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The Importance of Diet on Exposure and Effects of Persistent Organic Pollutants on Human Health in the Arctic

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Abstract

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Aim: To describe the importance of diet on exposure and possible health effects of persistent organic pollutants (POPs) in the Arctic. *Methods:* The study is based on a literature review. *Results:* Minor decreases in POPs and minor increases in Hg levels in Arctic populations in Greenland, Eastern Russia, Western Alaska and Eastern Canada are likely to occur by 2010 and major decreases in both POPs and Hg levels in these same populations by 2030. Levels of POPs and metals in populations in the Faeroe Islands and the Scandinavian countries are already reasonably low and are only likely to decline marginally by 2030. Estimates of effects are difficult based on current knowledge, but the combination of improved methodology and selection of risk groups will be a good step further in the process. Any strategies based on traditional food substitution should ensure that the value of the dietary components is sustained. *Conclusions:* In order to improve our understanding of health effects associated with contaminant exposure in the Arctic, we recommend that circumpolar epidemiological studies should be implemented on a larger scale. MeHg and POPs related effects are still the key issues. However, the role of newly discovered contaminants, like PBDEs and PCNs, should be investigated. For exposure assessment, epidemiological studies should consider mixtures and nutritional interactions. Epidemiological studies on nutritional benefits of

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traditional foods should be incorporated in risk assessment profiles. There is a need for a more nuanced view on human dietary exposure to xenobiotics. Risk should not be evaluated alone, but seen in relation to benefits from specific diets. It is essential that countries ratify and implement multinational environmental agreements.

KEYWORDS: diet, contaminants, effects, human, Arctic

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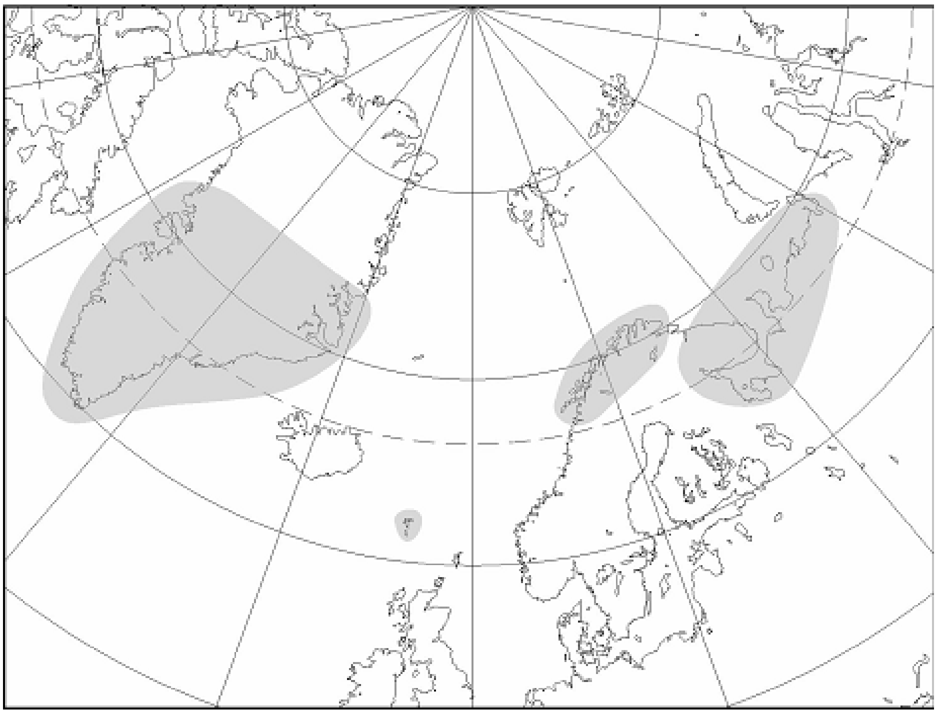
1. Introduction and Objectives

A comprehensive assessment of the contaminant situation in Arctic areas has been provided by the Arctic Monitoring and Assessment Programme (AMAP, 1998). The high levels of organic contaminants in the Arctic have caused serious concern regarding the health effects of indigenous populations in Greenland and Canada. Recent data indicate development of a similar situation in the Barents Region, especially the Russian Arctic. The exposure to pollutants through diet is of central concern and today food safety is essential in daily life in developed countries. However, the consumer‘s trust varies according to his country‘s regulatory systems and public opinion, often influenced by the persuasive power of the media. The objectives of this study are to describe the importance of diet on different exposures and possible health effects of persistent organic pollutants (POPs), based on a literature review. The report discusses recent information to prepare the basis for recommendations and dietary advice in the years to come. The study focuses on the coastal population in the European Arctic, the study areas are shown in Figure 1.

Fig. 1. Geographical areas of the study. Scale 1:20 000 000.



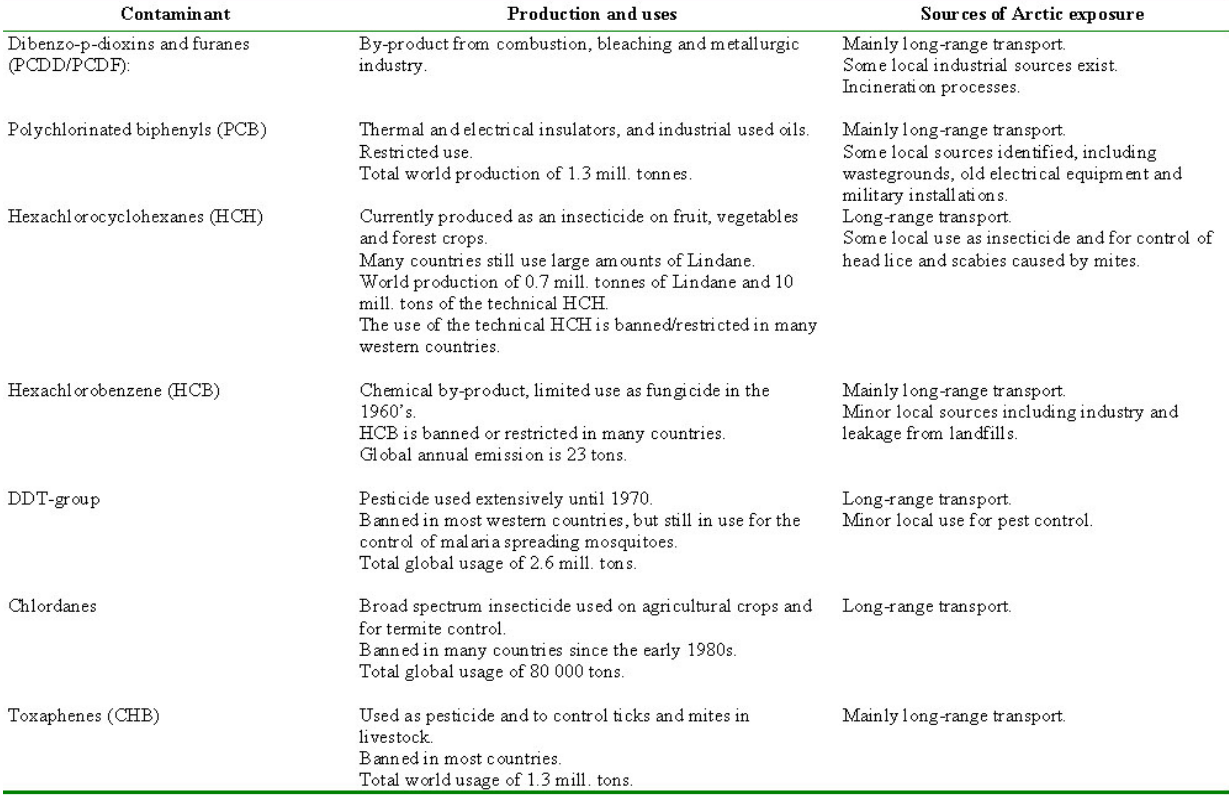
2. Relevant POPs in Euroarctic Coastal Populations

