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Transgenerational Exposures: Persistent Chemical Pollutants in the Environment and Breast Milk

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Many environmental threats to children's health are chemicals or pollutants that are currently used or released into the environment, such as pesticides, mercury, various chemicals in consumer products, and air pollutants. Some chemicals, however, remain significant health concerns even though they have been banned for more than a quarter-century in the United States. Many of these so-called "legacy pollutants" are also known as "persistent organic pollutants" (POPs). These substances are present within the food supply, and they are known to accumulate in breast milk. Because many POPs, such as dichlorodiphenyltrichlorethane (DDT), polychlorinated biphenyls (PCBs), and dioxins, are familiar names, there is a high level of concern among the general public about these contaminants. In addition, sporadic media attention about contaminants in food and breast milk

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generates questions to pediatricians about the likelihood and nature of potential health effects and about the advisability of breastfeeding.

POPs are synthetic organic compounds that persist in the environment for many years, resist biodegradation, accumulate in fatty tissues and in predator species, and travel long distances to be dispersed globally. Nearly all living organisms carry measurable concentrations of POPs in their bodies [1]. Although POP chemicals have a variety of structural characteristics, most are polyaromatic, and all are polyhalogenated hydrocarbons, usually containing chlorine or bromine as an important constituent. A dozen POPs have been targeted for global elimination under the Stockholm Convention on Persistent Organic Pollutants [2], an international treaty signed by 151 countries in May, 2001. The pesticides and industrial chemicals on the Stockholm POPs list were banned in most developed countries in the late 1970s, although many are still in use in the developing world. Other chemicals that share POPs' characteristics remain in widespread use in the United States and worldwide.

Extensive human cohort studies have shown associations between certain POPs, particularly PCBs and dioxins, and a wide array of adverse health effects in infants and children. Although the health effects generally are subtle, they are of significant concern because they have been shown to occur at exposure concentrations within the range commonly found in the human population worldwide. Epidemiologic studies have demonstrated adverse neurodevelopmental effects [3–10], endocrine alterations [11–20], immunotoxicity [21–28], and increased cancer risk [29–32] in populations with above-average exposures to these chemicals.

Persistence and bioaccumulation

An important characteristic of POPs is their ability to resist photolytic, biologic, and chemical degradation. They have half-lives that range from months to more than a decade. These chemicals are semivolatile, which allows them to evaporate into the atmosphere and deposit back to earth in precipitation. As this cycle is repeated, these substances are transported from equatorial regions toward the poles in a process called ''global distillation'' [33]. This process accounts for the high concentrations of POPs in Arctic wildlife [34]. POPs are also lipophilic and hydrophobic [2]. When these chemicals land in water, they precipitate rapidly from the water column and attach to organic material in the sediment, where they may be consumed by small organisms.

As organisms at the bottom of the food chain consume POPs, these substances are absorbed and stored in fatty tissue. Because POPs are not readily excreted, continued consumption over time results in bioconcentration. As higher-level predators consume lower-level organisms, the increasing concentration is accentuated in a process referred to as ''biomagnification.'' This phenomenon holds particularly true for aquatic ecosystems because there are more levels in the food chain. Native peoples in the Arctic regions derive a substantial portion of their diet from high on the food chain (ie, marine mammals); they are among the populations most highly exposed to POPs.

Breastfeeding infants are at the top of the food chain, and they consume bioaccumulated substances in mother's milk [35]. Infants are at additional risk because of their relatively high adipose concentrations, rapidly developing organs, and high intake of food or breast milk relative to body weight.

Sources

Diet is the major predictor for POPs exposures [36]. Although fruits, vegetables, and grains contain small amounts of POPs, the highest exposure comes from consumption of animal fats. Fig. 1 summarizes the main sources of dietary intake of dioxin for various age groups of children.

POPs are known to occur in human breast milk. Concentrations of various POPs are up to six times higher in breast milk than in maternal serum, and it has been estimated that infants breastfeeding for 6 months may receive as much as 14% of their cumulative lifetime exposure of dioxins and PCBs [37]. Because of the prolonged half-life of dioxin, this childhood exposure contributes significantly to the total body burden present during the

