Chapter 9

The Effects of Arctic Pollution on Population Health

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Summary

Very few major epidemiological studies on effects due to exposure to environmental contaminants have been conducted in the Arctic. Arctic studies are extremely difficult to undertake due to the remoteness of communities, the cultural context, climatic factors, small populations, and confounding social and behavioral factors, etc. The special characteristics of the Arctic raises the question as to how far results and conclusions from epidemiological studies conducted outside the Arctic can apply to this region. Human exposure to contaminants generally involves exposure to a mixture of many different substances simultaneously, it is therefore not appropriate, and currently not even possible, in epidemiological studies to establish the risk associated with individual substances. Nevertheless, serious consideration should be given to results from cohort studies into neurological disorders associated with prenatal methylmercury (MeHg) exposure (in the Faroe Islands) and immune dysfunction in children exposed prenatally to persistent organic pollutants (POPs) (in Nunavik). It is likely that the negative effects, although small, can be detected at sites outside the Arctic under similar exposure conditions. In adopting dietary recommendations intended to reduce the exposure of Arctic populations, public health authorities should give consideration to the possibility of negative effects on public health caused by changes in lifestyle.

Inuit from the east coast of Greenland, who consume large numbers of marine mammals, have the highest proportion of the population exceeding the (Canadian) guidelines for polychlorinated biphenyls (PCBs) in blood, followed by west coast Greenland Inuit populations and Inuit populations from the Baffin and Nunavik regions of eastern Canada. A similar pattern occurs for exceedance of the blood Hg guidelines, but the data are more limited. If the new U.S. EPA mercury guidelines are applied, then it is evident that most Inuit populations and a significant proportion of several other populations exceed these guidelines.

9.1. General considerations

There is considerably more information on the effects of environmental factors on the health of Arctic populations than existed at the time of the previous AMAP Assessment Report (AMAP, 1998), five years ago. This chapter updates that information.

In addition, this chapter examines the risks to Arctic peoples associated with exposure to the major contaminants, also taking into account some lifestyle factors. These factors, when integrated, can result in risks that are greater than or different to those resulting from any single effect alone. This combined effects risk assessment is problematic. While it is intuitively obvious that exposure to multiple risk factors should be of more concern than exposure to one or two defined health risks, it is extremely difficult to combine these risks in a quantitative or even qualitative manner. It is possible to investigate the estimated risks to populations based on their exceedance of health guidelines; however these are few in number, and change as scientific knowledge improves (Table 9·1).

Table 9·1. Guideline values for levels of environmental contaminants in human tissues.

Contaminant	Media	Guideline Value (µg/L)	Source
DDT and DDE	Plasma or serum	200 (total DDT)	WHO
PCBs[1]	Plasma or serum	*For women of reproductive age* <5: Tolerable 5–100: Concern >100: Action	Canada
		For men and post-menopausal women <20: Tolerable 20–100: Concern >100: Action	Canada
PCBs[1]	Breast milk	50: For protection of infants	Canada
Hg (total)	Whole blood	20: Normal acceptable range 20–100: Increasing risk >100: At risk	Canada
		>4.4[2]	United States
Cd	Whole blood	5: For occupational exposure	Canada
Pb	Whole blood	100: Action Level	Canada
Pb	Whole blood	100	United States

[1]PCBs measured as Aroclor 1260;
[2]Based on the US EPA's 1999 re-evaluation of mercury: a BMDL of 44 µg/L (58 µg/L in cord blood), and applying a 10-fold safety factor.

9.2. Epidemiological studies on mercury and persistent organic pollutants

The following discussion on epidemiology is restricted to studies on MeHg and POPs, specifically PCBs. Other contaminants such as cadmium (Cd) and lead (Pb) are now considered of lower priority as the main sources giving rise to human exposure (smoking for Cd and lead shot or industrial emissions for Pb) are not Arctic-wide environmental contamination and information on their toxicity is in most cases already available, validated and widely used. Furthermore, most of the health concerns associated with the presence of contaminants in the Arctic food chain are related to MeHg and POPs.