Most research and ongoing monitoring work on persistent toxic substances in the Arctic has focused on industrial compounds and by-products (e.g., PCBs and dioxins), pesticides (e.g., Lindane, DDT-group and cyclodiene analogues), as well as heavy metals (e.g., mercury, lead and cadmium) (AMAP, 1998; Jensen *et al.,* 1997; Hansen *et al.,* 1996; Lønne *et al.,* 1997). This fact is also reflected by the United Nations Environment Programme (UNEP) facilitated treaty on Persistent Organic Pollutants (POPs) (1999). However, during the last few years there has been an increased interest in "new" toxic substances and metabolites.

The group of "new" environmental toxins include a number of organic compounds and compound classes. Some of the more persistent polar pesticides currently in use belong to this group. Other examples are nitro- and aromatic musk and their metabolites from personal care products. Among the industrial chemicals and by-products, phthalates, octachlorostyrene (OCS), polychlorinated naphthalenes (PCN), polybrominated diphenyl ethers (PBDE), polychlorinated paraffins (PCA) as well as perfluoroorganic compounds (e.g., perfluorooctane sulfonate - PFOS) are found. Especially the three latter groups have recently received attention. The synthetic musks, phthalates and the new generation pesticides are, due to their distribution and accumulation pattern, generally not considered as a particular problem in the Arctic. None of these "new" compounds are on the UNEP list of most unwanted POPs.

Long-range transport by air and water from Central Europe and the USA allows many POPs to reach remote areas such as the Arctic, where only a few local sources for these contaminants exist. Depending on geographic location, weather conditions and the physical-chemical properties of the contaminant, transport to and within the northern regions can be carried out via the atmosphere, water currents, sea-ice drift and the great Arctic rivers (AMAP, 1998; Burkow & Kallenborn, 2002). Due to their persistency and high lipophilicity several of these compounds tend to bioaccumulate, presenting a possible risk for humans living on lipid-rich marine food. Among the many thousands of man-made bulk-chemicals in use today, only a limited number have been tested or evaluated for their hazard potential. In understanding the possible consequences for human health and the Arctic environment extensive evaluation is needed. The fact that the consequences are often only observed years to decades after emission to the environment should always be borne in mind. For example, perinatal dioxin exposure in The Netherlands was associated with premature neurodevelopment in children at the age of 2 ½ years (Ilsen *et al.,* 1996) and lung function deficit at the age of 7-12 years (ten Tusscher *et al.,* 2001). Perinatal exposure to PCBs and mercury was associated with respectively neurobehavioural and cognitive deficits in 7 year old children (Grandjean *et al.,* 1997; Grandjean *et al.,* 2001), and reduced sperm motility in Swedish men was associated with PCB exposure (Richthoff *et al.,* 2003). Evaluation criteria must include long-range transport ability, persistence, bioaccumulation potential and hazard for human health and the environment. A comprehensive overview of relevant contaminants in Euroarctic populations is discussed in the second AMAP Report (AMAP, 2003; Van Oostdam & Tremblay, 2003; Deutch, 2003; Dewailly & Weihe, 2003). An overview of production, uses and sources of exposure to some of the major persistent organic pollutants is shown in Table 1, and toxicological characteristics of selected persistent organic pollutants are presented in Table 2.

Table 1. Production, uses and sources of exposure to some of the major persistent organic pollutants.



Contaminant	Production and uses	Sources of Arctic exposure
Dibenzo-p-dioxins and furanes (PCDD/PCDF):	By-product from combustion, bleaching and metallurgic industry.	Mainly long-range transport. Some local industrial sources exist. Incineration processes.
Polychlorinated biphenyls (PCB)	Thermal and electrical insulators, and industrial used oils. Restricted use. Total world production of 1.3 mill. tonnes.	Mainly long-range transport. Some local sources identified, including wastegrounds, old electrical equipment and military installations.
Hexachlorocyclohexanes (HCH)	Currently produced as an insecticide on fruit, vegetables and forest crops. Many countries still use large amounts of Lindane. World production of 0.7 mill. tonnes of Lindane and 10 mill. tons of the technical HCH. The use of the technical HCH is banned/restricted in many western countries.	Long-range transport. Some local use as insecticide and for control of head lice and scabies caused by mites.
Hexachlorobenzene (HCB)	Chemical by-product, limited use as fungicide in the 1960's. HCB is banned or restricted in many countries. Global annual emission is 23 tons.	Mainly long-range transport. Minor local sources including industry and leakage from landfills.
DDT-group	Pesticide used extensively until 1970. Banned in most western countries, but still in use for the control of malaria spreading mosquitoes. Total global usage of 2.6 mill. tons.	Long-range transport. Minor local use for pest control.
Chlordanes	Broad spectrum insecticide used on agricultural crops and for termite control. Banned in many countries since the early 1980s. Total global usage of 80 000 tons.	Long-range transport.
Toxaphenes (CHB)	Used as pesticide and to control ticks and mites in livestock. Banned in most countries. Total world usage of 1.3 mill. tons.	Mainly long-range transport.

