persistants (POP) dans le lait maternal

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ABSTRACT

Persistent organic pollutants (POPs) are always components of human milk and can be transferred to infants through lactation. This paper describes the POPs and discusses the risks that POPs in human milk pose to nursing infants. Features of select POPs that are explained in this paper include their uses, toxicity and temporal trends. The levels of most POPs are declining in human milk due to a series of international bans and restrictions that have been placed on the manufacturing and/or use of the chemicals. However, there is still concern regarding the continued exposure to POPs from leaks in electrical equipment and vector control programs. Although these contaminants continue to be detected in human milk samples, women are still encouraged to breastfeed their newborn children. It is firmly believed that the benefits of lactation for both the mother and her child outweigh the health hazards that POPs present.

KEY WORDS

Persistent organic pollutants (POPs), breastfeeding, lactation, human milk, environmental contaminants

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RÉSUMÉ

Les polluants organiques persistants (POP) font toujours partis des composantes du lait maternel et peuvent être transférés au nourrisson lors de l'allaitement. Cet article décrit les POP et discute des dangers que les POP présents dans le lait maternel peuvent poser aux nourrissons. Les caractéristiques des POP décrient dans cet article inclus: leurs modes d'emplois, leur toxicité et leurs tendences temporelles. Le niveau des POP présents dans le lait maternel sont en déclin en raison d'une série d'interdictions et de restrictions mise sur la manifacturation et/ou l'emploi de ces produits chimiques. Cependant, il y a encore des préoccupations concernant l'exposition répétée aux POP en provenance d'écoulements d'équipements électriques et des programmes de lutte antivectorielle. Bien que ces polluants continuent d'être détectés dans les échantillons de lait maternel, les femmes sont encore encouragées d'allaiter leur nouveau-né. Il est fortement cru que les bénéfices de l'allaitement maternel, pour la mère et l'enfant, ont une plus grande importance que les risques que posent les POP pour la santé.

MOTS CLÉS

Polluants organiques persistants (POP), lait maternel, allaiter, contaminants environnementaux

Cet article a été évalué par des pairs.

INTRODUCTION

Breastfeeding is an essential component of newborn care since it bestows upon infants numerous benefits such as immunologic protection and a decreased lifetime risk of arthritis, diabetes and obesity.[1-3] However persistent organic pollutants (POPs) are ubiquitous and the main source of POP exposure in infants is human milk[2,4,5] so the advantages of milk are diminished by the risks of the POPs. This is a major concern for expectant and lactating mothers as they are particularly conscious of health issues and are determined to practice behaviors that will contribute to the growth of a healthy child.[6]

To determine whether the benefits offered by breastfeeding outweigh the effects of POP exposure it is important to identify the current contaminant load in human milk. The following paper aims to provide an overview of the POPs found in human milk as well as their temporal trends.

Persistent Organic Pollutants (POPs)

POPs are toxic substances known for their resistance to degradation through photolytic, biological and chemical means.[7] POPs are further characterized by low water solubility and high lipid solubility (lipophilicity) resulting in their accumulation in tissues and fluids with high fat content.[7,8] This combination of stability and lipophilicity allows POPs to reside in organisms for years as well as accumulate in the top of the food chain.[8,9] Humans are exposed to and accumulate POPs in large quantities due to their position at the top of the food chain.[8]

Lactation allows mothers to transfer portions of their POP burden to their children because milk fat sequesters the lipophilic contaminants.[1] There is wide variation but it is estimated that 20% or more of a mother's POP load may be passed to her infant in six months of breastfeeding,[10,11] and newborns are often being subjected to an average of 50 times an adult's daily intake of certain organic contaminants.[1]

POPs became an issue of global concern because of their ability to travel unchanged long distances into previously uncontaminated areas.[7] Known as the "grasshopper effect", POPs will evaporate and travel until they reach a climate that is sufficiently cold to promote their deposition.[12, 13] A major implication of this pole-ward migration of POPs is that extreme northern and southern communities receive a disproportionate amount of POPs in areas where POPs were never used.

This paper will focus on the following common POPs: dichlorodiphenyltrichloroethane (DDT), dichlorodiphenylchloroethane (DDE), hexachlorocyclohexane (HCH), hexachlorobenzene (HCB), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and bisphenol A (BPA). DDT, HCH, and HCB are pesticides while DDE is the metabolite of DDT and the remaining four substances serve as industrial chemicals.

