BY ÉRIC DEWAILLY AND ANTHONY KNAP

Food from the Oceans and Human Health

Balancing Risks and Benefits

Figure 1. Seafood-consuming populations.

Figure 2. Inuits consuming traditional diet.

THE OCEANS provide great health benefits to humans, ranging from food and nutritional resources to recreational opportunities and new cures for human disease. At the same time, increasingly, food from the oceans is contaminated with man-made pollutants. Globally, over one billion people rely on fish and other seafood as their main source of animal proteins (Figure 1). Dependence on a seafood diet is usually higher in coastal than in inland areas, and many small island states depend on fish exclusively, particularly native peoples. Therefore, the choice for those people who regularly consume seafood is increasingly a balance between the nutritional vs. the detrimental aspects of seafood (see case study by Dewailly, this issue).

FISH-EATING POPULATIONS

Remote maritime populations are intimately connected to the oceanic environments that nourish their daily life and culture. They rely on the oceans as a source for nutrition and are among the highest fish-consuming nations (Figure 2). In the small developing island states of the Pacific and Indian Oceans and the Caribbean Sea, several countries have fish consumption of over 50 kg a year per capita, compared to 16 kg per year for the world average (Food and Agricultural Organization [FAO], 2005).

The consumption of large quantities of fish raises the issue of the potential exposure to harmful natural and anthropogenic contaminants in seafood (Knap et al., 2002). These toxicants in the aquatic food chain are threatening all fishing communities that still rely on seafood for their subsistence. For example, the highest body burdens of methyl mercury and persistent organic pollutants (POPs) have been found in the remote maritime populations in the northern and southern hemispheres (see Figure 3). Populations from the circumpolar regions also have serious issues of contaminated seafood (Arctic Monitoring and Assessment Programme [AMAP], 2004).

Numerous studies have reported high levels of methyl mercury in predator fishes, while POPs such as polychlorinated biphenyls (PCBs), dioxin, and chlorinated pesticides accumulate in fatty fishes and sea mammals. Of note, while mercury bioaccumulates in the aquatic food chain in both hemispheres, the higher concentrations of organic compounds are reported mostly in the northern hemisphere. All of these pollutants potentially threaten human health, particularly that of the developing human fetus and infant, since pollutants are passed through the mother transplacentally and via breast milk.

Recently, reports have shown that the highest human concentrations and related health effects are found in children living in the Arctic (Faeroe Islands, Canadian Arctic, Greenland) and in remote Canadian fishing populations (Dewailly et al., 1994; case study by Dewailly, this issue). Neurobehavioral and immunological disturbances have been associated with high prenatal exposure to these seafood-borne contaminants. More recently, these compounds have been found to possess endocrine properties, and have been associated in animals and humans with male fertility problems (AMAP, 2004).

Hair Mercury in the World (ppm)