Table 2. Toxicological characteristics of selected persistent organic pollutants.*

Contaminant	Acute oral lethality (LD_{50} rats, mg/kg bw)	Teratogenity	Hormonal effect (relative to estradiol)	Human carcino-genity	Tolerable daily intake (WHO; µg/kg body weight)
Dibenzo-*p*-dioxins and furanes (PCDD/PCDF): 2,3,7,8-TCDD	0.013-0.043	+	-	+	10 (pg/kg bw)
Polychlorinated biphenyls (PCB): Aroclor 1260	1300	0	+	Possible	1.0
Hexachlorocyclohexanes (HCH)	88 (γ)	0 (γ)		Possible	0.3 (total)
Hexachlorobenzene (HCB)		0	+	Probable	
DDT-group: DDT	113	0	++(o,p)	Possible	20
DDE	880	0	0 (o,p /p/p)	Possible	20
Chlordanes	335-430	0	+	Probable	0.05 (total)
Toxaphenes (CHB)	80-90	+/0		Possible	0.2

*Adapted from Arctic Monitoring and Assessment Programme (AMAP, 1998)

3. Levels and Trends of POPs in Humans in Arctic Coastal Populations

The most recent levels of POP concentrations in human plasma and breast milk sampled in Euroarctic areas are shown in Table 3. It is difficult to assess human exposure to POPs. Several studies have measured environmental toxins in human fat or milk, both matrices useful indicators for long time exposure. For practical reasons human blood plasma can be used, and plasma is the preferred matrix for pesticides with short half-lifes. Examination of environmental contaminants in maternal samples from the arctic regions of the eight circumpolar countries has confirmed that the plasma levels of certain POPs and Hg are generally higher in the samples of arctic peoples who consume traditional foods (e.g., the Inuit of Greenland and of arctic Canada) (Van Oostdam & Tremblay, 2003; Deutch, 2003). For Greenland Inuit in particular, the levels of PCBs, HCB and total chlordanes are higher than those in maternal samples from Canada and other circumpolar countries, and likely reflect the higher consumption of these traditional foods. Since the lipophilic POPs freely pass the placenta, the developing fetus is exposed to the same contaminants as the mother and the POP levels in cord blood are practically identical with maternal blood levels (on lipid adjusted basis) (Deutch & Hansen, 1999). Consequently POP blood levels in young women is a good indicator of the exposure of future babies.

Other key findings include higher levels of total DDT in a non-indigenous population from Arkhangelsk, Russia, than in any other region, indicating a possible use of this pesticide locally or in Russian agricultural regions from which food is transported to the Arkhangelsk region. For â-HCH the highest levels were also seen in arctic Russia among the non-indigenous peoples (Van Oostdam & Tremblay, 2003).

There are few arctic populations for which more than one or two sequential data sets are available, so it is difficult to assess any time trends for the environmental contaminants of concern. Most environmental monitoring in the Arctic has taken place only over the last five to ten years, and this has enabled a much better assessment of the spatial variation in contaminant levels but may be too short a time span to detect any time trends.

Table 3. Levels of different persistent organic pollutants in plasma of younger women, pregnant or nonpregnant. Wet weight ug/L geometric means/ medians and range (AMAP, 1998; Ilsen *et al.*, 1996).

	PCB Arol260	β HCH	Chlordane	DDT	HCB	Toxaphene
Inuit, Northeast Greenland n=90	72 (2-263)	0.5 (0.01-2)	6.7 (0.3-24)	12.5 (0.4-43)	1.5 (0.1-5)	1.5 (0.1-7)
Inuit Southwest Greenland n=270	18.4 (3-95)	0.2 (0.03-0.8)	2.1 (0.05-19)	4.9 80.5-31)	0.9 (0.1-7)	0.8 (nd-4.7)
Faroe Islands n=148	14.9 (1-129)	0.1 (0.05-0.6)	0.5 (0.05-5.5)	3.6 (0.3-39)	0.3 (0.05-2)	0.4 (0.06-3.5)
Norway, Vestvågøy n=50	6.6 (2-17)	0.05 (0.02-0.4)	0.15 (0.06-0.4)	1.0 (0.2-5)	-	-
Sweden Kiruna n=40	6.1 (2.7-15)	0.09 (0.02-0.3)	0.06 (0.02-0.2)	0.8 (0.3-5.5)	0.2 (0.1-0.3)	-
Finland , Lapland n=13	3.8 (1.5-5.3)	-	0.08 (0.04-0.12	0.6 (0.2-0.8)	0.2 (0.1-0.3)	-
Russia non-indigenous n=107	3.8 (0.2-9)	0.6 (0.04-4)	0.15 (0.1-0.25)	1.5 (0.3-4)	0.3 (0.05-0.6)	-
Russia Indigenous n=30	2 (0.5-5)	0.4 (0.02-0.9)	0.1 (0.04-0.2)	0.8 (0.3-2)	0.2 (0.02-0.7)	-

4. Dietary Studies in the Arctic Areas

Levels of persistent organic pollutants in selected food items are shown in Table 4. Dietary surveys serve several purposes, namely to describe and analyze the food choice and nutritional adequacy of the diet and to assess the role of food components as sources/carriers of anthropogenic pollutants including heavy metals, organochlorines and radionuclides. Dietary surveys have been performed among Arctic populations both as part of the AMAP-Human Health program and as independent studies, discussed in the second AMAP Report (Deutch, 2003). In particular, a large body of dietary information has been accumulated in Canada over the last twenty years by the Centre for Indigenous Peoples' Nutrition (CINE) (Kuhnlein & Receveur, 1996; Kuhnlein & Receveur, 2001). An ongoing project of the Russian Arctic will give new insights, where a knowledge-chasm exists, in the area from the Kola Peninsula to the Chukotka Peninsula. We have reasons to believe that the amount of food containing residues above the maximum residue limit is considerably higher in the Arctic areas and especially in the Russian Arctic (Klopov *et al.,* 1998).

There are large variations in dietary patterns in the Euroarctic area, but the general tendency is clear that traditional/country food consumption is gradually decreasing, as imported foods are becoming more available and culturally acceptable to Arctic peoples. This is most clearly shown by the use of dietary indicators, e.g., human blood lipid profiles of n-3 and n-6 polyunsaturated fatty acids among which the n-3 to n-6 ratio is a strong marker of traditional food intake, consisting mainly of marine mammals, but also of fish and game. The high relative content of n-3 fatty acids in the