Pesticides

DDT

DDT is an insecticide widely recognized for its uses on agricultural crops and in vector control.[4,14-16] The main current use of DDT is for the control of mosquitoes responsible for the spread of malaria and the sandflies responsible for carrying leishmaniasis. This chemical is especially important in the discussion of POPs in human milk because it was the first environmental contaminant to be found in this fluid and has been detected in almost all human milk samples since 1951.[1] DDT is highly persistent in the environment with 50% of the substance remaining in the soil for 10-15 years following its application.[7,15] Food acts as the greatest source of DDT exposure for the general public.[7,15,16]

The health effects of DDT have been studied since it began to be used for vector control in the Second World War. In 1950, a study involving 77 rats exposed to 0.25 - 0.5 mg/kg/day DDT in the diet observed increases in liver cell size consistent with hepatitis.[17] In 1974, offspring of rats given 34.3

mg/kg/day DDT during gestation and lactation showed impaired learning and memory function when tested one and two months after weaning.[18] Studies have also shown DDT to exhibit toxic effects on the nervous systems of both humans and animals following acute, subchronic, and/or chronic oral exposure.[19-22]

To aid in making the results of these studies relevant to human health, the Agency for Toxic Substances and Disease Registry (ATSDR) has established Minimal Risk Levels (MRLs) for several harmful compounds. MRLs are approximations of daily exposure levels of a chemical that present nominal risks to humans.[15] The MRL for both acute and intermediate duration exposure to DDT is 0.0005 mg/kg/day.[15]

To determine whether the benefits offered by breastfeeding outweigh the effects of POP exposure it is important to identify the current contaminant load in human milk.

DDT levels in Canadian human milk samples have been following a downward trend since the early 1970s.[11] In 1968, a mean value of 5.50 mg/kg lipid was observed for human milk samples collected across the country.[23] This number decreased significantly to 0.39 mg/kg lipid, as shown in a study published in 1986.[24] A more recent analysis of human milk samples from Ontario demonstrated the continuation of this temporal trend with the finding of 0.06 mg/kg lipid as the mean DDT concentration.[25] This translates into an exposure level of 0.000345 mg/kg body wt/day for a 4.0 kg infant consuming milk at one month, a value that is just below the MRL for both acute and intermediate duration exposure to DDT.

Canadian human milk samples generally contain lower DDT concentrations than samples collected from other areas of the world. Recently reported mean concentrations of DDT include 0.34 mg/kg lipid in Japan,[26] 0.66 mg/kg lipid wt. in Russia,[27] and 1.50 mg/kg lipid in New Delhi, India.[28] A study in 2004 estimated the daily intake of DDTs by infants in the Vietnamese cities of Hanoi and Ho Chi Minh to be 0.007 and 0.011 mg/kg body wt/day respectively.[29]

Attention was brought to the detrimental impact of DDT on humans, animals and the environment in the early 1970s, which initiated a series of bans or heavy restrictions on the chemical across the world.[7,30] The Stockholm Convention, a global treaty to minimize or eliminate the use of POPs,[31] is one such restriction that has played a large part in reducing DDT levels worldwide. Under the Convention, the use of DDT is only permitted for vector control.[30] There is a particular emphasis on utilizing DDT to control mosquitoes in the hopes of combating malaria, a disease that is still responsible for millions of deaths across the world.[30] The World Health Organization (WHO) has also approved the use of DDT in controlling the spread of malaria and has incorporated the chemical into its Indoor Residual Spray (IRS) Programs.[32]

DDT is currently being manufactured in India, China, and the Democratic People's Republic of Korea, with the largest amounts of production and consumption occurring in India.[14] DDT usage is also being seen in various African countries where the pesticide is being reintroduced as part of the WHO's IRS Program.[14]

DDE

DDE is the main breakdown product of DDT and although it has no commercial use,[15] it represents an area of concern due to its ability to persist to a greater degree in the environment than DDT.[7] The predominant organic pesticide detected in human milk samples is *p, p'*- DDE an isomer of DDE. This pesticide residue is responsible for about 90% of

the sum of DDT-DDE.[28,29,39-41] The concentration ratio of DDE to DDT is helpful for determining whether individuals are still being exposed to DDT.[33,34] Since DDE is formed as a result of DDT degradation, a low ratio would indicate recent exposure to the parent compound, while a high ratio would imply that a large amount of time has passed since DDT was last introduced.[33,34]

Research has suggested that *p,p'*-DDE exposure is linked to pre-term birth, lower weight of infants and decreased baby size at birth.[35] The compound is also found to be an androgen receptor antagonist, a substance that interferes with the functioning of male sex hormone receptors.[36-38] In 1995, Kelce et al. administered 100 mg/kg/day *p,p'*-DDE to Long-Evans rats during gestation days 14 to 18 and exposed the male pups to the substance via lactation.[36] This resulted in the pups being born with significantly reduced anogenital distance and retaining their thoracic nipples on postnatal day 13.[36] The same study also treated weanling rats with 100 mg/kg/day *p,p'*-DDE from either day 21 or 25 until day 57 of age.[36] A significant delay in the onset of puberty was noticed and attributed to the aforementioned impact of DDE on androgen receptors.[36] No MRL has been derived for DDE.