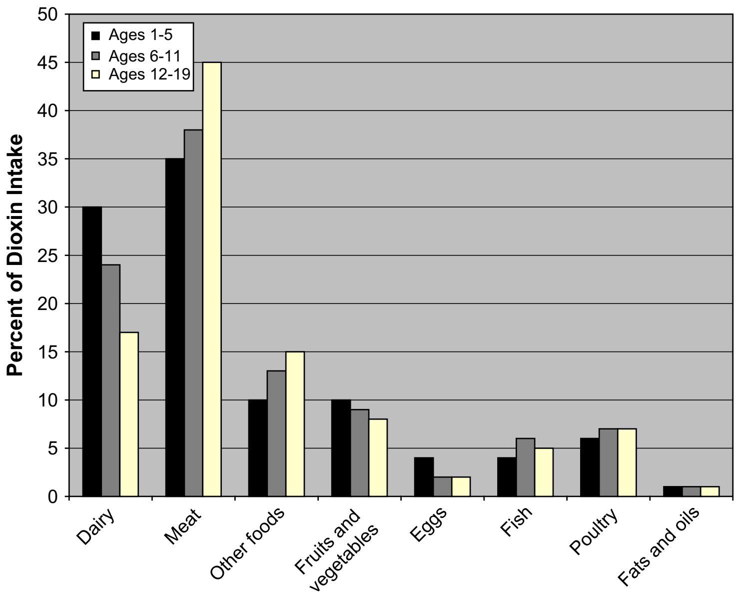

Fig. 1. Estimated percent contribution of various foods to dioxin intake among children. (*Data from* The Committee on the Implications of Dioxin in the Food Supply. Dioxins and dioxin-like compounds in the food supply: strategies to decrease exposure. Washington, DC: National Academies Press; 2003. p. 116–20.)

reproductive years. Fortunately, the concentrations of most POPs in breast milk have shown a significant decline in the past few decades as a result of increasing restrictions on production and use worldwide. Fig. 2 illustrates the decline of several major POPs in breast milk. The World Health Organization and the American Academy of Pediatrics have concluded that the health benefits of breastfeeding are not outweighed by the presence of pollutants [38,39].

Persistent organic pollutants controlled under international treaty

The Stockholm Convention on Persistent Organic Pollutants was signed by 151 countries, including the United States [2]. Its goal is to eliminate or restrict the use of 12 major POPs (Table 1). Additional chemicals have been nominated to join these original 12. Although the United States has not ratified the Stockholm Convention, most of these chemicals have been banned in the United States for many years. These chemicals can be classified generally into three major categories: pesticides, industrial chemicals, and byproducts.

Nine of the 12 Stockholm POPs were used as pesticides for vector control and agriculture. These chemicals came into widespread use after World War Two and initially had the advantage of minimal acute toxicity. Concerns about persistence and chronic toxicity led many countries to ban their use in the 1970s. Some of pesticides banned by the Stockholm Convention, such as DDT, are still used for vector control in developing countries.

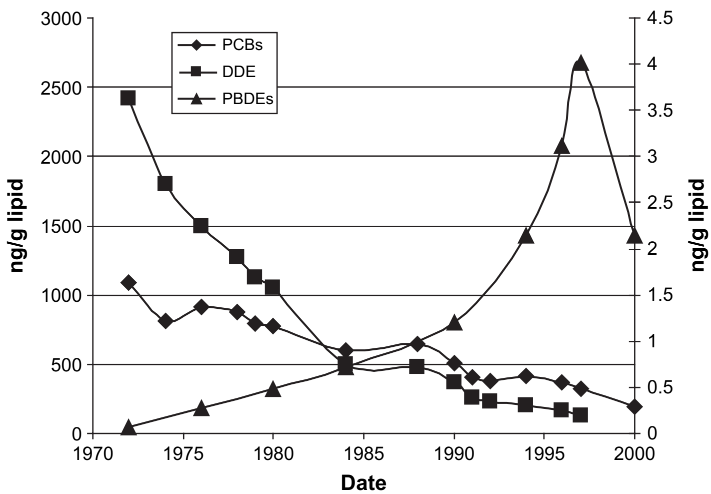

Fig. 2. Time trends of representative persistent organic pollutants in human breast milk. DDE, dicholorodiphenyldicholoroethylne; PCBs, polychlorinated biphenyls; PBDEs, polybrominated diphenyl ethers. (*Data from* Meironyte NK. Certain organochlorine and organobromine contaminants in Swedish breast milk in perspective of past 20–30 years. Chemosphere 2000;40(9–11):1111–23.)