Table 4. Levels of persistent organic pollutants in selected food items.*

Country	Food item	Concentration of POPs
North-West Russia	Arctic char muscle	Sum PCBs: 26.6 µg/kg ww Sum HCH: 2.9 µg/kg ww Sum DDTs: 5.65 µg/kg ww Sum Chlordanes: 3.01 µg/kg ww Toxaphenes: 35.4 µg/kg ww
	Cod muscle	Sum PCBs: 9.6 µg/kg ww Sum HCH: 1.42 µg/kg ww Sum DDTs: 2.12 µg/kg ww Sum Chlordanes: 1.75 µg/kg ww
	Ringed seal blubber	Sum PCBs: 710-4 200 µg/kg ww Sum HCH: 34-180 µg/kg ww HCB: 14-28 µg/kg ww Sum DDTs: 490-3 600 µg/kg ww Sum Chlordanes: 180-470 µg/kg ww
Greenland	Whale blubber	Sum PCBs: 3 700-5 400 µg/kg ww Sum DDTs: 2 700-4 100 µg/kg ww Sum Chlordanes: 1 800-2 400 µg/kg ww Toxaphenes: 3 000-3 500 µg/kg ww
	Cod liver	Sum PCBs: 63-107 µg/kg ww Sum HCH: 7-9 µg/kg ww HCB: 12-20 µg/kg ww Sum DDTs: 60-98 µg/kg ww Sum Chlordanes: 40-57 µg/kg ww
	Salmon muscle	Sum PCBs: 75 µg/kg ww Sum HCH: 14 µg/kg ww HCB: 7 µg/kg ww Sum DDTs: 40 µg/kg ww Sum Chlordanes: 15 µg/kg ww Toxaphenes: 300 µg/kg ww
Faroe island	Pilot whale muscle	Sum PCBs: 640 µg/kg ww (mean) Sum DDTs: 280 µg/kg ww (mean)
	Whale blubber	Sum PCBs: 17 000-39 000 µg/kg ww γ-HCH: 500 µg/kg ww Sum DDTs: 10 000-24 000 µg/kg ww
	Cod liver	Sum PCBs: 52-68 µg/kg ww Sum HCH: 4-5 µg/kg ww HCB: 9-11 µg/kg ww Sum DDTs: 42-50 µg/kg ww Chlordanes: 22-30 µg/kg ww
	Halibut muscle	Sum DDTs: 780 µg/kg ww
Northern-Norway	Cod liver	Sum PCBs: 240 µg/kg ww Sum HCH: 11 µg/kg ww HCB: 41 µg/kg ww Sum DDTs: 309 µg/kg ww Sum Chlordanes: 196 µg/kg ww
	Cod muscle	Sum PCBs: 1.1 µg/kg ww Sum HCH: 0.1 µg/kg ww HCB: 0.2 µg/kg ww Sum DDTs: 1.0 µg/kg ww Sum Chlordanes: 0.3 µg/kg ww
	Seagull eggs	Sum PCBs: 1830 µg/kg ww (mean)
	Reindeer fat	Sum PCBs: < 80 µg/kg ww Sum HCH: < 20 µg/kg ww Sum DDTs: < 10 µg/kg ww
	Harp seals blubber	Sum PCBs: 3800 µg/kg ww (mean) Sum DDTs: 3000 µg/kg ww (mean)
	Shrimp muscle	Sum PCBs: 0.1 µg/kg ww (mean) Sum HCH: 0.1µg/kg ww (mean) HCB: 0.3µg/kg ww (mean) Sum DDTs: <dl Sum Chlordanes: <dl

* Adapted from (AMAP, 1998; SNT, 1997; Fromberg *et al.*, 1999; Stange *et al.*, 1996).

traditional/country foods presumably provides some protection against cardiovascular diseases, and diabetes. On the other hand human blood levels of marine n-3 fatty acids are strongly associated with POPs, because the main sources of POPs are fats (blubber) from marine animals (Deutch, 2003).

A Norwegian survey on the levels in foodstuffs and dietary intake of dioxins and PCBs showed that the analysed foodstuffs were low in dioxins and dioxin-like PCBs (SNT, 1997). The highest concentrations were found in fatty marine food such as cod liver and brown crabmeat. Commercial fish oil products are refined during production and not regarded as a problem.

The average weekly dietary intake of dioxins and PCBs in the Norwegian population, based on data from household budget surveys, was estimated to be well below the tolerable weekly intake recommended by the Nordic Expert Group (SNT, 1997). However, for consumers of fish liver and crab from areas locally contaminated with dioxins and PCBs, it is likely that the intake may exceed the tolerable weekly intake. Fatty seafood, especially fish liver and crab, from such areas should not be used for food.

Contaminant levels of fish used in the Norwegian diet have big local variations. Fish from the Barents Sea and the Norwegian Sea are normally found to have very low concentrations of contaminants. A substantial part of the fish used in the general diet is caught in these areas. Local fjords might have higher levels of POPs, leading to restrictions in the consumption of fish, fish liver and crabmeat (SNT, 2002). For milk and meat products local variations seem to be minor (SNT, 1997; SNT, 2002). Recently, eggs of sea gulls were reported to be highly PCB contaminated (SNT, 2002). However, recent data from a preliminary study in a high fish consumption community in Northern Norway did not show elevated levels of PCB and pesticides (Furberg *et al.,* 2002). Concentrations of brominated flame retardants in plasma samples from three different occupational groups in Norway were recently reported, finding large variations of individual concentrations within the groups (Thomsen *et al.,* 2001). The conclusion was that Norwegian populations are exposed to a variety of brominated flame retardants, probably with food as the major source. A more complete assessment of human exposure pathways is needed before we can offer public health advice.

The diets of Arctic indigenous peoples consists of both traditional food and imported (market) foods. Although it varies by country, locality, sex, and age group the traditional food yields 10-40% of the total energy intake and this percentage has decreased over the last 30-40 years. The traditional foods are the main contributors of protein, fat, and most minerals (Fe, Zn, Se, I), vitamin D, and especially of the essential long chain n-3 fatty acids, which supply some protection towards heart disease and diabetes. On the other hand the imported foods are the main contributors of carbohydrates, water-soluble vitamins, vitamin A, and calcium. In general the composite diets are sufficient regarding most nutrients. However the nutrients most at risk are vitamin A, vitamin C, and folic acid due to the low intake of vegetables and calcium due to the low intake of milk products. The iodine intake of inland indigenous populations is sometimes below recommended levels.

Chemical analyses of food items of animal origin have provided ample proof that traditional food is a major source of heavy metals (Hg, Cd, Pb) and persistent organic substances. Exposure estimates of heavy metals calculated from dietary intake data show good correlation with human tissue concentrations. Dietary exposure estimates of persistent organic pollutants (POPs) have so far only been compared with human body burdens of POPs on a population basis. Correlation between estimates of individual dietary intakes and individual blood levels of xenobiotics are not yet available. However, several studies show very significant positive associations between n-3 fatty acids in human lipid fractions and blood levels of both Hg and POPs which makes the connection between intake of marine mammal fat (e.g., blubber) and organic pollutants highly probable. It is also evident that the POP concentration in animal fat varies with the age and sex of the animals and the geographic location (AMAP, 1998).