Over the past decades, epidemiological studies on human health effects related to exposure to PCBs and mercury (Hg) have been oriented toward prenatal exposure and children's health. Although, these have largely focused on neurological systems, hormonal effects (related to reproduction and cancer), immune deficiency and cardiovascular effects have recently gained considerable attention.

Very few epidemiological studies have been conducted in the Arctic. This is because knowledge about levels and exposure of northern residents to lipophilic pollutants is relatively recent (dating from the mid 1980s). In addition, communities in this vast territory are small and scattered, hence travel and fieldwork are extremely expensive and the power of epidemiological studies is weakened by small population size. However, problems associated with Hg contamination have been known for many years; and recognized in the Arctic for nearly 25 years. As a consequence, effect studies have been conducted all over the world, including the Arctic.

9.2.1. Neurobehavioral effects

9.2.1.1. Mercury

Mercury is a heavy metal that enters the environment from both natural and anthropogenic sources. The main anthropogenic sources include combustion of fossil fuels, and waste incineration. Inorganic Hg is converted to MeHg by bacteria in aquatic systems and this then bioaccumulates in marine and freshwater food chains. MeHg is highly fetotoxic. The developmental neurotoxicity of MeHg first became evident during the 1950s when Minamata Bay, Japan, was heavily contaminated by industrial effluents discharged to the bay. Infants born to women who had eaten fish from the bay exhibited a range of impairments to the central nervous system, including mental retardation, primitive reflexes, cerebral ataxia, and seizures (Harada, 1995). A second well-documented MeHg poisoning occurred in Iraq in the 1970s when seed grain treated with a MeHg fungicide was used in households to make bread (Amin-Zaki *et al.*, 1976). The affected Iraqi population was exposed to higher levels than that in Japan, and the exposure took place over a much shorter period of time, yet the neurodevelopmental effects were similar, including severe sensory impairment, general paralysis, hyperactive reflexes, cerebral palsy, and impaired mental development (Marsh *et al.*, 1987).

Three well-designed, prospective, longitudinal studies have been performed which examine the effects of prenatal exposure to low doses of MeHg; in New Zealand, the Faroe Islands, and the Seychelles (Davidson *et al.*, 1998; Grandjean *et al.*, 1997; Kjellstrom *et al.*, 1986; Myers *et al.*, 1995a). High dietary MeHg exposure in the Faroe Islands population results from consumption of pilot whale (*Globicephala melaena*) (Grandjean *et al.*, 1992), while consumption of deep-sea and reef fish is the source of exposure for the Seychelles (Myers *et al.*, 1995b) and New Zealand populations (Kjellstrom *et al.*, 1986). All these prospective MeHg studies involved children without overt clinical symptoms of MeHg poisoning. Cord blood Hg was the main indicator of prenatal exposure in the Faroe Islands study, although maternal hair Hg concentration during pregnancy was also determined. Maternal hair Hg concentration during pregnancy was the indicator of prenatal MeHg exposure in the Seychelles and New Zealand studies. Hair Hg is approximately 90% MeHg and has the advantage of providing an historical record of MeHg exposure, whereas the MeHg half-life in human blood is approximately 50 days (Cox *et al.*, 1989; Kershaw *et al.*, 1980; Sherlock *et al.*, 1984). Average maternal hair Hg concentrations in these studies varied from 4.3 to 8.8 µg/g, and a significant number of infants studied had hair Hg concentrations higher than 10 µg/g.

Two other studies investigated the effects of prenatal Hg exposure resulting from fish consumption, the first in Canada – more specifically in the James Bay Cree population – and the second in Peru. However, these did not consider neurobehavioral outcome (Marsh *et al.*, 1995; McKeown-Eyssen *et al.*, 1983).