A study published in 2003 observed that DDE levels in Canadian human milk samples were declining over time.[11] Furthermore, samples collected between 2005 and 2006 in Canada displayed concentrations of 0.10 mg/kg lipid[42] and 0.09 mg/kg lipid.[25] This means a 4.0 kg nursing infant consuming these concentrations at one month would be receiving 0.000575 mg/kg body wt/day and 0.000518 mg/kg body wt/day respectively.

When these concentrations of DDE in Canadian

Table 1: *Importance, toxicity and temporal trend of POPs.*

POPs	Importance	Toxicity	Trend
Pesticides			
DDT	★★★	✖✖✖	↓ 23,33,34,39,105
DDE	★★★	✖✖	↓ 9,105,126,127
HCH	★★	✖✖✖	↓ 28,33,126,127
Industrial Chemicals			
PCB	★★★	✖✖✖✖✖	↓ 9,33,105,126,127
HCB	★★	✖✖✖	↓ 33,105,126,127
PBDE	★★★★	✖✖✖	↔ 103, 105
Bisphenol A	★	✖	-

human milk samples are compared to global levels, it can be concluded that Canadian values are very low. Samples from Melbourne, Australia contained a mean DDE concentration of 0.38 mg/kg lipid,[41] while 1.10 mg/kg lipid wt. in Chennai, India[28] and 1.20 mg/kg lipid in Hanoi, Vietnam[34] were also observed.

HCH

Technical HCH, also abbreviated as HCCH or BHC, is an insecticide composed of eight different isomers.[28,33,43] The γ-HCH isomer is well known as lindane, a substance still used as a second-line treatment of lice and scabies. Recognition of the different forms of HCH is critical because each has a different level of persistence, bioaccumulation and toxicity.[33,43] β-HCH is the most persistent and bioaccumulative isomer with 90% of HCH in human milk being contributed by this specific compound.[28,33,44] This high percentage is partly due to the conversion of the α-and γ-HCH isomers into β-HCH once they have entered an organism.[33] Sources of HCH exposure include food, water and topical treatments for insects.[33,43]

As mentioned earlier, each HCH isomer has a different level of toxicity. γ-HCH is the most toxic in terms of acute exposure, followed by α-, δ- and β-HCH.[43] A three-generation study of mink exposed to 1 mg/kg/day dietary γ-HCH found reduced litter size and testicular size as results.[45] 10 - 20 mg/kg/day γ-HCH yielded hematological and immunological effects in mice,[46] while pathologic changes in the liver and kidneys were seen at 72 mg/kg/day.[47] The ATSDR has thus assigned an MRL of 0.003 mg/kg/day for acute-duration oral exposure to γ-HCH.[43]

In contrast, β-HCH is the most toxic isomer when exposure is on a chronic basis.[43] Chronic studies in rats and mice have confirmed the liver as a target of action for β-HCH.[43,48] Five mg/kg/day β-HCH during gestation and lactation led to increased liver weights in pups while 20 mg/kg/day during gestation was associated with increased neonatal mortality.[49] Although the MRL for chronic exposure to β-HCH is not available, exposure to the chemical for intermediate duration has been given an MRL of 0.0006 mg/kg/day.[43]

Levels of HCH are generally quite low in Canadian human milk, as demonstrated by the finding of concentrations such as 0.0063 mg/kg lipid.[25] These low levels lead to an exposure of only 0.0000362 mg/kg body wt/day if they were to consume this concentration for their first month. This exposure level is far below the MRLs for both γ- and β-HCH.