The uptake, metabolism and excretion of organochlorine compounds is influenced by genetic factors. The tissue levels are influenced by various lifestyle factors such as smoking and body mass index (Lagueux *et al.,* 1999; Deutch & Hansen, 2000). Therefore identification of individuals at risk of accumulating high POP burden is not just a question of dietary exposure but also a more complex question of interacting genetic and biochemical factors. These should receive more attention in future studies.

5. Assessment of Exposure to Levels of POPs Presently Found in the Arctic

In the Canadian Arctic 43% of the blood samples from Inuit women from North West Territoires/Nunavut had blood PCB at a Level of Concern; of these, 87% were less than 20 microg/L, and none exceeded 100 microg/L. Among women of child-bearing age in the Greenland regions of Disko Bay, Ilullissat, Nuuk and Ittoqqortoormiit (Scoresbysund), the Level of Concern of > 5 microg/L for PCBs such as Aroclor 1260 was exceeded by 95, 52, 81 and 81% of the mothers, respectively (Van Oostdam & Tremblay, 2003; Dewailly & Weihe, 2003). In Ittoqqortoormiit, 12% of pregnant women exceeded the Canadian Action Level of 100 microg/L for PCBs such as Aroclor 1260, while 52% of non-pregnant women exceeded this blood guideline. These markedly higher proportions of the populations exceeding the Level of Concern reflect the considerably higher PCB levels in Greenland Inuit. The exceeding values for maternal blood samples from Norway, Sweden and Finland were 70%, 68%, and 7.7% respectively. These higher level of exceedances of the Canadian Level of Concern among the Norwegian and Swedish mothers may be due to higher fish intake and resulting higher PCB levels. The PCB levels in fish are so much lower than in mammals that it is hard to believe that this can be the whole explanation. Table 5 presents a more detailed overview of blood guidelines.

Table 5. Guideline values for levels of selected environmental contaminants in human tissues.

Contaminant	Tissue	Guideline Value	Organization/country
DDT/DDE	Plasma/Serum	200 microg/L (total DDT)	WHO
PCBs[1]	Plasma/Serum	For women of reproductive age (µg/L): < 5: Tolerable 5-100: Concern > 100: Action	Canada
PCBs[1]	Plasma/Serum	For men and post-menopausal women (µg/L): < 20: Tolerable 20-100: Concern > 100: Action	Canada
PCBs[1]	Breast Milk	50 µg/L: For protection of infants	Canada
Mercury (total)	Whole Blood	<20 µg/L: Normal acceptable range 20-100 µg/L: Increasing risk > 100 µg/L: At risk	Canada
Cadmium	Whole Blood	5 µg/L (for occupational exposure)	Canada
Lead	Whole Blood	100 µg/L: Action Level	Canada, USA

[1] PCBs measured as Aroclor 1260

5.1. Epidemiological Studies

Arctic residents are exposed to a variety of contaminants present in the food chain. POPs are composed of numerous compounds, most of them accumulating in the food chain and in humans. It is then difficult to ascertain which compound is responsible of any associated observed effect. This makes any risk assessment of limited relevance for regulators. Similarly, concomitant exposure to MeHg and POPs is often observed.

In The Faeroe Islands, prenatal exposure to PCBs was examined by analyses of cord blood from 435 children from a Faroes birth cohort, established in 1986/87 (Grandjean *et al.,* 1997; Grandjean *et al.,* 2001). Among 17 neuropsychological outcomes determined at age 7 years, the cord PCB concentration was associated with deficits on the Boston Naming Test, the Continuous Performance Test reaction time, and, possibly, on long-term recall on the California Verbal Learning Test. The association between cord blood PCB and cord blood Hg (r=0,42) suggested possible confounding. While no PCB effects were apparent in children with low Hg exposure, PCB-associated deficits within the highest tertile of Hg exposure indicated a possible interaction between the two neurotoxicants. PCB-associated increased threshold were seen at two of eight frequencies on audiometry. No deficits occurred on evoked potentials or contrast sensitivity. The limited PCB-related neurotoxicity in this cohort appears to be affected by concomitant MeHg exposure.

Neurotoxic effects of MeHg might be attenuated by protective effects of nutrients such as selenium (Se) and n-3 polyunsaturated fatty acid (n-3 PUFA). Increased intake of these nutrients would be expected in a population such as the Inuit who consume relatively large quantities of fish and marine mammals. Although the protective effects of Se on MeHg toxicity have not been adequately documented in humans (National Research Council, 2000), there is strong evidence from animal studies that Se can influence the deposition of MeHg in the body and some evidence that Se can protect against Hg toxicity (Ganther *et al.,*1972). n-3 PUFA (polyunsaturated fatty acids), especially docosahexaenoic acid (DHA), are essential for brain development (Crawford *et al.,* 1976). DHA deficiency impairs learning and memory in rats (Greiner *et al.,* 1999). Studies have shown that supplementation of n-3 PUFA can enhance visual acuity and brain development in preterm infants (Bjerve *et al.,* 1999; Uauy *et al.,* 1990), but it is not clear whether increased levels of these nutrients during the fetal period can protect full term infants against neurotoxicity associated with prenatal exposure to environmental contaminants.

Except for Hg and organochlorine- induced neurodevelopmental effects studied in the Faeroe Islands (Grandjean *et al.,* 2001), POPs and the immune system in Nunavik (Canada) (Belles-Isles *et al.,* 2002; Dewailly *et al.,* 2000) and pregnancy outcomes and metals in the Kola Peninsula (Odland *et al.,* 1999), very few major environmental epidemiological studies have been conducted in the Arctic. There are several reasons for this situation. Conducting Arctic studies is extremely difficult due to the remoteness of communities, e.g., the cultural context, climate, small size populations, and social and behavioral confounders. The specificity of the Arctic raises the question of how far results and conclusion from epidemiological studies conducted outside the Arctic can apply to this region. Mixtures of contaminants are different. Due to the diffuse properties of contaminants, the exposure profile found in the Arctic might differ from those reported at mid-latitudes where local sources could contribute to the mixture. Patterns of exposure could be influenced by hunting and fishing seasons and constant exposure versus occasional high exposure could have different toxic consequences. Arctic residents consume wild animals and plants. This country food contains specific nutrients, which could influence or counteract the toxicity of contaminants. For example, Inuits are exposed to similar amounts of Hg as the Faeroe's people, but their selenium intake is much higher. Finally local ethnic population groups may have specific genetic background that might influence their susceptibility to toxic agents.