The Faroe Islands study reported associations between maternal hair Hg concentration corresponding to the pregnancy period and children's performance in neurobehavioral tests, particularly concerning fine motor function, concentration, language, visual–spatial abilities and verbal memory (Grandjean *et al.*, 1997). However, neuropsychological dysfunction was the parameter most closely associated with cord blood Hg concentration (Grandjean *et al.*, 1999a).

The New Zealand study also found adverse effects of prenatal MeHg exposure (Kjellstrom *et al.*, 1986). More specifically, higher hair Hg levels were associated with poorer neurodevelopmental test scores for similar domains to those observed in the Faroe Islands study.

In the Seychelles study, in which the exposure and research design were similar to that of the New Zealand study, however, prenatal MeHg exposure was not found to be related to neurobehavioral effects (Davidson *et al.*, 1995, 1998; Myers *et al.*, 1995b).

Thus, prenatal MeHg exposure from marine food consumption was associated with neurobehavioral deficits in the Faroe Islands study but not the Seychelles study. Less consideration has been given to the outcome of the New Zealand study because, until recently, it had not been subject to peer review. Differences in the neuropsychological test battery, Hg exposure, age at testing, and the source of Hg exposure are suggested to account for the differences between the findings of the Faroe Islands and Seychelles studies. When the New Zealand data are considered, these factors no longer seem determinative, because the exposure and research design of the New Zealand study were similar to those of the Seychelles study, yet adverse neurobehavioral effects were

observed (as they were in the pilot study conducted in the Seychelles) (NRC, 2000). One limitation of the Faroe Islands study was that, owing to the confounding effects of prenatal exposure to both Hg and PCB (r = 0.41 to 0.49) (Grandjean *et al.*, 1997, 1999a), it was difficult to determine whether several of the neurodevelopmental deficits observed at age 7 years, especially those in language and memory function, were due to prenatal Hg exposure, to prenatal PCB exposure, or to both exposures. However, patterns of neurobehavioral damage produced by developmental Hg exposure in animals resemble those found in humans and include sensory system effects, motor or sensorimotor system effects, and cognitive effects.

The relationship between prenatal exposure to MeHg and neurological and developmental abnormalities was ascertained among 234 Cree Indian children aged 12 to 30 months from four northern Quebec communities (McKeown-Eyssen *et al.*, 1983). A pediatric neurologist, 'blinded' to the children's level of exposure, assessed neurological, physical, mental, and psychosocial development. MeHg exposure was estimated from maternal hair segments representing the period of pregnancy. Abnormality of the tendon reflexes, observed in 13 boys (11%) and 14 girls (12%), was positively associated with MeHg exposure in boys only and there was no consistent dose–response relationship. Other neurological disorders were less prevalent and none were positively associated with exposure; indeed, incoordination was positively associated with exposure in girls.

Cord blood samples (n=42) from Qaanaaq (northwest Greenland) were collected and analyzed in 1982 and the children examined at 7 to 12 years of age. Clinical neurological examination did not reveal any obvious deficiencies. However, neurophysiological tests (auditory evoked potentials) showed possible Hg exposure-associated deficiencies, although in only a few cases reaching levels of statistical significance (Weihe *et al.*, 2002).

9.2.1.2. **Polychlorinated biphenyls**

The developmental toxicity of heat-degraded PCBs was first recognized in Japan in the late 1960s and in Taiwan in the late 1970s. In similar industrial accidents in both countries, infants born to women who had consumed rice oil contaminated with mixtures of PCBs and polychlorinated dibenzofurans (PCDFs) had skin rashes and exhibited poorer intellectual functioning during infancy and childhood (Chen *et al.*, 1992; Yu *et al.*, 1991).