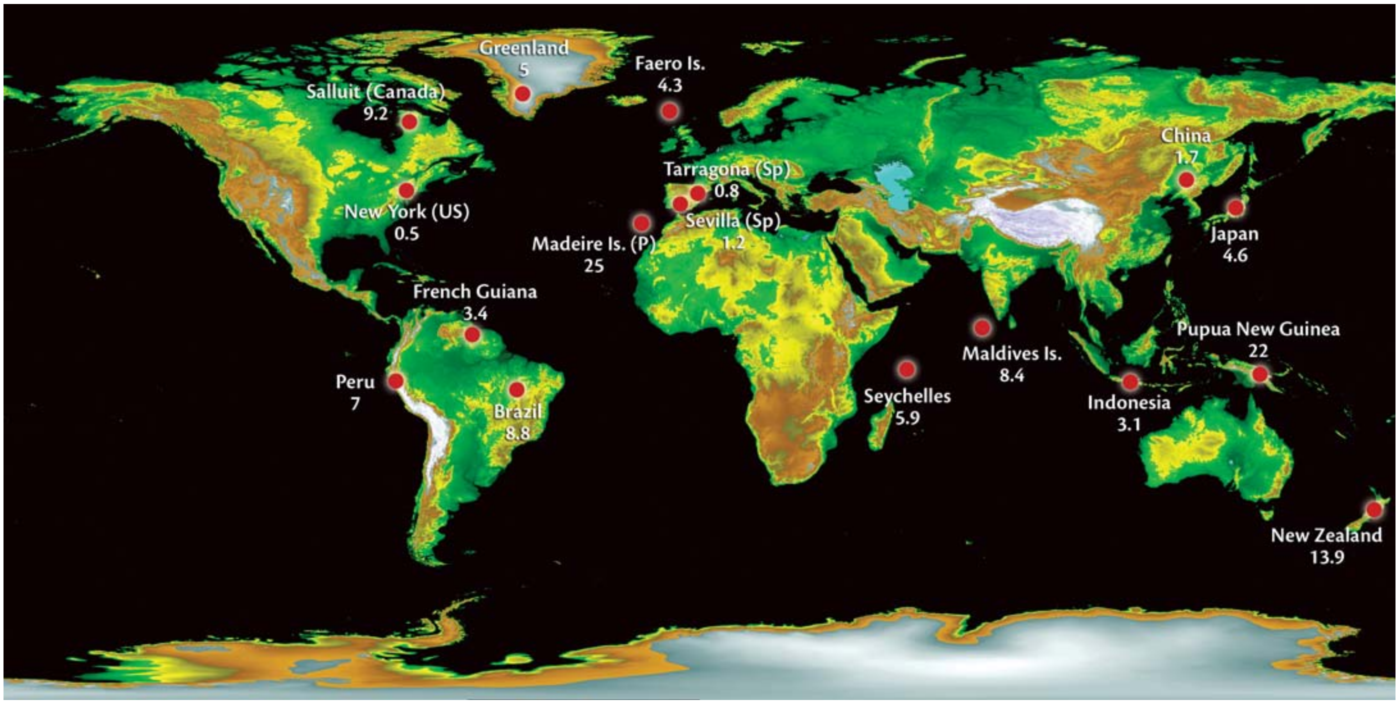

Figure 3. Hair mercury levels in the world. Background map from http://www.ngdc.noaa.gov/mgg/topo/globegal.html.

On a more positive note, these fish-eating populations also receive important nutrients through fish consumption. Maritime populations have a generally high intake of omega-3 fatty acids, the most important compounds being eicosapentanoic acid (EPA) and docosahexanoic acid (DHA). Omega-3s have been associated with a reduction of coronary heart diseases, increased pregnancy duration, and protection again inflammatory diseases, to name a few of the established benefits (Ruxton et al., 2004). In addition, fish is a very good source of selenium (Se), which as well as being an important antioxidant, has a role as possibly being antitoxic for mercury. Selenium is also extremely beneficial in the prevention of oxidative stress-related diseases, particularly for the prevention of prostate cancer (Rayman, 2000). Selenium is also reported to prevent cardiac diseases (Salonen et al., 1982).

GENERAL DEBATE ABOUT FISH CONSUMPTION

Balancing the risks and benefits of the consumption of seafood is an active debate not only for subsistence communities, but also for more urban populations. This subject is a global issue following recent reports on anthropogenic contaminants identified in salmon (Hites et al., 2004) and other commonly consumed species, and followed by reaction from nutritionists (Willett, 2005).

Several health organizations have recommended that the general population eat fish twice a week (Kris-Etherton et al., 2002; Harris, 2004). Fish consumption is also recognized as beneficial for brain development (Cunnane et al., 2000; Uauy et al., 2001) and protective against cardiovascular diseases (Harper et al., 2001; Bucher et al., 2002; He et al., 2004), mental disorders (Cunnane et al., 2000; Emsley et al., 2003; Casper, 2004), and various inflammatory conditions (such as bowel diseases, asthma, and arthritis) (Ruxton et al., 2004). Long-chain omega-3 polyunsaturated fatty acids are arguably the most important nutrients in fish.

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However, because fish flesh also contains persistent and bio-accumulative chemicals (such as PCBs, dioxins/furans [PCDD/Fs] and methyl mercury), at the same time fish advisories are regularly issued by various governmental agencies. One recent example is an advisory issued by the U.S. Food and Drug Administration (USFDA) informing women of reproductive age to avoid the consumption of four species of fish that are highly contaminated by methyl mercury (i.e., king mackerel, shark, swordfish and tilefish) (USDHH/USEPA, 2004). The USFDA thus recommends for pregnant women a weekly consumption of up to 12 oz (360 g) of varieties of other fish species with more optimal nutrient to contaminant ratios.