Table 1
Persistent organic pollutants (POPs) subject to the Stockholm convention

Chemical	Category	Sources	Potential health effects	Half-life	California carcinogen classification
Aldrin	Insecticide	Agriculture, food	Neurotoxic, immune	5 years (soil)	Yes
Chlordane	Insecticide	Termite, agriculture, food	Neurotoxic, liver, immune	1 year (soil)	Yes
DDT	Insecticide	Vector control, agriculture, food	Lactation, liver, development, reproduction	10–15 years (soil)	Yes
Dieldrin	Insecticide (metabolite of Aldrin)	Agriculture, food, termite control	Neurotoxic, immune	5 years (soil)	Yes
Dioxins	Incineration byproduct	Food, waste sites	Development, immune, endocrine	7 years (humans); 10–12 years (soil)	Yes
Furans	Byproduct contaminant	Food, waste sites	As dioxin above	10–12 years (soil)	Yes
Endrin	Insecticide	Agriculture, food	Neurotoxic, development	12 years (soil)	No
Heptachlor	Insecticide	Fire ants, termite, agriculture, food	Development, neurologic, reproductive	2 years (soil)	Yes
Hexachlorobenzene	Fungicide, industrial by product	Agriculture, food	Liver, immune, endocrine	3–6 years (soil)	Yes
Mirex	Insecticide	Fire ants, termite, agriculture, food	Liver, neurologic, reproductive	10 years (sediment)	Yes
PCBs	Industrial Chemical	Food, leaking transformers, waste sites	Neurologic, development, immune, endocrine	2–6 years	Yes
Toxaphene	Insecticide	Agriculture, food	Immune, development	12 years (soil)	Yes

PCBs are halogenated hydrocarbons with paired phenyl rings having varying degrees of chlorination. Billions of pounds of these chemicals were produced for use in capacitors, transformers, and carbonless copy paper because of their fire-resistant properties [40]. In 1978 these products were banned in the United States and in many other countries, but they are still detectable in human tissue. Dioxins and furans are byproducts of combustion, waste incineration, paper bleaching, and chlorine production. There are hundreds of potential congeners, the most potent of which is 2,3,7,8-tetrachlorodibenzodioxin (TCDD). This substance has an estimated half-life in the human body of up to 7 years [41] and sometimes is referred to as the most toxic synthetic chemical known to man. Although pollution controls have reduced these chemicals, there is still ongoing release into the environment.

Human health effects of banned persistent organic pollutants

Neurodevelopmental effects

A variety of sources have presented compelling evidence of the impact of PCBs and dioxin on children's neurodevelopment. Animal research has demonstrated negative effects of in utero PCB exposure on neurodevelopment, cerebellar functioning, and short-term memory [42]. In a cohort of humans exposed prenatally to a mass poisoning from PCB-contaminated rice oil in Taiwan, exposed children demonstrated developmental delays, behavioral abnormalities, and poor cognitive development lasting past age 11 years, as well as dermatologic effects including hyperpigmentation of the skin and nails [43].

Several prospective cohort studies have demonstrated adverse developmental and neurodevelopmental findings at significantly lower exposures typical of fish-eating populations from the Netherlands, Michigan, North Carolina, and New York. An ongoing study in the Netherlands recruited mothers during pregnancy and followed the development of their children. The researchers estimated prenatal PCB exposure based on levels in maternal plasma during the last month of pregnancy; and postnatal exposure to PCBs and dioxin was based on levels in breast milk samples and duration of breastfeeding. At birth, the more exposed children had statistically significantly smaller head circumference [44]; by age 3 months, psychomotor and neurologic development was negatively associated with prenatal PCB exposure [45]. At age 7 months, although the breastfed infants were doing better by neurologic measures than the formula-fed infants, those exposed to higher concentrations of PCBs and dioxins in the breast milk were behind their breastfed peers. Additionally, General Cognitive Index and memory scores on the McCarthy Scales of Children's Abilities remained impaired by 8% ($P < .01$) at 7 years of age among those children who had highest PCB and dioxin exposures and whose home environment was rated "less advantageous" [3].

Cohorts of children whose mothers ate fish from the Great Lakes have been followed for years in New York and Michigan. Higher in utero exposures to PCBs as measured in maternal serum and cord blood were associated with significantly smaller head circumference, lower birth weight (by an average of 180 g) [4], poorer neonatal neurologic scores [5], poorer visual recognition memory on the Fagan Test of Infant Intelligence at ages 6 and 12 months [6], and persistent cognitive deficits in verbal and numeric memory at 4 years [7]. Further, at age 11 years, the children with the highest prenatal exposure were found to have a 6.2-point decrement in IQ scores and delayed reading abilities [8]. These children were three times more likely to have low-average IQ scores and twice as likely to be at least 2 years behind in reading comprehension. Another prospective cohort study in North Carolina found that infants exposed to higher in utero PCB concentrations were significantly more likely to be hyporeflexive [9] and had seven-point lower scores, on average, on the psychomotor section of the Bayley Scales of Infant Development up to 24 months of age but had no detectable cognitive deficits at 5 years [10].