Effects of prenatal exposure to background levels of PCBs and other organochlorine compounds (OCs) from environmental sources have been studied since the 1980s in prospective longitudinal studies in Michigan, North Carolina, the Netherlands and Oswego (New York). The source of PCB exposure was fish consumption from the Great Lakes in both the Michigan (Schwartz *et al.*, 1983) and Oswego (Stewart *et al.*, 1999) studies, and consumption of dairy products in the Netherlands (Koopman-Esseboom *et al.*, 1994a). Newborn infants from the North Carolina cohort were exposed to background levels of PCBs, and there was no specific source of exposure (Rogan *et al.*, 1986b). PCB exposure was associated with less optimal newborn behavioral function (e.g., reflexes, tonicity and activity levels) in three of the four studies (Huisman *et al.*, 1995a; Rogan *et al.*, 1986a, Stewart *et al.*, 2000). Adverse neurological effects of exposure to PCBs were found up to 18 months of age in the Netherlands study (Huisman *et al.*, 1995b). In Michigan and the Netherlands, higher cord serum PCB concentrations were associated with lower birth weight and slower growth rate (Fein *et al.*, 1984; Jacobson *et al.*, 1990b; Patandin *et al.*, 1998). In Michigan, prenatal PCB exposure was associated with poorer visual recognition memory in infancy (Jacobson *et al.*, 1985, 1990a, 1992), an effect recently confirmed in the Oswego study (Darvill *et al.*, 2000), and was linked to poorer intellectual function at 4 and 11 years (Jacobson *et al.*, 1990a; Jacobson and Jacobson, 1996), a finding recently confirmed in the Netherlands study at 42 months (Patandin *et al.*, 1999). In North Carolina, deficits in psychomotor development at up to 24 months were seen in the most highly exposed children (Gladen *et al.*, 1988; Rogan and Gladen, 1991). Although much larger quantities of PCBs are transferred to nursing infants by breast feeding than prenatally across the placenta, virtually all the adverse neurobehavioral effects reported to date are linked specifically to prenatal exposure, indicating that the embryo and fetus are particularly vulnerable to PCBs.

A German cohort of 171 children showed average PCB concentrations (based on CB138, CB153 and CB180) in cord serum and maternal milk that were similar to those reported in the Netherlands study (Winneke *et al.*, 1998). Negative associations between maternal milk PCB levels and mental/motor development were reported at all ages, becoming significant from 30 months onwards. Over 30 months of age, for a PCB increase from 173 to 679 ng/g lipids in milk there was a decrease of 8.3 points in the Bayley Scales of Infant Development mental scores, and a 9.1 point decrease in the Bayley Scales of Infant Development motor scores. There was also a negative effect of postnatal PCB exposure via breast feeding, at 42 months. Home environment had a positive effect from 30 months onwards (Walkowiak, 2001).

A prospective, longitudinal study set up to examine the effects of prenatal exposure to low doses of MeHg resulting from fish and pilot whale consumption was performed in the Faroe Islands (Grandjean *et al.*, 1992, 1997). Because pilot whale tissues contain other neurotoxins this cohort was also exposed to PCBs. This is the only cohort studied to date where the main source of PCB exposure was the consumption of marine mammals, as is the case for the Inuit. However, it was difficult to determine whether several of the neurobehavioral deficits observed at age 7 years, especially on language and memory function (Budtz-Jorgensen *et al.*, 1999), were due to prenatal MeHg exposure, to PCB exposure or to both. Nevertheless, after determining PCB concentrations in cord tissue for 50% of the cohort, detailed statistical analyses showed that confounding factors were limited, and interaction with MeHg-associated effects was unlikely. A complete review of epidemiological studies related to PCB exposure and neurodevelopmental effects in newborn infants was published recently (Ribas-Fito, 2001).

New findings on the effects of both MeHg and PCB exposure have been made since the previous AMAP Assessment Report, increasing significantly the body of sci-

entific evidence linking neurodevelopmental effects during infancy and childhood with prenatal exposure from maternal consumption of fish and marine mammals. One prospective longitudinal study on this topic involving Nunavik and Greenland mothers and infants has been ongoing since 1997 (Dewailly and Bjerrgard, pers. comm., 2001). The data are still being analyzed and no results have yet been published. In the Faroe Islands, the cohort established in 1986/87 (Grandjean *et al.*, 1992) was re-examined at age 14 years. The examination was basically the same as that undertaken when the children were 7 years of age. However, at 14 years special attention was given to the maturation of the body. In 2001 and 2002 a cohort of 182 7-year old children was examined in same manner as for the 1986/87 Hg cohort at 7 years. A third cohort of 650 children will be examined neuropediatrically during 2002 to 2004 at 54 months (4.5 years), however the main emphasis of this study will be on immunological deficits related to POPs.