RISKS RELATED TO SEAFOOD CONTAMINANTS

As discussed earlier, seafood-borne substances of particular concern are the heavy metals and POPs (such as PCBs, chlorinated dioxins, and some industrial solvents). Pesticides and herbicides also pose potential hazards to human health; some synthetic organic chemicals have been linked to possible endocrine-disrupting functions. Herbicide and pesticide exposures seen in wildlife, including marine and freshwater organisms, may be linked with reproductive and developmental problems seen in humans (Heindel and Levin, 2005).

Human exposure to synthetic organics occurs primarily from eating contaminated foods. A large number of studies (AMAP, 2004) related to consumption of contaminated foods have been performed in remote fishing communities in the Arctic, because these lipophilic contaminants are transported by the atmosphere, deposited in the land and water, ingested by wildlife, and biomagnified up the marine food web, ultimately being consumed by humans living in these regions. Unfortunately, because the "environmental soup" has many different contaminants, relating a deleterious effect in specific marine organisms to the action of a specific compound is very difficult. However, studies suggest that the PCBs have a variety of adverse health effects on human reproduction, neurobehavioral development, liver function, birth weight, immune response, and tumorigenesis. Studies in Arctic populations have linked fetal cord blood PCB concentrations with low birth weight, small head circumference, and immunosuppression (AMAP, 2004).

Most epidemiological and experimental studies on health effects related to heavy metals (Pb, Hg) and POP exposure (mainly PCBs) suggest that prenatal life is the most susceptible period for induction of adverse effects on physical and neurological development. Indeed, several studies have reported different developmental, immune, and/or cognitive deficits in newborns exposed to POPs during prenatal and/or postnatal development, with some of these deficits persisting into later childhood.

Other organic contaminants are also of concern. For example, human exposure to dioxins is a concern for public health. The commonly used pesticide, dichlorodiphenyltrichloroethane (DDT), was banned in the United States and Europe in 1972, but it is still being used in tropical and subtropical countries for malaria control. The International Agency for Research on Cancer (IARC) considers DDT to be *possibly* carcinogenic. DDT is regarded as an "estrogen mimic," and dichlorodiphenyldichloroethylene (DDE) is an androgen receptor antagonist. Subacute levels of exposure show effects on the central nervous system of humans.

Although we have much information on the transfer of organochlorine residues through the marine food web, our knowledge of the transfer of these substances to humans through this pathway has been limited to a few classes of contaminants. However, evidence suggests that the organochlorine pesticide dieldrin (the epoxide of aldrin) affects the central nervous system and liver in humans. Generally, how to discern specific compounds and their effects in a large pool of contaminants present in the ocean environment is unclear.

NEW ORGANIC CONTAMINANTS

New formulations of synthetic chemicals enter the environment continually and end up in the ocean. Notably, several new compounds have emerged as potential concerns to the oceans and humans. Organobromine compounds are among these more recent contaminants, including brominated flame retardants (BFR) such as brominated diphenyl ethers (BDEs), commonly added in the composition of electronic equipment, plastics, and textiles. BDEs share some physico-chemical and toxicological properties with the organochlorines. However, while the production, sale, and use of the organochlorines have generally decreased, the use and environmental and human occurrence of the BDEs have dramatically increased since the

CASE STUDY

Canadian Inuit and the Arctic Dilemma

BY ÉRIC DEWAILLY

THE SITUATION

Human exposure to anthropogenic contaminants is now a well-known phenomenon in the Canadian Arctic. Early work conducted on Baffin Island and in Nunavik has demonstrated that because of their traditional dietary habits (Dewailly et al., 1989; Dewailly et al., 1993; Kinloch et al., 1992; Muckle et al., 2001), Inuit populations are exposed to environmental contaminants by eating their traditional foods, and their infants are exposed through transplacental and breast milk transmission from the Inuit mother (Figures 1 and 2).