The highest proportions of exceedance of blood guideline parallels the concentrations of contaminants in blood. The Inuit from the east coast of Greenland who consume large amounts of marine mammals have the highest proportion of blood concentrations exceeding the PCB guidelines used by Canada followed by west coast Greenland Inuit populations and Inuit populations from the Baffin and Nunavik regions of eastern Canada. Similar patterns can be seen for exceedances of the Hg blood guidelines (used by Canada and USA) but the data are more limited. When the new US-EPA Hg guidelines are applied it can be seen that most Inuit populations and a significant proportion of several other populations exceed these guidelines. Lead levels are also elevated among some inuit groups in Arctic Canada and Greenland and these are also reflected in the increased proportions exceeding the action level. It seems that most of the lead comes from the use of lead shot for hunting of game rather than from long range atmospheric transport. Northern Europeans from Norway, Sweden, and The Faeroe Islands have higher levels of PCBs and markedly higher proportions exceeding the PCB blood guideline than Caucasians from Arctic Canada (Van Oostdam & Tremblay, 2003; Dewailly & Weihe, 2003).

5.2. Studies on Risk Assessment

In many studies on risk assessment, exposures have not been entirely ”pure” and most have included more than one neurotoxicant. The Faeroes studies offer some insight and a potential for separating the effects, because PCB and mercury showed only a moderate association, and because lead exposures were very low (Grandjean *et al.,* 2001). However, the most serious problem in interpreting research in this field may rather be that PCBs in the environment is not one well-defined chemical but consists of 209 congeners. Several of the congeners are thought to be neurotoxic (Sauer *et al.,* 1994), but few of them are included in routine analyses and as a result they are not considered in risk assessment of persistent congeners. Further, PCBs occur in conjunction with other organochlorine substances, such as *p,p´*-DDE, which may contribute to their combined toxicity. The PCB exposure estimate may not address differences in PCB profiles and other contaminant profiles in different settings, and comparison between epidemiological studies must therefore be performed with caution.

Among the reasons for different study outcomes are differences in concomitant exposures and nutritional factors. In addition, imprecision in exposure assessment and outcomes as well as statistical power needs to be taken into account. For seafood-mediated exposures, confounding due to n-3 polyunsaturated fatty acids must be considered, because these nutrients are essential also for the development of the nervous system. Thus, birth weight and fatty acid statuses are important cofactors to consider.

Whenever possible risk assessment of contaminants should be based on epidemiological evidence. However, Arctic epidemiological studies are few in number. Serious consideration should be given to cohort studies on neurological disorders associated with prenatal MeHg (Faeroe Island) and the study of immune dysfunctions in children exposed prenatally to POPs (Nunavik). As human exposure to contaminants is to a mixture of many different substances simultaneously it is not reasonable and presumably not even possible to deal with the risk of single substances in epidemiological studies. The effect study from the Faeroe Islands has shown that there are negative effects related to both Hg and PCBs and perhaps DDT, DDE and other organochloric substances (Grandjean *et al.,* 2001). However, the most recent review concludes that in the Faroese population methyl mercury seems to be the greater hazard as a neurotoxicant (Schantz *et al.,* 2003). Similar exposure levels as observed in the Faroe Islands can also be found in other places in the Arctic area, e.g., in Greenland. It seems likely that the negative effects, although small in the Faeroe Islands, can be found at other places with a similar exposure.

In the risk assessment of exposure at levels presently found in the Arctic it is reasonable to conclude that the traditional diet in the Arctic contains xenobiotic substances which have a negative influence on health.

6. Toxicological Consequences of Persistent Organic Contaminants in Food

The health of humans is, in large, determined by the quantity and the quality of the diet, which means, that it should provide sufficient nutrients, both macro-and micro nutrients, and contain a low level of harmful pathogenic micro organisms and toxic compounds. In many cases chemical contaminants are unavoidable in food. E.g., MeHg occurs at a natural background level in marine mammals and fish, and PCBs and pesticides are globally spread, bioaccumulated and biomagnified in the marine food chains with the result that some Arctic peoples are exposed to these components, often at a level in excess of internationally accepted limits for safe intake (AMAP, 1998).

Animal experiments have demonstrated that there are interactions between toxicants, also that specific components of the diet modulates the toxicity of specific toxicants whether these are ingested via food or absorbed via other routes. Many examples point to the importance of interactions between dietary components and toxicants after absorption in the body. Such interactions occur at every level of biological organisation from the molecular to the whole organism. Some may be synergistic, others antagonistic. Some may involve direct chemical reactions between the nutrient molecule and the toxicant, e.g., the reaction between the micronutrient Se and Hg, others may occur by indirect action at the molecular level, such as enhanced gene expression by toxicants. Presently we are beginning to understand the molecular basis of the regulation of gene expression by dietary factors and how genetic changes can effect response to toxicants. Recent advances in technology and a more detailed understanding of disease etiology has increased the possibility to study molecular determinants of disease risk. Research programmes still provide new mechanistic models for effects of toxicants and at the same time increases the understanding of interactions between toxicants and between toxicants and nutrients. In addition development of a system of relevant and applicable biomarkers of effects will be of importance for future studies of risks from dietary contaminants. The body of present knowledge clearly points to the importance of considering the composition of the diet when evaluating the response to toxicants in human populations.

A theoretical model for diet-toxicant interaction is shown in Figure 2, showing the dose related negative effect of a given toxicant and the effects of the same toxicant ingested through two different diets. The toxicant will *per se*, as a xenobiotic, theoretically exerts a negative effect at all dosage levels, disregarding a potential stimulating effect at the low levels of intake. However, when ingested from different diets the response may be altered depending on the nutritional composition of the diets.