9.2.2. **Reproduction**

Typical OC mixtures found in highly exposed human populations contain a large variety of OCs, including substances with estrogenic, anti-estrogenic or anti-androgenic properties. Arnold *et al.* (1996) showed that compounds such as endosulfan, dieldrin, toxaphene and chlordane, which are practically devoid of estrogenic activity on their own, caused synergistic activation of the estrogen receptor when tested in combination in a yeast estrogen system. It may thus be anticipated that complex real life mixtures, composed of numerous compounds, which can interact with different receptors, may result in impaired male fertility in adulthood.

9.2.2.1. **Hormones**

No studies on hormones have been conducted in the Arctic to date. However, a pilot study was recently undertaken in Greenland (n=48 males) and the following male hormones measured: DHEA, δ5-diol, δ4, testosterone, DHT, E1, and E2. There were no correlations between hormone levels and POP levels adjusted for age, body mass index (BMI) and smoking (Dewailly, pers. comm., 2001). A multi-center fertility study involving 600 males and 200 pregnant women began in Greenland in 2002. Male fertility parameters and time-to-pregnancy are the most important endpoints of the study. POPs are part of the exposure assessment (Pedersen, pers comm., 2001).

9.2.2.2. **Pregnancy outcome**

From 1989 to 1991 Dewailly *et al.* (1993) undertook a cohort study on the health effects of Inuit newborn prenatally exposed to OCs. A statistically significant association was found between male newborn length and PCBs and PCDD/Fs, even after adjustment for potential confounding factors.

A study was initiated in 1994 because of public concern about adverse reproductive health effects and pregnancy outcome in the Russian–Norwegian border zone near the nickel (Ni) producing industry on the Kola Peninsula. The original objective was to assess the health of delivering women and their outcome within the general population of the area, including an assessment of essential and toxic trace elements. Over the course of the study, the health of an occupationally exposed population of female Ni industry workers and children living on the Kola Peninsula also became an important focus. Between April and June 1994, maternal information, delivery information, and maternal and neonatal blood and urine samples were collected for approximately 50 deliveries in each of the Russian cities Arkhangelsk, Nikel, and Monchegorsk; the three Norwegian study areas were Kirkenes, Hammerfest, and Bergen. Urinary Ni concentrations were significantly higher in the Russian study groups. Sources of Ni exposure for the Russian population that could account for this remain unidentified. Environmental Ni exposure, as measured by urinary Ni excretion, was not shown to be a predictor variable of either low birth weight or newborn BMI. The mineral status of delivering women in Arctic and subarctic areas of Norway and western Russia was adequate, with the exception of zinc (Zn). The variation in serum Zn concentrations demonstrated differences between Arctic and subarctic areas across national borders. Maternal serum Zn was a positive predictor variable for birth weight. Maternal blood Pb was a negative predictor of birth weight, even at the relatively low concentrations in this study. The inclusion of maternal Pb in a multivariate model caused the non-specific country difference to lose statistical significance. Blood Pb concentrations in school children living in remote areas of the Kola Peninsula were up to a level of medical concern. Mean birth weight and BMI were significantly lower in the Russian study groups, suggesting possible nutritional deficiencies during pregnancy in Russia. Congenital malformations were too scarce to be assessed.

With the exception of the negative effects of maternal Pb concentrations, the other pollutants studied had no observed effects on pregnancy outcome, birth weight or BMI. The statistically significant difference between the Norwegian and Russian mean BMIs suggests that malnutrition during pregnancy may occur in the Russian study groups. Blood Pb concentrations up to a level of medical concern were observed in children living in remote areas of the Kola Peninsula (Odland *et al.*, 1999a,c, 2001).