On a global scale, Canadian values of HCH concentrations in human milk are one of the lowest. This is in comparison to 0.019 mg/kg lipid wt. in the United States,[50] 0.31 mg/kg lipid in Beijing, China,[44] and 4.50 mg/kg lipid wt. in Chennai, India.[51] One study estimated mean exposure rates to be 0.00265 and 0.00274 mg/kg/day in Beijing, China and Shenyang, China respectively.[44]

The α-, β-, and γ-HCH isomers were officially added to the Stockholm Convention's list of pollutants in 2009.[8] They are regarded as chemicals whose use and production must be eliminated.[8] The eradication of γ-HCH or lindane is especially important due to the fact that the α- and β-HCH isomers arise as unintentional by-products during manufacture and metabolism.[8] Several countries have placed regulations on lindane, which has led to a considerable reduction in the production and use of the chemical.[8,52] A report published in 2006 noted that lindane has been banned in 52 countries and restricted in 33 countries.[52]

However, the Convention recognizes that lindane remains a practical remedy for lice and scabies in many nations including Canada and the United States.[8,52] It has therefore made an exception and has allowed the medical use of lindane.[8]

Industrial Chemicals

HCB

HCB is both a by-product of industrial processes and a fungicide that has been used for seed grains since 1945.[7,33,53] It poses a significant threat to the environment due to its high water insolubility and

extreme resistance to degradation.[7,53] These qualities contribute to HCB being very persistent in the environment, with estimations of its half-life in soil reaching up to 23 years.[7] Food constitutes a major source of HCB exposure for humans, while contaminated water, soil and fumes from factories act as minor routes.[53,54]

Much of HCB's toxic effects were discovered in the 1950s after a widespread exposure in Anatolia, Turkey. The epidemic began when an estimated 3,000 to 4,000 individuals consumed bread made from grain that had been treated with fungicides composed of 10% HCB.[53] It was reported that the average adult ingested approximately 0.7 - 2.9 mg/kg/day HCB during the epidemic.[55] Children were also affected, as seen by the 95% mortality rate of infants less than two years of age who had been breastfed by mothers exposed to the chemical.[53] Poisoned infants were diagnosed with pembe yara or "pink sore", which included symptoms of skin lesions, weakness and convulsions.[56,57] Further studies have shown that women who were most heavily exposed had proportionally fewer males and a greater likelihood of spontaneous abortion.

Studies have shown HCB to display hepatic, reproductive and developmental toxicity.[53] HCB targets the liver by causing the accumulation of porphyrins, important building blocks of hemoglobin and other biological molecules, in the organ.[53] This leads to the development of porphyria, the excessive excretion of porphyrins in the urine, a disease that was widely seen during the epidemic in Turkey.[53] Doses of 5-12 mg/kg/day have been reported to elicit porphyrinogenic effects in female rats exposed to HCB for intermediate durations.[58-60] The occurrence of porphyria is concerning because the disease has been associated with an increased risk of liver cancer.[61] This information, as well as HCB's ability to induce tumors in the liver, thyroid and kidney of three rodent species, has led the U.S. Department of Human Health Services to deem HCB an expected carcinogen in humans.[62] Studies have also shown that HCB accumulates in the ovaries[63,64] and can cause adverse effects in the organ at doses as low as 0.01 mg/kg/day.[53,65] HCB's developmental toxicity was observed when the pups of female Rhesus monkeys exposed to 64 mg/kg/day were fed their mother's milk for 15-38 days and as a result experienced neurological effects, lung edema, liver damage and death.[66,67] HCB has an MRL of 0.008 mg/kg/day for acute exposure, an MRL of 0.0001 mg/kg/day for intermediate exposure, and an MRL of 0.00005 mg/kg/day for chronic exposure.[53]

Studies have shown that women who were most heavily exposed had proportionally fewer males and a greater likelihood of spontaneous abortion.

HCB is another POP found in small quantities in Canadian human milk samples. Studies conducted between 2005 and 2006 found concentrations of 0.0061 mg/kg lipid[42] and 0.0063 mg/kg lipid[25] in Canadian samples. For a 4.0 kg nursing infant at one month, this translates into an exposure level of 0.0000351 mg/kg body wt/day and 0.0000362 mg/kg body wt/day respectively. Although these exposure levels are below the MRLs for all durations of exposure to HCB, it is important to note they are not far behind the limit for chronic exposure.