Overall, the results of these studies and others suggest that exposures to PCBs and dioxins that are only slightly higher than the average exposure in the general population may have a long-term impact on cognitive function in children. Although some studies also have pointed to an association between breast-milk levels and negative newborn neurologic scores, the breast-milk levels may represent markers for in utero exposure; these studies also indicate that breastfed infants did better than formula-fed infants regardless of the presence of PCBs and dioxins in the breast milk. The exact mechanism by which PCBs or dioxins may cause long-term cognitive impairment is unclear. The leading hypothesis points to the role of PCBs and some of the dioxins in disrupting normal thyroid function. The regulatory role of thyroid hormones on brain development has long been recognized [46]. Other factors, including incomplete development of the blood–brain barrier, lack of detoxification systems within the fetus, and the sensitivity of migratory cells undergoing mitosis, may play a role.

In a recent study conducted in the United States, prenatal exposure to DDT was associated with neurodevelopmental delays in early childhood [47]. The mothers were immigrants from Mexico and had substantially higher exposures than women born in the United States. Decreases in the Mental Development Index scores corresponding to 7 to 10 points across the exposure range were found. Breastfeeding was found to be beneficial even among highly exposed women.

Endocrine effects

Many POPs have developed notoriety for being "endocrine disruptors." The similarity of their structure to many hormones, including thyroid hormone, can, depending on the dose and congener, cause these chemicals to act as an agonist, partial agonist, or antagonist to a variety of endogenous hormones. Many organochlorine pesticides (including DDT, methoxychlor, and dicofol) have shown estrogen-like effects [11] or anti-androgen effects in animals [12]. Male children of mothers exposed to high doses of PCBs in Taiwan were found to have alterations of serum estradiol, serum testosterone, and follicle-stimulating hormone levels [13], as well as alterations in external genitalia [14]. In boys in the North Carolina PCB study, higher prenatal exposure to dicholorodiphenyldicholoroethylene (DDE), the DDT metabolite, was associated with greater height and weight at puberty [15]. Even as recently as 15 years ago, serum concentrations of DDE in humans were found at 100-fold greater levels than endogenous estradiol in premenopausal women and at about the same concentration as testosterone in men [16].

Thyroid hormone is essential for normal neurodevelopment of the fetus and young child. Various studies performed around the world have found alterations of thyroid hormones related to either in utero or childhood exposure to PCBs or dioxins [17,48,49]. Despite the variable effects of chemicals on thyroid-stimulating hormone, it seems that some of these compounds also may act on biologic systems that are not directly the result of thyroid hormone action (eg, through calcium signaling and increased reactive oxygen species) [18]. Additional studies in rats have demonstrated that PCBs can interfere with thyroid hormone signaling in the fetal brain by direct action on the fetus, absent changes in maternal thyroid status [19]. Recent studies have provided evidence that the effects of thyroid-disrupting chemicals are additive [20]. These findings in animal studies combined with the known influence of thyroid hormone on human neurocognitive development observed in epidemiologic studies have led to concerns about the effects of POPs on thyroid regulation and neurodevelopment in infants.

Two separate studies have demonstrated an association between DDE concentrations in maternal milk and shortened lactation time [50,51]. In developing nations longer duration of lactation is associated with increased infant survival. Although in some developing countries DDT has continued to be used in malaria control, a recent analysis suggests that the lives saved by DDT malaria control may be more than offset by infant deaths caused by reduced nutrition and increased diarrheal diseases attributable to the adverse effects of DDT on duration of lactation and increases in preterm birth [52].

Immune effects

Animal research has shown dioxin exposure to be associated with thymic atrophy, down-regulation of cytotoxic T- or B-lymphocyte differentiation, poorer antibody response, and reduced lymphocyte activation [21]. For the Taiwanese cohort exposed in utero, children were found to have a 25% decrease in IgA levels ($P < .01$), a 40% decrease in IgM levels ($P < .001$), and a 50% reduction in helper/suppressor T-cell ratio. A five- to six-fold increased risk of pneumonia/bronchitis and middle ear disease was reported in these children [22]. Similarly, a study of Inuit children revealed a significant association between elevated prenatal pesticide exposures to DDE and hexachlorobenzene and a higher incidence of otitis media in the first year of life (an approximately 50% increase) [23]. A significant negative association between serum dioxin levels and plasma IgG was still evident 20 years after exposure resulting from a large industrial accident in Seveso, Italy, with a nearly 25% difference in IgG levels between the highest and lowest exposed quartiles [24].