9.2.3. **Cancer**

Results from early human studies generally supported the existence of a relationship (Dewailly *et al.*, 1994a; Falck *et al.*, 1992; Mussalo-Rauhamaa *et al.*, 1990; Wolff *et al.*, 1993) or suggested a possible link (Krieger *et al.*, 1994) between breast cancer risk and OC exposure, more specifically exposure to *p,p'*-DDE, the main metabolite of DDT. In contrast, recent studies involving larger sample sizes yielded negative results (Høyer *et al.*, 1998; Hunter *et al.*, 1997; López-Carillo *et al.*, 1997; Moysich *et al.*, 1998; van't Veer *et al.*, 1997). In particular, Hunter *et al.* (1997) and Høyer *et al.* (1998) using a nested case control study design, failed to observe a relationship between *p,p'*-DDE or PCB plasma concentrations and breast cancer risk. However, Høyer *et al.* (1998) reported that high plasma concentrations of dieldrin were associated with breast cancer risk. Previous

studies have focused solely on the risk of developing a new breast cancer. However, hormonally active OCs might also modulate cancer growth and prognosis (Demers *et al.*, 2000).

Rubin *et al.* (2001) reported on levels of DDT, DDE, other chlorinated pesticides, and PCBs in serum samples collected from 131 Alaska Native women between 1980 and 1987 to enable a comparison with other published studies of DDE and PCB exposure in U.S. women. The data collected during this case-control study of the relationship between OCs and breast cancer showed minimal differences between cases and controls. Data for case and control women were consequently pooled in the statistical analysis. More than 99% of the women had detectable levels of *p,p'*-DDE (mean 9.1 µg/L). The mean total PCB level was 7.6 µg/L. Levels of exposure varied according to geographical location and ethnic identification, and may reflect dietary differences. Five of the OCs were detected in at least half of the study population. Alaska women had levels similar to those reported for the United States.

9.2.4. Immune system effects

Several OCs display immunotoxic properties in both laboratory animals and humans. In children and young adults accidentally exposed to PCBs and PCDFs in Taiwan ('Yu-Cheng disease'), serum IgA and IgM concentrations as well as percentages of total T-cells, active T-cells and suppressor T-cells, were decreased compared to values of age- and sex-matched controls (Chang, 1981). An investigation of delayed type hypersensitivity responses further indicated that cell-mediated immune system dysfunction was more frequent among patients than controls. Infants born to Yu-Cheng mothers had more episodes of bronchitis and/or pneumonia during their first six months of life than unexposed infants from the same neighborhoods (Rogan *et al.*, 1988). The authors speculated that the increased frequency of pulmonary disease could result from a generalized immune disorder induced by transplacental or breast milk exposure to dioxin-like compounds, probably PCDFs (Rogan *et al.*, 1988). Eight- to 14-year old children born to Yu-Cheng mothers were shown to be more prone to middle-ear diseases than matched controls (Chao *et al.*, 1997).

Organic and inorganic Hg possess cytotoxic activities for cellular components of immune systems in several species of rodent. Moreover, it has been demonstrated that MeHg can affect the functions of B-cells and therefore reduce the humoral-mediated response (Daum, 1993). Exposure to inorganic Hg induces allergies and auto-immune problems in hypersensitive individuals. There is limited evidence from epidemiological studies.

In Nunavik, an epidemiological study investigated whether OC exposure was associated with the incidence of infectious diseases in Inuit infants and with immune dysfunction (Dewailly *et al.*, 2000a). The number of infectious disease episodes in 98 breast-fed and 73 bottle-fed infants was compiled during the first year of life. Organochlorine concentrations were measured in early breast milk samples and used as surrogates for prenatal exposure levels. Biomarkers of immune system function (lymphocyte subsets, plasma immunoglobulins) were determined in venous blood samples collected from infants at 3, 7 and 12 months of age. None of the immunological parameters were associated with prenatal OC exposure.