The aforementioned HCB concentrations are lower than most of the levels found in human milk samples of other world populations. Observed global values include 0.081 mg/kg lipid in China,[68] and 0.10 mg/kg lipid wt. in Russia.[27] The estimated infant exposure rate to HCB in Vietnam is 0.00001 mg/kg/day.[29]

The Stockholm Convention included HCB in its initial list of pollutants as both a pesticide that must be eliminated, and a substance whose unintentional production in industrial processes must be reduced.[8] Actions to achieve the goals of the Convention have already been undertaken, beginning with the implementation of various bans and restrictions on the production and use of

HCB in the 1970s.[69,70] Both the United States and Canada have prohibited the production and use of HCB as a pesticide.[69,70] However, it has been reported that the chemical continues to be emitted from sources such as metal industries, combustion and chemical processes, and through volatilization and leaching from landfills.[69,71]

PCBs

PCBs are industrial chemicals that have been widely used since 1930 in products such as electrical equipment, paint additives and plastics.[7,33,72] They have been utilized extensively in different sectors because they are stable, non-conducting, non-flammable and heat resistant.[7,72] As their name suggests, PCBs are composed of carbon, hydrogen and a varying number of chlorine atoms. The structures of these chemicals play a key role in determining their ability to bioaccumulate and linger in the environment, since a greater number of chlorine atoms is associated with higher lipid solubility and degree of persistence.[7,72] PCBs are produced and used in a mixture of up to 209 congeners (different conformations of PCB). Each congener manifests its own level of prevalence and toxicity.[33,72] To estimate the risk of the congeners, a Toxic Equivalency Factor (TEF) has been assigned to each of them.[72] The TEF is a comparison of a congener's relative toxicity with that of 2,3,7,8-TCDD, the most toxic dioxin.[72] Dioxins are compounds structurally similar to PCBs[72,73] and therefore allow for accurate comparisons. Individuals are subjected to PCBs primarily through food, but exposure can also occur through PCB leaks in products and living near waste sites that contain the contaminant.[7,72]

Determining the health effects of PCBs is made difficult by the varying composition of PCB mixtures.[72] The toxicity of each congener and the interactions that take place between them play a large part in influencing the toxicity of the overall mixture.[72] Thus, mixtures with different compositions may yield dissimilar effects in exposed individuals.

One type of mixture that is used in studies to assess the risks of environmental exposure to PCBs is a commercial mixture such as Aroclor 1254.[72] Monkeys exposed to 0.005 mg/kg/day Aroclor 1254 during gestation and lactation for 22 weeks displayed ocular, nail and gum lesions, as well as inflammation and/or enlargement of the tarsal glands.[74,75] Another study fed female monkeys either 0.1 or 0.2 mg/kg/day Aroclor 1248 for 15 months, a period that included breeding, gestation and lactation.[76] Signs of PCB intoxication were evident in the offspring at two months of age and included facial acne, swollen eyelids, loss of eyelashes, and hyperpigmentation of the skin.[76] Thyroid toxicity has also been associated with oral exposure to Aroclor 1254.[77-79]

Researchers also utilize an experimental mixture that resembles the PCB congener composition of human milk.[72] The use of this particular mixture allows these studies to be especially helpful in determining the risk of PCB exposure by a nursing human infant.[72] One such study administered doses of 0.0075 mg/kg/day to male monkeys from birth to 20 weeks of age.[80] This dose level matched the approximate daily intake of a human infant whose mother's milk contains 0.05 mg/kg (50 ppb) PCBs, the Health Canada guideline for maximum PCB concentration in human milk.[72] The exposed monkeys showed increased errors at short delay task responses, impaired learning, and perseverative behavior.[77] Based on the studies conducted on PCBs, an MRL of 0.00003 mg/kg/day has been given for intermediate oral exposure to PCBs.[72] The MRL for chronic exposure is 0.00002 mg/kg/day.[72]

Information regarding the toxicity of PCBs was also gathered from the Yusho incident in Japan and the Yu-Cheng incident in Taiwan when the consumption of PCB-contaminated rice led to mass poisonings.[72] Exposed individuals displayed both dermal and ocular effects, as well as neurological symptoms of numbness, hypesthesia (insensitivity) and headaches.[72,81,82] However, PCBs were not solely responsible for inducing these effects because other compounds containing chlorine atoms, such as chlorinated dibenzofurans, were also present.[72] These chemicals were produced in high

concentrations from the heating of the PCB mixture.[72] It is therefore difficult to discern what effects were caused by PCBs alone. Instead, the findings from these incidents are used to indicate how humans might respond to dioxin-like PCB congeners.[72]

In Canada, PCBs are present in human milk in larger quantities than other POPs such as HCB and HCH. Recent studies have found Canadian human milk samples to contain PCB concentrations of 0.04 mg/kg lipid[42] and 0.07 mg/kg lipid.[25] These concentrations result in a daily infant exposure level of 0.00023 mg/kg body wt/day and 0.000403 mg/kg body wt/day respectively. This is concerning because these levels exceed the MRLs for both intermediate and chronic exposure to PCBs, thus putting the health of Canadian nursing infants at risk.