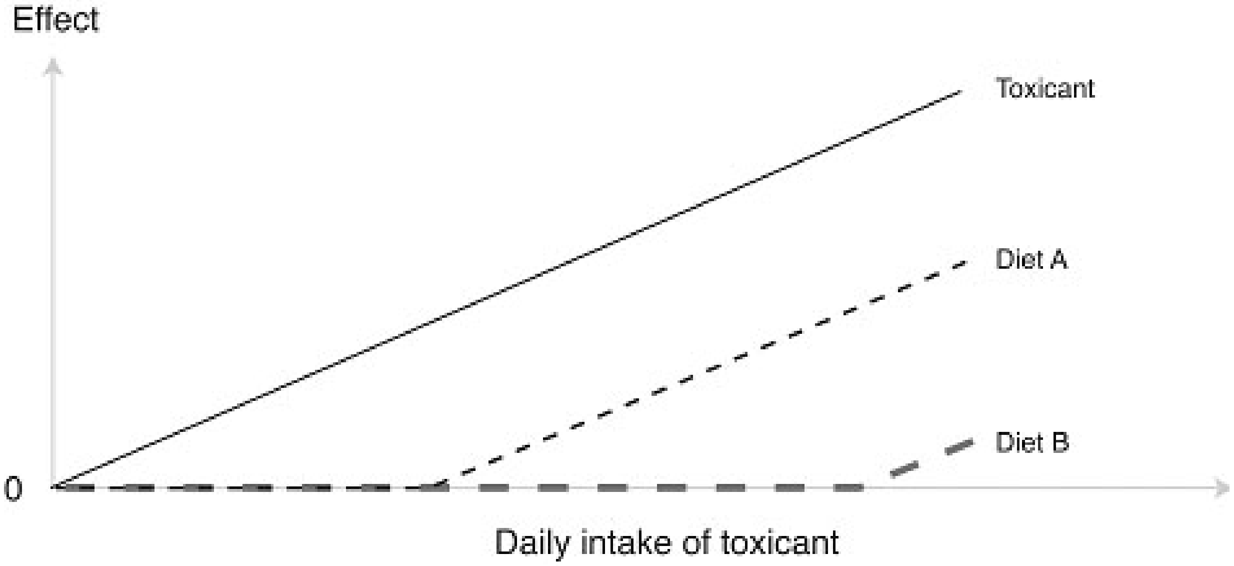
The model shown in Figure 2 can illustrate why different studies so often reach different conclusions. One example is MeHg, where the Faeroese study reported developmental effects in children related to dietary intake of methyl mercury from pilot whale meat (Grandjean *et al.,* 1997), while no effects were observed, at a similar exposure level, in the Seychelles study (Davidson *et al.,* 2002) where the mercury was provided through a fish diet. Contrary to the Faeroese study in the Seychelles study there was a better performance outcome among the children who had the highest exposure *in-utero* compared to the group with the lowest exposure. This is interpreted by the authors as an influence by nutrients that overweigh the negative effects of methyl mercury. This example clearly points to the need to evaluate diet in environmental monitoring programmes together with the toxicants in order to provide relevant risk information.

Traditional risk assessments for non-cancer effects are commonly based on determination of a NOAEL (no observed adverse effect level) from controlled studies in animals. An "acceptable safe" daily dose for humans is then derived by dividing the NOAEL with a safety factor, usually 10 to 1000, to account for sensitive subgroups of the population, data insufficiency, and extrapolation from animals to humans. This procedure does not take into account any forms of interactions, and the use of the NOAEL has become controversial because of the inherent uncertainties. There is an increasing interest in new approaches based on dose-response modelling techniques. Crump suggested application of the lower 95% confidence limit of the dose corresponding to a predefined increase (usually 5% or 10%) over the background rate (Crump, 1984). The author defined the Benchmark Dose (BMD) as the estimated dose that correspond to the specific risk above the background risk, while the Benchmark Dose Lower 95 % Limit (BMDL) is the lower 95% limit. This notation has now become standard usage in risk assessment (Budtz-Jorgensen *et al.,* 2001). However, the benchmark calculations depend on the assumed dose-response model, which will depend on nutritional conditions (Figure 2). This approach will not provide a universal estimate of the real risk from a given toxicant under varying environmental conditions and the BMDL can only be taken as indicative of approximate orders of magnitude.

The risk management process is, based on scientific evidence and taking into account certain societal factors, administratively to set guidelines for tolerable exposure, the TDI (tolerable daily intake). As the scientific basis for doing this is ambiguous the TDIs should only be regarded for what they are; namely an administrative tool for regulation of human exposure to potential harmful chemicals, and not as an indication of a real risk level.

In some cases the TDI is fixed at a level below the Toxicologically Determined Reference Dose (RfD) with the intention to minimise the use of a hazardous compound. This is true for some pesticides, e.g., DDT. In other cases the reverse attitude is taken and the TDI is above the RfD. An example is MeHg where the RfD is calculated by US-EPA to be 0.1 ug/kg body weight/day, while the WHO recently had decided to maintain the PTWI (provisional tolerable weekly intake) of 3.3 ug/kg bw corresponding to 0.47 ug/kg/day. This is justified from the point of view that the US-EPA RfD will limit fish consumption to a level far below what is recommended for protection from cardiovascular diseases. On the other hand a RfD to TDI ratio <1 indicates the presence of a potential environmental problem calling for a reduction of environmental MeHg of anthropogenic origin.

Fig. 2. Theoretical model for the modifying effect of various diets on the effect of a toxicant (as a function of toxicant intake).



7. Conclusions and Abatement Strategies

Well-designed epidemiological studies with standardized questionnaires are now being created and validated. Estimates of effects are difficult based on current knowledge, but the combination of improved methodology and selection of risk groups will be a good step further in the process. Data from these studies are of importance in designing local abatement strategies. A model for interactions and feedback mechanisms for POPs; exposures, levels, effects, and abatement strategies including dietary advice is suggested in Figure 3.

The authors‘ suggestions for possible local abatement strategies are visualized in Figure 4.

The most effective strategies must be adapted locally with the community they are designed to assist. Once evaluated for their effectiveness, they can be used as case studies to assist the development of risk reduction strategies in other parts of the Arctic. The best strategies are those developed with the affected people strongly engaged in the decision making process. Any strategies based on traditional food substitution should ensure that the value of the dietary components is sustained.

It is essential that countries ratify and implement multinational environmental agreements, as these will be the only effective long-term solutions for reducing human exposure to POPs and metals.

The complexity of changing conditions and the need for inclusion of multiple determinants of health in decision-making makes forecasting future population trends very difficult. Based on current global trends and activities to manage risks minor decreases in POPs and minor increases in Hg levels in Arctic populations in Greenland, Eastern Russia, Western Alaska and Eastern Canada by 2010 are likely to occur (AMAP, 2003) and major decreases in both POPs and Hg levels are likely in the same populations by 2030 (AMAP, 2003). Levels of POPs and metals in populations in the Faeroe Islands, Norway, Sweden and Finland are already reasonably low and are only likely to decline marginally by 2030. These predictions will be influenced by prompt ratification and implementation of multinational environmental agreements.

There remains a key need to fill in data gaps to validate and update exposure and disease estimates for various regions of the Arctic. Special emphasis should be placed on children and youth for whom data are difficult to gather.

In order to improve our understanding of health effects associated with contaminant exposure in the Arctic, we recommend that circumpolar epidemiological studies be implemented on a larger scale. MeHg and POPs related effects are still the key issues. However, the role of new discovered contaminants, like PBDEs and PCNs, should be investigated. For exposure assessment, epidemiological studies should consider mixtures and nutritional interactions. Epidemiological studies on nutritional benefits of traditional food should be incorporated in risk assessment profiles. Tissue banking for samples collected in the course of epidemiological studies should be carefully organized to allow further assessment of new contaminants and time trend studies.