The two main groups of contaminants that may affect human health are the heavy metals (e.g., mercury), and the persistent organic pollutants (POPs) (e.g., polychlorinated biphenyls [PCBs], DDT, and other pesticides). POPs form a class of persistent organic pollutants including polychlorinated dibenzo *p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), PCBs, and various chlorinated pesticides or industrial products. A new generation of POPs has recently been found in the Arctic food chain. These new chemicals include the brominated flame retardants, in particular polybrominated diphenyl ethers (PBDEs), and the perfluorinated alkane compounds (PFAs). These new POPs were first measured in freshwater and marine organisms, then subsequently in Inuit foods. Furthermore, there is also concern because the levels of all these substances are increasing. The high lipophilicity and resistance to biodegradation of POPs allow their bioconcentration and prolonged storage in the fatty tissues of animals. As the Inuit diet is comprised of large amounts of tissues from marine mammals, fish, and terrestrial wild game, the Inuits are more exposed to food chain contaminants than human populations living in temperate regions.

Figure 1. Inuit capturing a seal.

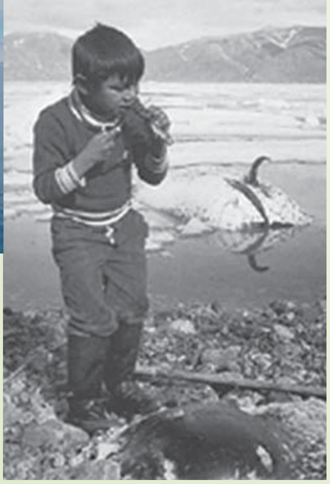

Figure 2. Inuit boy eating traditional diet.

EPIDEMIOLOGIC STUDIES

Various studies have been conducted in Nunavik (northern Québec) over the past decade on the characterization of exposure of Inuit populations. Moreover, biological markers were also validated to detect and evaluate early biological changes that could result in altered immune and nervous system function, oxidative stress, and in subsequent chronic diseases. Most of these studies have focused on maternal and cord-blood analyses because of the susceptibility of the fetus to contaminant exposures.

In Nunavik, an epidemiological study conducted from 1989–1991 investigated whether organochlorine exposure was associated with the incidence of infectious diseases and immune dysfunction in Inuit infants (Dewailly et al., 2000b). The number of infectious-disease episodes during the first year of life of 98 breast-fed and 73 bottle-fed infants was determined. Concentrations of POPs were measured in early breast-milk samples and used as surrogates for the prenatal exposure levels. Otitis media (middle-ear infection) was the most frequent disease, with 80 percent of breast-fed and 81 percent of bottle-fed infants experiencing at least one episode during the first year of life. However, the risk of otitis media was significantly increased with a history of prenatal exposure to dichlorodiphenyldichloroethylene (DDE), hexachlorobenzene (HCB), and dieldrin. The relative risk for the 4- to 7-month-old infants most exposed to DDE was twice that of the less exposed infants. Furthermore, the relative risk of *recurrent* otitis media (i.e., three or more episodes) increased with prenatal exposure to these compounds. Therefore, prenatal and breast-milk exposures to the POPs was associated with an increased risk for infection in this Inuit population.

A second study investigated the effect of prenatal exposure to PCBs and DDE on the incidence of acute infections in Inuit infants. The medical charts of a cohort of 199 Inuit infants during their first 12 months of life were reviewed, and the incidence rates of upper and lower respiratory tract infections, otitis media, and gastrointestinal infections evaluated. Maternal blood plasma during delivery and infant blood plasma at seven months of age were sampled and assayed for PCBs and DDE. Compared to the rates for the less exposed, the infants whose mothers had the highest levels of PCBs and DDE at their birth had generally a 30 percent excess of infections during their first six months of life. These results demonstrated a possible association between prenatal exposure to organochlorines and acute infections early in life in this Inuit population, and supported previous findings (Dallaire et al., 2004)

RISK MANAGEMENT

Taking action to modify life-style habits and diets in order to reduce environmental exposure to POPs and heavy metals must be done carefully, taking into consideration not only the risks associated with diets including fish, seafood, and sea mammal meals (i.e., exposure to contaminants), but also the benefits of such diets and the benefits of breast feeding.