When compared to levels worldwide, Canadian milk PCB concentrations are one of the lowest. Recent global values include 0.023 mg/kg lipid in New Delhi, India,[28] 0.07 mg/kg lipid in the Philippines,[83] 0.089 mg/kg lipid in Belgium,[84] and 0.153 mg/kg lipid in Poland.[85] The estimated infant exposure rate in Tunisia is 0.00083 mg/kg body/day[86] while the rate in Hanoi, Vietnam is 0.00025 mg/kg body wt/day.[29]

The dangers of PCBs were brought to light in the 1970s and this consequently led to international calls for bans and/or restrictions on their use.[87,88] By 1977, both the United States and Canada had prohibited the manufacturing, processing, distribution and use of PCBs.[70,87] Japan and various western European countries also took part in similar bans.[88] Although these policies prevented PCBs from being created, they did not target PCB-containing electrical equipment.[87] The continued use and improper disposal of these devices poses a threat to human and animal life due to the potential for the chemical to leak from the equipment into the environment.[72,89] Countries have therefore established controls for the handling, storage and disposal of PCB-containing equipment.[87,89]

PCBs were placed on the Stockholm's Convention original list of pollutants and remain important chemicals of interest.[8] PBCs are labeled as both pollutants whose production and use must be eliminated, and substances whose unintentional releases must be minimized.[8]

PBDEs

PBDEs are substances similar to PCBs in both chemical structure and application as flame-retardants in products including electrical appliances and carpets.[90] They are commercially available in the following three forms: pentaBDE, octaBDE, and decaBDE.[91,92] These products are composed of a mixture of individual PBDE congeners with each congener having anywhere from one to ten bromine atoms attached.[93] PBDEs do not chemically react with the materials they are applied to which enables them to evaporate into the environment.[33,92] The pentaBDE and octaBDE congeners, containing on average five and eight bromine atoms respectively, are easier to absorb due to their small size. The absorption of the decaBDE congener is made difficult by its average ten bromine atoms per molecule.[92] Therefore, the compounds with fewer bromine atoms are usually seen in human milk.[92]

The toxicity of PBDEs is discussed in terms of the three commercial products in which they are made available: penta-, octa-, and decaBDE. DecaBDE has been shown to exhibit a lesser degree of toxicity than the pentaBDE and octaBDE products.[92, 94] This is likely due to decaBDE's poor absorption pattern, rapid elimination in the body, and the greater retention of the lower brominated products in tissues with high lipid content.[92.95]

Studies have suggested that the lower brominated PBDEs target the liver, thyroid and developing neurobehavioral systems. Although exposure to 2000 - 8000 mg/kg/day high purity decaBDE for 13 weeks did not induce any liver effects in rats,[94] the separate administration of 5 mg/kg/day octaBDE for 4-13 weeks and 9 mg/kg/day pentaBDE for 28 days induced changes in the liver such as increased liver weight and liver cell size.[92] The thyroid toxicity of PBDEs is supported by experiments such as the one

conducted by Zhou et al., where acute oral exposure to decaBDE did not cause any thyroid effects in weanling rats, but similar exposures to octaBDE and pentaBDE products led to decreases in the serum T_4 and T_3 levels of the rats.[96]

The impact of PBDEs on the neurobehavioral system of neonates has been examined using lower brominated congeners such as BDE 47 and BDE 99. Eriksson et al. administered single doses of 0, 0.7 or 10.5 mg/kg BDE 47 or 0, 0.8 or 12 mg/kg BDE 99 to mice on postnatal day 10, a stage characterized by rapid brain development.[92,97] A prominent result of these studies was the display of non-habituating behavior, such as decreased locomotion, by mice exposed to both PBDE congeners.[97] This behavior was also observed in an additional study that subjected mice to a single 8 mg/kg dose of BDE 99 on postnatal day 10.[98] Evidence presented by these studies led the ATSDR to assign an MRL of 10 mg/kg/day for intermediate oral exposure to decaBDE.[92] In contrast, the lower brominated PBDEs have been given an MRL of 0.03 mg/kg/day for acute exposure and 0.007 mg/kg/day for intermediate exposure.[92]

Similar to PCBs, PBDEs are often found in higher concentrations than other POPs in Canadian human milk. Samples collected in Vancouver showed a mean PBDE concentration of 0.043 mg/kg lipid,[99] while 0.096 mg/kg lipid wt. was observed in the Pacific Northwest of the United States and Canada.[100] These translate into exposure levels of 0.000247 mg/kg body wt/day and 0.000552 mg/kg body wt/day for a 4.0 kg nursing infant at one month. These values fall below the MRLs for PBDEs.