In the Dutch cohort described previously, prenatal PCB and dioxin exposure was found to be associated with changes in T lymphocytes [25]. A follow-up study in this group of children demonstrated that immune effects associated with prenatal PCB exposure (including higher number of lymphocytes and T-cell markers and lower mumps and measles antibodies) persist into childhood [26]. Further evidence for an alteration of immune function was seen in a study of Flemish children in whom there was a negative association between PCB levels and IgG, IgE, and allergic responses [27].

The mechanism for immunosuppression by POPs is poorly understood. Some hypotheses suggest that these molecules bind to the aryl hydrocarbon receptor and thereby alter the expression of genes involved in cell differentiation and proliferation of immune cells. In vitro studies also have suggested that dioxins and PCBs may alter thymus maturation and thymocyte differentiation [28].

Cancers

Many of the POPs are classified as possible or probable human carcinogens. Heptachlor epoxide, dieldrin, oxychlordane, and DDE have been associated with an 80% to 240% increase in risk of non-Hodgkin's lymphoma [29]. In the case of DDT, animal data suggest an increase in liver cancer, lung cancer, and lymphoma [30], and human studies report an association with non-Hodgkin's lymphoma (odds ratio, 4.5; 95% confidence interval, 1.7–12.0) [31]. Table 1 summarizes the cancer classifications in the California Safe Drinking Water and Toxic Enforcement Act of 1986, the most comprehensive authoritative list of carcinogens. PCBs have been classified as probable human carcinogens based on limited human data and significant animal data. In humans, studies of occupationally exposed electrical workers reveal an increased risk of malignant melanoma, biliary cancer, stomach cancer, and thyroid cancer. In the Taiwanese cohort exposed to PCB-contaminated rice oil, there was excess mortality from all types of malignancies, especially of the liver and lung [30].

Dioxin, specifically 2,3,7,8-TCDD, has the notoriety of being classified as a known human carcinogen based on both human and animal data. In animals, low-dose exposure to 2,3,7,8-TCDD and other dioxins causes cancer in several sites in multiple species. Four cohorts of occupationally exposed workers demonstrate that dioxins are a potent multisite carcinogen (including non-Hodgkin's lymphoma, soft tissue sarcoma, and respiratory cancers), similar to smoking and ionizing radiation [28].

Emerging persistent organic pollutants

The experiences from the mostly banned Stockholm POPs provide a framework for understanding the possible range of toxicities that POPs may have on human health. This experience also has emphasized the importance of prevention and global regulation. Several other emerging POPs have come to public attention. These newer POPs pose potential concerns, although they do not yet have strong epidemiologic data to support negative effects on human health. These concerns arise from their similarities, both structurally and functionally, to previous POPs combined with characteristic bioaccumulation, transplacental transfer, and transfer to breast milk. Although many human health risks are not yet proven, a precautionary approach can be helpful for minimizing human risk.

Polybrominated diphenyl ethers

(PBDEs) have been used for the past 30 years as flame retardants in plastics, wire insulation, electrical parts, printed circuit boards, polyurethane foam, and textiles (such as carpets and draperies). They are structurally similar to PCBs and seem to have a mode of action that also includes disruption of the thyroid hormone system [32]. Animal studies suggest the PBDEs, like PCBs, have effects on learning and behavior and that the neurobehavioral effects of PBDEs and PCBs may be additive [53]. In utero exposure to PBDEs in rats has resulted in delayed puberty and decreased ovarian follicles in females and in decreased circulating sex steroids and feminization of sexually dimorphic behavior in adult males [54]. At this time, there are only limited animal data and insufficient human data for carcinogenicity classification.

Like other POPs, the PBDEs resist degradation and are lipophilic, thus accumulating in fat. The half-lives of various congeners of PBDEs in humans vary from 1 week to 3 months. Until recently, an estimated 70,000 tons were produced each year, mostly as pentaBDE, octaBDE, and decaBDE, (named for the number of bromine atoms). Although increasing levels have been detected in aquatic sediment, public health concern was raised when these chemicals were detected in the Swedish breast milk–monitoring program in 1998 [55]. Comparison with archived breast milk samples detected a logarithmic increase in concentrations over a 20-year period, as depicted in Fig. 2. There has been evidence of a decline in breast milk levels of PBDEs (Fig. 2) in Sweden since efforts began to eliminate use there.