In conclusion there is a need for a more nuanced view on human dietary exposure to xenobiotics as risk should not be evaluated alone, but seen in relation to benefits from specific diets. Table 6 is a suggestion for a model connecting food consumption and a POP Contamination Impact Factor (CIF) in Greenland, based on current knowledge of levels and available effect studies. So far Greenland is the only area we have enough information on the key issues; contamination of food items, dietary intake, biological levels, and human effect studies to suggest such a model in the strategic discussion of risk understanding, risk assessment and risk communication. The definitions of Low, Medium and High are arbitrarily set, based on results discussed in the Arctic Monitoring and Assessment Programme (AMAP, 2003). In other geographical areas the information is still too scarce to develop such models.

In future risk analysis it is important to have a good and ongoing communication between scientists and administrative and political authorities to maintain a balance between risk and benefit of traditional diet and its possible content of pollutants. New chemical and epidemiological methodology will contribute to develop good abatement strategies.

Fig. 3. Interactions and feedback mechanisms for POPs: Exposures, levels, effects, and abatement strategies including dietary advice.

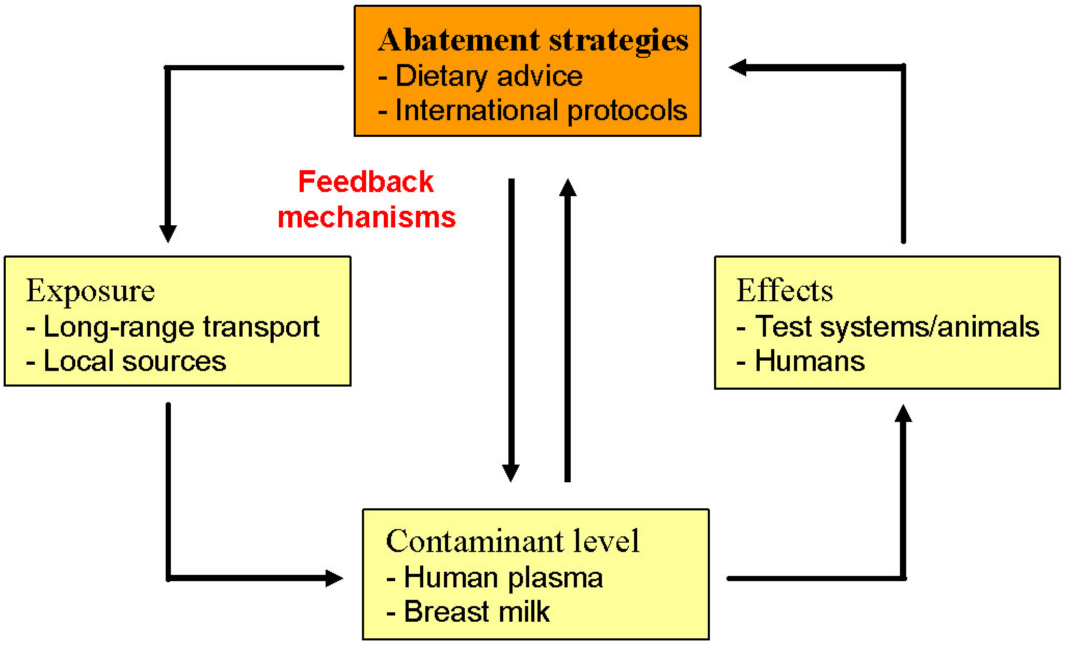


Fig. 4. Local abatement strategies.

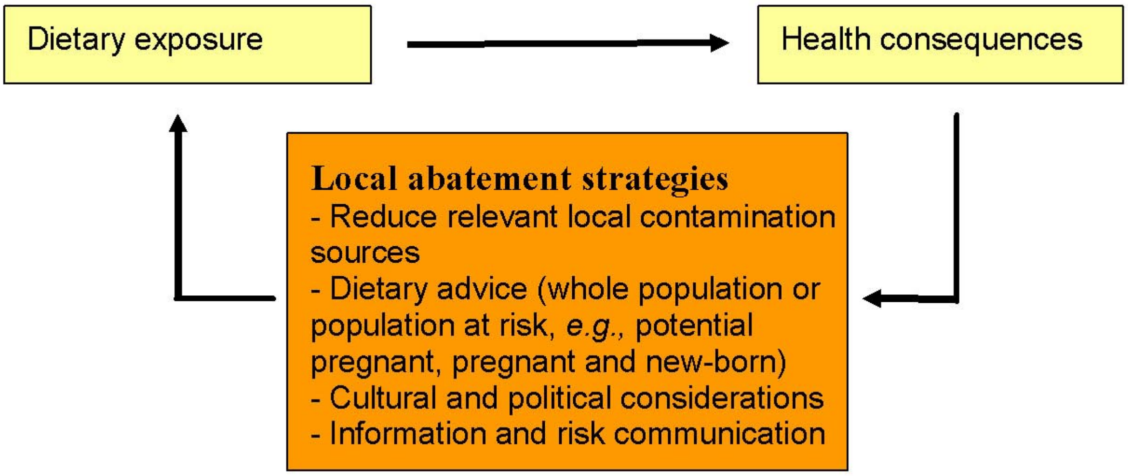


Table 6. Food consumption and POP Contamination Impact Factor (CIF) in Greenland.

Population group	Basic food items	Consumption factor*	Contamination factor*	Impact factor (CIF)*
Greenland (Inuit)	Marine mammals	H	H	H
	Terrestrial mammals	M	L	L
	Birds	M	H	H
	Fish	L	L	L
	Imported food	H	L	L

*L=Low, M=Medium, H=High; arbitrarily set definitions based on results shown in Arctic Monitoring and Assessment Programme (Ilsen *et al.*, 1996).

8. Relevance for Brazil

So far, no systematic studies of environmental pollutants and reproductive health have been initiated in Brazil. In the State of Sao Paulo many different sources of pollutants with known or suspected impacts on human health and development are known; pesticides used in agriculture, chemical pollutants in and toxic metals in industry, and toxic substances related to the urban pollution of Sao Paulo. It is of urgent importance to localize sources and the impact those have on the human health, especially on reproductive and developmental health.

A new cooperation project between the Arctic Monitoring and Assessment Programme and the University of Botucatu, Sao Paulo County, starting autumn 2005, introduces a new scientific field in Brazil.

The project design includes;

- To facilitate risk assessment related to exposure to persistent toxic substances (PTS), including food security and malnutrition through assessment of environmental toxins in maternal blood of selected populations
- To elucidate food as a source of exposure of contaminants
- To create data for future dietary advises and pollution control protocols
- To improve pregnancy care and mother-and-child health conditions of the population
- To cooperate in basic training of health workers in research, field work, sampling technique and questionnaire handling, as well as to facilitate exchange of health workers, laboratory personnel and students for educational purposes and scientific cooperation
- To introduce local laboratories in international laboratory networks for PTS-analysis and to develop quality controlled (QA/QC) analytical capabilities
- To develop a regional birth registry to facilitate research on environmental contaminants and human health.

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