The Canadian levels of PBDEs in human milk are significant in a global context because they are between 10-40 times higher than those found in other areas such as Europe.[90, 91,101] For example PBDE levels of 0.0038 mg/kg lipid and 0.0089 mg/kg lipid have been found in Norway[39] and England[91] respectively. A study in the Philippines noted that the estimated daily intake of total PBDEs by infants remains below the reference dose for chronic oral exposure and is not posing a large threat currently.[83]

PBDEs represent a very significant area within the issue of human milk contamination because they are one of the only POPs whose levels were increasing until recently. Their production and use increased since the 1970s,[33,102] which corresponds with the time when efforts were being made to reduce PCB utilization. Recent studies have shown that PBDE levels are beginning to decrease or, at worst, stabilize in the human milk samples of certain countries.[103-105]

In contrast to most of the aforementioned POPs, regulations on the manufacturing, use and distribution of PBDEs were created fairly recently and are continuing to be developed. California banned the manufacturing or distribution of any product containing pentaBDE or octaBDE in 2003, with Hawaii and Illinois passing similar laws.[106] In 2004, a ban against the marketing and use of pentaBDE and octaBDE was implemented throughout the European Union.[93,107] This year also saw the Great Lakes Chemical Corporation, the only producer of commercial pentaBDE and octaBDE in the United States, cease the manufacturing of the two products.[93,106] Canada passed legislation in 2008 that forbade the production, use, sale and import of select PBDE congeners and mixtures, polymers and resins containing those substances.[107]

Although several bans and restrictions have been placed internationally on the manufacturing and use of certain PBDE congeners and products, there is a lack of legislation passed on decaBDE. A study in 2005 noted that decaBDE is the world's most widely used PBDE product, and is still being produced and sold in the United States.[102] Unlike the other two commercial products, decaBDE is not subject to a great number of bans and restrictions.[106] The Stockholm Convention has targeted the tetra-, penta-, hexa-, and heptaBDE congeners for elimination, as they are the main components of the pentaBDE and octaBDE products, but has not done so for decaBDE.[8] This is a potential problem, as congeners with a greater number of bromine atoms may lose those constituents and become lower, more

toxic congeners.[8]

The safe disposal of PBDE-containing products is also a concern since the pollutant has been known to leak from equipment into the environment.[93, 106] Countries have therefore developed or are in the process of creating strategies for handling PBDE-containing waste.[93, 108]

BPA

BPA is an industrial chemical used in the synthesis of polycarbonate plastic and epoxy resins, and thus is a component of numerous consumer products such as metal cans and toys and, most conspicuously, some plastic baby bottles[109,110] BPA has one of the highest production volumes of industrial chemicals in the world, with about 3 million tonnes produced per year.[110] BPA is not generally considered a POP since it does not tend to accumulate in lipid-rich materials to the same extent, and is broken down more rapidly, than the "classic" POPs like DDE and PCBs. Sometimes BPA is referred to as a semi-persistent organic pollutant. BPA is similar to PBDEs in that it can also leach from objects into the environment and enter the food chain.[110,111] Since BPA is used in many consumer products and can be released from these goods with relative ease, particularly under hot or acidic conditions, sources of this contaminant are many and are not limited to simply food, air or water.[110]

The estrogenic properties of BPA have been the focus of many studies conducted on the chemical.[112,113] BPA was originally produced as a chemical estrogen and thus it is no surprise that it exhibits endocrinological activity.[114,115] An animal study involving perinatal exposure to 0.1 or 1.2 mg/kg/day BPA observed increases in body weight, changes in estrous cycles, and reductions in plasma concentrations of luteinizing hormone as results.[116] Findings from other animal studies include the early onset of sexual maturation in females at maternal doses ranging from 0.0024 mg/kg/day to 0.500 mg/kg/day,[117,118] an increase in prostate size in male offspring at maternal doses of 0.002 to 0.050 mg/kg/day,[119,120] and behavioral effects at 0.030 mg/kg/day.[121] No MRL exists for BPA.