Ensuing studies in animals, food, and humans revealed a similar pattern of rapidly increasing levels worldwide [30]. The levels of PBDEs are estimated to be 10 to 40 times higher in North American populations than in Europeans [56].

The major routes of exposure to PBDEs seem to be dietary intake and direct indoor exposure to PBDEs in air and dust. Some studies have indicated that meat and fish currently may be a less important source of exposure than for PCBs [57]. Although originally there was little concern about decaBDE, because it is not as readily absorbed after oral intake, recent studies suggest that decaBDE is biologically available and can accumulate in predator species [58]. In addition, decaBDE may degrade in the environment to lower brominated forms that are more easily absorbable and more toxicologically active [59]. Perhaps 5% of the United States population (15 million people) carry body burdens of PBDEs associated with alterations of reproductive organs in rats and within an order of magnitude of those causing neurodevelopmental effects in mice [60]. Current exposures to inhabitants of the United States leave little margin of safety.

Nitromusks

Synthetic musks are a component of many fragrances including soaps, cosmetics, and detergents. Most industrial musk production consists of two major classes of compounds, monocyclic nitroaromatic musks (nitromusks) and polycyclic musks. Musk xylene and musk ketone belong to the nitromusk category of compounds. Production is estimated to be 2000 tons per year. The high lipophilicity and propensity to bioconcentrate have led to comparisons with PCBs and other POPs. These chemicals have been detected in surface water and fish [61]. Further, the presence of these substances in human milk and adipose tissue has attracted concern [62]. Half-life in the human body has been estimated at approximately 3 months [63]. Current opinion favors the hypothesis that most nitromusk exposure occurs through dermal application of musk-containing products [64].

Comprehensive toxicologic studies on long-term effects are lacking for this class of compounds. Some animal studies have shown evidence for neurologic and hepatic toxicity [65]. There also is evidence of increased rates of benign and malignant liver tumors in mice [62]. Although there is no evidence for genotoxicity, some studies have suggested that musk ketone may act as a comutagen. Additionally, musk ketone has been shown to be a potent inducer of cytochrome P-450 enzymes; musk xylene can either inhibit or induce these enzymes [66].

Many countries have taken action to limit production of nitromusks. Japan has banned their use, German industry has voluntarily halted production, and the United States forbids their use in products that may be ingested but allows their use in products for dermal application. Preliminary evidence suggests that there has been a decrease in human serum levels in Germany since the discontinuation of production in 1993 [67].

Lindane

Lindane (gamma-hexachlorocyclohexane) has been used since the 1940s throughout the world as a pesticide on crops and animals and as treatment for human head lice and scabies. Because of concerns about this chemical's persistence and bioaccumulation, potential carcinogenicity, and effects on the endocrine systems of animals, it has been banned or severely restricted in at least 85 countries. In the United States most agricultural uses have been eliminated. Extensive use in many countries persists and has resulted in contamination of products significant to children, such as milk and butter [68]. In the United States and elsewhere, its poor safety profile and marginal efficacy has resulted in lindane being considered of limited pharmaceutical usefulness. Currently the Food and Drug Administration provides cautions about the use of lindane in persons weighing less than 110 pounds because of potential neurotoxicity [69].

In 2002 California banned the use of pharmaceutical lindane. The Los Angeles Sanitation District reported that one application for head lice could contaminate 6 million gallons of waste water above acceptable limits for aquatic ecosystems. A public draft report from the Commission on Environmental Cooperation suggests there have been no reports of significant difficulties resulting from the California ban [70].

Perfluorooctanesulfonate and perfluorooctanoic acid

Perfluorooctanoic acid (PFOA) and perfluorooctanesulfonate (PFOS) are perfluorinated compounds that are used as synthetic surfactants in lubricants, paints, cosmetics, and fire-fighting foam, on water-repellent clothing, in food packaging, and in nonstick pans. They are stable in the environment, and some studies have shown no evident biodegradation and a half-life of 96 years. In studies in occupationally exposed workers, biologic half-life has been estimated at 4.4 years. Further, these chemicals now have been detected in blood sera of the general pediatric population [71]. In a study of blood concentrations of various chemicals around the world, the United States and Poland were found to have the highest levels of PFOS [72].