Although the contaminants found in Inuit foods (especially those from the aquatic food chain) may pose a public-health risk, dietary studies conducted recently have shown that these traditional foods are important sources of nutrients such as protein, vitamins, minerals, and omega-3 fatty acids (EPA and DHA) (Blanchet et al., 2000). For example, high exposure to omega-3 fatty acids during prenatal life increases birth weight and visual acuity of newborns. Inuit people, in particular, have very high levels of omega-3 fatty acids in their blood due to their high consumption of fish and marine mammal meals. These substances are transmitted to the fetus during pregnancy and have a direct effect on the weight of the newborn and on beneficially prolonging the gestational time. Furthermore, the Inuit diet, which is rich in fish and marine mammals, has been linked to a lower incidence of thrombotic disease; this beneficial effect can be attributed to the high omega-3 fatty-acid intake obtained from seafood consumption. A recent study conducted by our team among the Inuit of Nunavik showed that their high plasma concentrations of omega-3 fatty acids protect them against some cardiovascular risk factors (Dewailly et al., 2001b).

Selenium (Se) is another essential nutrient found in sea products. This element is an antioxidant, as well as a micronutrient that regulates the action and/or enters in the composition of several essential enzymes. Furthermore, Se interacts with mercury in an antagonistic way; hence, it exerts a protective effect with regards to mercury-induced toxicity (AMAP, 2004). In addition, it is currently believed that Se has a role of antioxidant in the prevention of atherosclerotic diseases and prostate cancer (Dewailly et al., 2003).

Figure 3. Inuits shopping for western diet.

Of note, changes in lifestyle and dietary patterns have been observed among Inuit populations during the last decades. Because of rapid societal transitions, a shift away from traditional lifestyle and diet has been observed in these populations (Bjerregaard and Curits, 2002; Kuhnlein and Receveur, 1996). Traditional food use is declining rapidly, although not uniformly across the Arctic. For most circumpolar regions, dietary intake from store-bought foods now exceeds those from traditional foods (Figure 3). As a result, in Greenland, Alaska, and Canada, ischemic heart disease and diabetes are on the increase among native populations (Young et al., 1993). Thus, while there is clearly a need to reduce the exposure of Inuits to POPs and heavy metals, there is, at the same time, a need for preventive action to ensure that the levels of protective factors in their diet are not diminished.

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1980s (Meironyte et al., 1999, Noren and Meironyte, 2000; Ikonomou et al., 2002) (Figure 4). Only a few studies have addressed the toxic effects of the BDEs, but their structural similarity to other polyhalogenated aromatic hydrocarbons and laboratory evidence suggest that they may exert similar toxic effects through common mechanisms with PCBs, PCDDs, and some other organochlorines (i.e., embryotoxicity, interference with thyroid hormone signalling, neurotoxic effects, etc.) (Darnerud et al., 2001; Zhou et al., 2002).

Some halogenated phenolic compounds (HPCs) are also considered emerging contaminants. Unfortunately, they have not been routinely measured with the conventional suite of POPs and heavy metals in global or regional contaminant monitoring studies. These HPCs include the hydroxylated metabolites of PCBs (OH-PCBs) and halogenated phenols (such as pentachlorophenol [PCP]). These HPCs have been found in humans (such as the Canadian Inuits), as well as in seafood samples from the lower north shore of the St. Lawrence River and Quebec City (Sandau et al., 2000; Sandau et al., 2002).

Perfluorooctanesulfonate (PFOS) and related compounds are other emerging contaminants that require monitoring in the ocean food web. These chemicals have been produced commercially for over 40 years. PFOS is very stable, repels water and oil, and was largely used as a stain repellent ("ScotchGuard"). Kannan et al. (2001) have reported widespread occurrence of PFOS in marine mammals from the Mediterranean and Baltic Seas. PFOS have also been detected in marine mammals from the North American Great Lakes (Kannan et al., 2005). Endocrine effects (decreased estradiol and T3 serum levels) have been observed in sub-chronic toxicity experiments in monkeys (Seacat et al., 2002). However, human exposure to these compounds in the northern regions is scarce, and therefore, dietary exposure to PFOS and related compounds in the Inuit population, as well as potential toxic effects in these populations, remain to be addressed.