As mentioned earlier, sources of exposure to BPA vary widely and can range from food packaging to dental sealants.[110, 114] It has been suggested that humans are exposed to the chemical on a steady basis and in significant amounts, as BPA continues to be detected in several body fluids even though it is metabolized rapidly.[112] BPA levels are seldom measured in human milk and are more commonly reported in fluids such as urine and blood. Recent studies that have included an analysis of BPA in human milk have observed mean concentrations of 0.017 mg/kg lipid[122] and 0.054 mg/kg lipid.[123] The European Food Safety Authority (EFSA) has estimated that the exposure of infants to BPA ranges from 0.0002 to 0.0083 mg/kg/day.[124]

Debates continue as to whether BPA poses a human health threat due to inconsistencies and quality control-related issues in research studies published on the chemical.[113] These issues include the use of non-oral routes of administration, small numbers of animals, and single dose levels.[113] A recent report by the WHO affirmed that regulatory authorities generally believe that the low-dose effects of BPA in rodents have not been shown in a way that is robust and reproducible.[113] The data inconsistencies have meant that there are varying responses by countries to BPA and varying interpretations of its potential impact on human health.

The government of Canada considers BPA to have harmful effects on the environment and humans and is continuing to implement regulations to ban the importation, sale and advertising of polycarbonate baby bottles that contain BPA.[113] Various individual states in the U.S., such as Connecticut and Minnesota, have banned the sale of polycarbonate baby bottles, food containers and cups that contain BPA.[125] In contrast, Japan, the European Union and the EFSA have all concluded that studies showing low dose, endocrine-disrupting effects of BPA are insufficient for an accurate risk assessment.[125] Furthermore, they have agreed that the current estimated exposures to BPA do not pose a threat to human health.[125]

Temporal Trends

Table 1 outlines the temporal trends displayed by the aforementioned POPs. The contaminants are also evaluated for their importance, judged by concentration, prevalence and toxicity.

CONCLUSION

The objective of this paper was to provide descriptions of select POPs in terms of their traits, uses, sources of exposure, toxicity, applicable regulations and temporal trends. As demonstrated by Table 1, PBDEs lead in importance due to the stabilization, rather than definite decrease, of their levels in human milk. This contrasts with the other pollutants, whose levels have been steadily decreasing in human milk. In addition, the continued use of decaBDE is a concern that is yet to be fully addressed. DDT, DDE and PCBs are not far behind PBDEs in importance as they are highly prevalent in human milk and exposure to these chemicals is likely continuing due to leaks from electrical equipment and vector control programs. Much of the significance of PCBs is also derived from its relatively high toxicity, as confirmed by the MRLs assigned to them by the ATSDR. In contrast, bisphenol A is ranked lower in importance since it is not yet a widely measured substance in human milk and conclusions on its prevalence and temporal trend are therefore difficult to make. The debates on bisphenol A's toxic effects further complicate the determination of the chemical's threat to human health and the importance it holds in the topic of human milk contamination.

It should be noted that although the toxicity of the pollutants was evaluated based on studies conducted on each contaminant, this is not representative of the scenarios faced by nursing infants. Human milk is most often a mixture of these pollutants, resulting in infants being exposed to multiple chemicals simultaneously. Research experiments that involve the administration of a single contaminant therefore do not take into account any synergistic or antagonistic effects the pollutant may have in the presence of other chemicals. To further the discussion of the dangers facing infants through lactation, the need for studies focusing on the combined effects of organic contaminants increases greatly.

On a positive note, the bans, restrictions and international treaties targeting these POPs have been largely successful at reducing the levels of the chemicals found in human milk.[26,124,125] The Stockholm Convention, adopted in 2001 and implemented in 2004,[126] is one treaty that has contributed to the downward temporal trends of many POPs. It represents the global community's pledge to continue these trends and achieve either a complete eradication or a minimized use of several POPs. The Convention currently has 170 Parties and 152 Signatories.[126]

It has been widely agreed upon that women should continue to breastfeed their children, regardless of the fact that contaminants remain present in human milk at detectable levels.[1,2,127] Miriam Labbok, a physician-epidemiologist who directs the Carolina Breastfeeding Institute at the School of Public Health of the University of North Carolina in Chapel Hill, affirmed that, "no environmental contaminant, except in situations of acute poisoning, has been found to cause more harm to infants than does lack of breastfeeding…I have seen no data that would argue against breastfeeding, even in the presence of today's levels of environmental toxicants."[1] Though lactating mothers have little control over the contaminants that become integrated into their milk, they can contribute to a healthier environment for their infants by making positive dietary choices. Seeing as diet acts as a major source of POP exposure for humans, and individuals who eat meat tend to accumulate more POPs than those following a largely vegetarian diet,[1] making better food choices can go a long way for the health and future of nursing infants.

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