In animals, studies have shown decreased hematocrit and thyroid hormones associated with PFOA. PFOA seems to interfere with fatty acid metabolism and cholesterol synthesis [73]. Cancer bioassays have shown an increase in testicular, liver, and mammary tumors from PFOA exposure. At high doses in monkeys, PFOS has been associated with lower triiodothyronine and estradiol levels and with increased liver weight [74]. PFOS at high doses also has been associated consistently with lowered cholesterol and metabolic wasting in animals [75]. In contrast, human epidemiologic data have shown a positive association between PFOA levels and cholesterol, triglycerides, and triiodothyronine [76]. In studies of PFOS, there has been possible association with bladder cancer [77], malignant melanoma, and colonic tumors [78].

At this point, it is unclear whether current levels could be harmful to humans. The persistence and prolonged half-life of these substances may cause a gradual increase in background levels, however. Although in 2000 the largest producer of PFOA compounds voluntarily announced the intention to stop producing these chemicals, a different major chemical company quickly began producing them. In 2006 the US Environmental Protection Agency (EPA) announced the voluntary PFOA Stewardship Program that aims to elicit corporate commitments to reduce emissions and use of these chemicals by 95% by 2010 globally. At this time, it is unclear what exposures carry the highest risk. Some data have suggested that drinking water [79] and residential area [80] may play the largest role. Other research has pointed out that perfluorochemicals are used in small quantities in substances that come into contact with food, such as nonstick cookware coatings (PFOA) and paper coatings for moisture resistance (eg, microwave popcorn bags, pizza boxes, PFOS) [81]. The extent to which these chemicals are transferred to food and the impact of heat on this process is not yet clear.

Anticipatory guidance

In the United States, research has shown a significant decline in the body burden of dioxins and PCBs from 1972 to 1999; however, this decrease seems to have leveled off from 1999 to 2003 [82]. The decreases probably are attributable to bans on many of these substances. Exposure to most POPs occurs gradually over time without any overt symptoms. Because these substances are pervasive in the environment, highly persistent within the body, and lack any viable elimination options, the most important factor in minimizing adverse health effects is reduction of exposure. Although reducing exposure ideally involves removal of these chemicals from commerce, or regulation of their use, there is some role for measures to reduce individual exposure. Counseling patients, especially young women before childbearing age, on avoidance of potentially high sources of POPs exposures and allaying unnecessary fears about breastfeeding can promote good health habits across generations.

Diet

The EPA estimates that 90% of dioxin exposure occurs from diet. Foods that contain the highest concentrations of POPs include high-fat cuts of beef, bacon, frankfurters, full-fat cheeses, butter, and fatty fish (eg, farm-raised salmon) [83]. Within these same categories are foods with lower concentrations of these contaminants, including shrimp, lean ham, lean steak, cottage cheese, and margarine [36]. Other recommendations include using vegetable oils instead of animal fats, trimming the excess skin and fat from meat, and choosing lean cuts of meat. Also, washing vegetables and peeling root and waxy-coated vegetables is recommended [84]. Changing a mother's diet during pregnancy or lactation will not significantly reduce the levels of most POPs and resulting exposures to the fetus or infant, because the mother's contribution reflects her long-term exposure. Rather, efforts to counsel and educate individuals about a diet low in animal fats should begin in childhood, so that women enter their reproductive years with a minimal body burden of potentially fetotoxic substances.

Researchers have demonstrated an association between increasing half-life of dioxins and increasing age and adiposity. This finding suggests that the youngest children may be able to excrete these substances more readily. By adolescence, however, the stability of these substances within the body becomes prolonged. For this reason, institution of a diet that is relatively low in animal fat at a young age is helpful. Fatty fish, although a source of important nutrients, is also a significant source of POPs exposure. Therefore, cooking fish in a manner that allows juices to drain away and moderate consumption (one or two meals per week) of a variety of fish types is suggested.

Breastfeeding

Much public concern has arisen regarding the concentrations of POPs in breast milk and the effects on the neonate. Overall, the epidemiologic research has demonstrated the strongest adverse effects on cognitive function to be associated with prenatal concentrations of PCBs and dioxins in cord blood, rather than with concentrations in breast milk. Presently, there is no recommendation to reduce breastfeeding. In fact, the American Academy of Pediatrics recommends exclusive breastfeeding until the age of 6 months [38]. The benefits of breastfeeding to the infant, mother, and society are clear and positive and outweigh the potential risks posed by pollutant exposure. Although infant formula does not contain significant amounts of POPs, studies comparing formula-fed and breastfed infants consistently show that breastfed babies are healthier and have better neurologic functioning [85]. Additionally, it has been demonstrated that prolonged breastfeeding leads to progressively lower levels of PCBs and dioxins in breast milk; therefore, there does not seem to be a benefit to shortening the duration of breastfeeding [86].