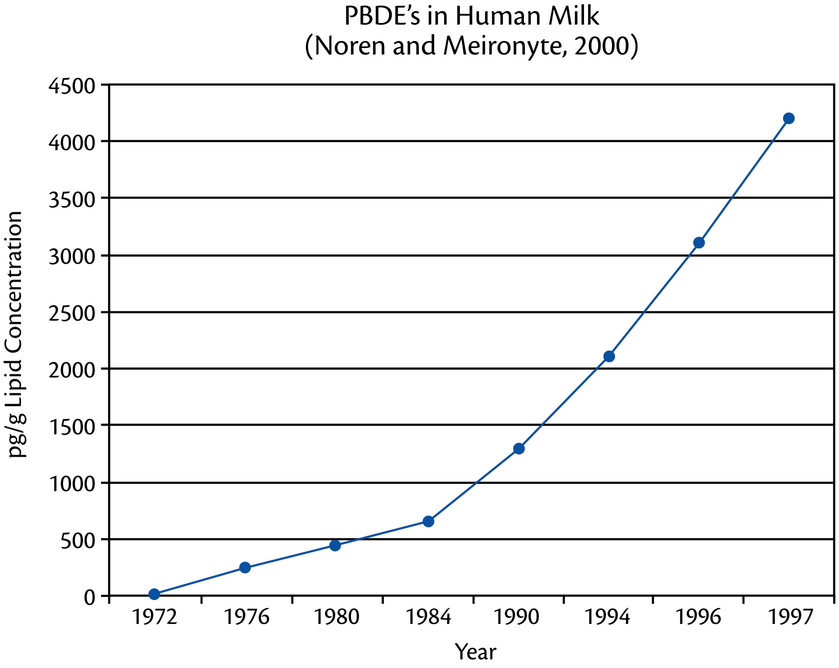

Figure 4 . PBDE's in human milk (Noren and Meironyte, 2000).

METALS

The metals group is composed of all metals and metalloids in the marine environment. It is important to distinguish between the introduction of metals from anthropogenic activities, and those from natural weathering processes. Although the sources of metals in the marine environment are numerous and diverse (e.g., elevated metal levels accompany almost every type of effluent), little evidence of widespread adverse biologic effects exists other than the risks to human health posed by metals in seafood. For example, a human pathway of metal contamination in people from direct seawater contact (even in the immediate vicinity of point sources) is very unlikely, due in most cases to the rapid removal of metals in solution by adsorption to suspended particulate materials.

Tributyl-tin (used as a constituent in anti-fouling paints on boats) and methyl mercury (formed by the microbial methylation of mercury) are two highly toxic compounds that have been responsible for well-recorded marine-pollution incidents. The basis of bioaccumulation and toxicity for these substances lies in their forms of speciation. Thus, special attention may be required to identify specific forms of other metals in the future.

Mercury is used in a wide range of industrial processes and mining practices. Once it is released into anoxic environments, bacteria can rapidly methylate this metal. Methyl mercury is highly lipophilic, and is biomagnified in the environment. Its half-life is 60–120 days in humans, and up to two years in fish. Methyl mercury causes cytotoxic, kidney, and brain damage, with concentrations of 1–2 mg/kg in brain tissue producing neurotoxic effects. Fetal and infant exposure to methyl mercury is of great concern via transplacental and/or breast-milk exposure.

Humans who consume seafood have the highest concentrations of methyl mercury in their tissues. The average concentrations of methyl mercury in human hair of persons eating 10–20 g/day of fish are less than 1 ppm, whereas those individuals deemed poisoned by methyl mercury in Japan and Iraq had methyl mercury concentrations of 50–100 ppm. Environmentally chronic exposures have occurred worldwide in populations dependent on fishing, including Amazonia, coastal Peru (Marsh et al., 1995), Seychelles (Davidson et al., 1998), Faroe Islands (Grandjean et al., 1997), the Arctic (Dewailly, 2001a), and New Zealand (Kjellstrom et al., 1986).

Cadmium can also bioaccumulate in the environment, including the ocean environment. The IARC has labeled cadmium as a Group I carcinogen (known human carcinogen). The major health risk associated with cadmium is nephrotoxicity (i.e., proteinuria and renal failure), however, the pathway from fish to people is not known, and most human contamination from cadmium tends be caused by tobacco smoking (Rey et al., 1997).

Like cadmium, environmental exposures but no cases of lead poisoning related to a marine source have been documented. The use of leaded gasoline in the developed world has decreased, but remains an issue in less-developed areas of the world. Arsenic is also a highly toxic metal, but, as with lead and cadmium, no known arsenic poisonings have occurred as a result of marine exposures or consumption of seafood. Both arsenic and lead occur in marine sediments as a result of industrial discharge. Like mercury, arsenic can be converted to more lipophilic and toxic methyl forms. Although the effects of these metals on marine ecologic health are known, the specific mechanisms of transfer to humans require more attention in the future.

UNCERTAINTY

Specific clinical effects related to contaminants have been the subject of numerous epidemiologic studies. In general populations exposed to low doses, only subtle effects are expected to occur. For lead and cadmium, epidemiologic studies and animal experiments have provided sufficient data to set thresholds for human exposure. For example, the general consensus is that 10 μg/dL is the maximum blood lead concentration acceptable for children. In this case, measuring blood lead in a group of children is a relatively easy, inexpensive, valid, and manageable biomarker to assess both exposure and risk in children. It should be re-emphasized that eating contaminated seafood has not yet been linked to human exposure.

However, for most ocean-related contaminants (such as methyl mercury and the persistent organic pollutants), the results from epidemiologic studies are more contradictory. Cohort studies in Michigan (Jacobson and Jacobson, 1996) and North Carolina (Rogan et al., 1986) have provided conflicting results on neurobehavioral changes in children who were exposed prenatally to PCBs through their mother's consumption of PCB-contaminated fish. Conflicting results were also reported on neurologic impairments in children who were exposed to methyl mercury during fetal development; a study in the Seychelles did not report any deleterious effects (Davidson et al., 1998), whereas a cohort study in the Faroe Islands found significant neurotoxic effects (Grandjean et al., 1997). There may be many reasons for these discrepancies, including differences in metal measurement methods, pollutant exposure mixtures, nutritional interactions, and genetic susceptibility of the particular populations.

Unfortunately, appropriately large epidemiologic studies are extremely expensive to perform in terms of both time and resources, and require large multidisciplinary scientific groups. In addition, new xenobiotics or metabolites are regularly identified by analytical chemists, and health officials may not be able to react in a timely manner. Multichemical interactions of ecologically relevant mixtures (at relevant concentrations in seafood) can have an effect different from the sum of the effects of each individual component of the mixture. Seafood contains a mixture of contaminants that may differ from those found in other parts of the world. How important these differences are is not known. Effects of mixtures need to be better understood. The possibility that nutrients present in seafood could modify or counteract the toxicity of contaminants is highly probable and specific to fish-eating populations. These interactions need to be better understood.

CONCLUSIONS

Globally, the diet of the world's maritime populations makes them particularly sensitive to seafood contamination. Therefore, monitoring these populations will provide the best early warning of pollution in the marine environment. Indicators for environmental and human health surveillance have recently been proposed (Dewailly et al., 2000a; Knap et al., 2002; De Guise et al., 2001).

Given the potential health hazards related to these environmental contaminants, worldwide agreements have been established to decrease the occurrence of these substances in the environment, and therefore decrease human and wildlife exposure (e.g., the Stockholm Convention, and the POPs and Heavy Metals Protocols of the UN/ECE Long-Range Transboundary Air Pollution Convention). Included in these Conventions are measures aimed at assessing current exposure levels in human populations and deriving the spatial and temporal trends for these environmental contaminants. These data are needed in order to follow and understand the behavior of these contaminants in the environment, to evaluate the efficiency of intervention programs, and to undertake appropriate actions to efficiently decrease potentially hazardous human exposures (e.g., recommendations on dietary habits). With seafood ingestion as a major pathway of contaminants to people, and the related health effects, especially in the young, it is important to expand these conventions well beyond the oceans.

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