Although breastfeeding is the general recommendation for the public, some subgroups may warrant further consideration. Women with occupational exposures to POPs or other related chemicals (eg, waste-incineration workers, cosmetics industry workers, electronics workers, farm workers) or people involved in a disaster incident may require biomonitoring and risk–benefit evaluation. Additionally, families who fish for subsistence or ethnic groups that consume large quantities of seafood may require more careful assessment. In unusual circumstances, the advice of state health department officials may be sought for specific regions in which high concentrations may be present in the environment.

Consumer products

In addition to dietary counseling, anticipatory guidance may include education about consumer products. Theoretically, bleached paper products (eg, coffee filters, tampons, diapers) may contain small amounts of dioxin. The reaction between chlorine and lignins in wood fiber can result in the formation of many chlorinated organic compounds including dioxin. The amounts are very small, however, especially compared with the magnitude of dietary exposures. Concerned consumers generally can find unbleached or chlorine-free paper products if they choose.

PBDEs may be present as an additive flame retardant in polyurethane-foam mattresses, cushions, and pillows as well as in draperies and carpet padding. Unlike reactive flame retardants, additive flame retardants are more likely to leach and volatilize into the environment. Additionally, there is a risk of PBDE volatilization from the plastic casing of computers, television sets, and other electronic devices. There are very few data on the magnitude of exposure to PBDE from these sources. The type of PBDE used as a flame retardant in polyurethane foam has been banned recently in several states and in the European Union. The EPA has come to a voluntary agreement with the major manufacturer of this product to phaseout production, so it is likely that newer mattresses, cushions, and pillows will be free of these chemicals. Many major corporations now report on their Web sites that they manufacture PBDE-free computers, televisions, monitors, electrical equipment, and mattresses.

Recent concern over the potential release of PFOS/PFOA from nonstick cookware and from food packaging has caused some alarm [75]. The health effects of low-level exposure from food cooked or stored in contact with these substances or from inhalation of material off-gassing during cooking are uncertain. PFOS also is used as a rain repellent in clothing, as a carpet spot cleaner, in fire-fighting foams, and as an artificial wax for some sporting equipment such as skis and snowboards. Because there is no centralized list of products that contain PFOS/PFOA, and because the exposures from existing sources have not been quantified, it remains difficult for physicians to give useful anticipatory guidance to patients at this time.

Nitromusk exposure can occur from a variety of consumer products in the United States. Although the use of nitromusks has been banned for products that may be ingested, they are still present in many cosmetics including laundry detergents, perfumes, air fresheners, hand creams, and soaps. Because these chemicals seem to penetrate the skin, dermal exposure is a concern. The precautionary principle suggests that it may be prudent to minimize the use of nitromusk-containing cosmetics in children and women of childbearing age. Unfortunately, nitromusk compounds are not specifically identified on product labels, which instead simply indicate the presence of "fragrance." Products that are unscented or that contain only natural fragrances are not likely to contain nitromusks.

The issue of POPs in consumer products affects individual patients and also the environment as a whole. These products can cause environmental contamination and possible health effects in future generations if the chemicals persist and bioaccumulate after disposal. Although there currently is no program for appropriate disposal of many products that contain newer POPs, some states have begun to collect electronic waste for recycling and proper disposal.

Laboratory testing

Laboratory testing for the presence of POPs in blood or breast milk in the general population is not generally recommended. Testing can be expensive and difficult to interpret. Most laboratories do not have standard procedures for these tests, and government laboratories may be required. For many POPs, laboratories do not have an established reference range, especially for media such as breast milk. In the setting of occupational exposures to chemicals, an occupational physician can arrange biomonitoring for specific chemicals or their metabolites. Overall, routine laboratory testing carries high expense and poor reliability and therefore is not a good screening method. The best method for reducing exposure to most POPs is prevention through timely patient education.

Summary

Diagnosis of elevated exposures to POPs can be difficult, and treatment options are limited or nonexistent. The optimal method for prevention involves international elimination of these chemicals. Efforts to counsel and educate individuals should begin in their childhood, so that good eating habits are established and women enter their reproductive years with a minimal body burden of potentially fetotoxic substances. Breast milk remains the healthiest and safest form of nutrition for newborn babies. Despite increasing regulatory efforts to curtail production of most POPs, they will continue to persist in the environment, ecosystem, and food supply for years to come.

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