Otitis media was the most frequent disease with 80.0% of breast-fed and 81.3% of bottle-fed infants experiencing at least one episode during the first year of life. During the second follow-up period, the risk of otitis media increased with prenatal exposure to *p,p'*-DDE, hexachlorobenzene (HCB) and dieldrin. The relative risk (RR) for 4- to 7-month old infants in the highest tertile of *p,p'*-DDE exposure as compared to infants in the lowest was 1.87 (95% confidence interval (CI) 1.07–3.26). The relative risk of otitis media over the entire first year of life also increased with prenatal exposure to *p,p'*-DDE (RR 1.52; 95% CI 1.05–2.22) and HCB (RR 1.49; 95% CI 1.10–2.03). Furthermore, the relative risk of recurrent otitis media (≥3 episodes) was augmented by prenatal exposure to these compounds. No clinically relevant differences were noted between breast-fed and bottle-fed infants with regard to biomarkers of immune function and prenatal OC exposure was not associated with these biomarkers. It was concluded that prenatal OC exposure could be a risk factor for acute otitis media in Inuit infants (Dewailly *et al.*, 2000a).

In another cohort, the risk of experiencing frequent infectious disease episodes was assessed in 89 children exposed to PCBs and DDT in northern Quebec during their first year of life. The risks were related to maternal PCB and DDT blood levels during pregnancy. Ratios were estimated using logistic regression and the results were adjusted for maternal smoking during pregnancy, the number of smokers in the house, crowding, breast feeding duration, and gender. This study supports the hypothesis that the high incidence of infections observed in Inuit children (mostly respiratory infections) is due in part to high prenatal exposure to POPs (Dewailly *et al.*, 2001b).

9.2.5. Cardiovascular effects

While there are no studies that report an association between cardiovascular disease and POPs, Salonen *et al.* (1995) suggest that the high mortality from cardiovascular disease observed among fish eaters from Finland could be explained by the high Hg content in fish (mainly non-fatty freshwater species). They noted a significant association between Hg concentration in the hair of eastern Finnish men and the risk of coronary heart disease. Mercury can promote the peroxidation of lipids, resulting in more oxidized low-density lipoprotein, which has been implicated as an initiator of arteriosclerosis. An enhanced risk of death from coronary heart disease in subjects with low serum selenium (Se) concentrations, an antioxidant that can block the Hg-induced lipid peroxidation, was previously observed in this population (Salonen *et al.*, 1982).

That both Hg and Se can modulate the risk of coronary heart disease is also suggested by observations of fish-eating coastal populations such as Inuit in Arctic regions. Inuit consume large amounts of fish and marine mammals and consequently receive large doses of Hg. However, contrary to the situation in eastern Finland, the mortality rate from coronary heart disease in Inuit is extremely low (Dewailly *et al.*, 2001a). This could be

due to the high intake of Se in this population, through the consumption of traditional food items rich in Se, such as muktuk (beluga and narwhal skin) and marine mammal liver or polyunsaturated fatty acids.

Blood pressure in childhood is an important determinant of hypertension risk later in life and MeHg exposure is a potential environmental risk factor. A birth cohort of 1000 children from the Faroe Islands was examined for prenatal exposure to MeHg, and blood pressure, heart rate, and heart rate variability were determined at seven years of age (Sorensen *et al.*, 1999). After adjustment for body weight, diastolic and systolic blood pressure were shown to increase by 13.9 mmHg (95% CI 7.4–20.4) and 14.6 mmHg (95% CI 8.3–20.8) respectively, when cord blood Hg concentrations increased from 1 to 10 µg/L. Above this level, which corresponds to the current exposure limit, no further increase was seen. Birth weight acted as a modifier, with the Hg effect being stronger in children with lower birth weights. In boys, heart rate variability decreased with increasing Hg exposure, particularly from 1 to 10 µg/L cord blood, at which point the variability was reduced by 47% (95% CI 14–68%). These findings suggest that prenatal exposure to MeHg might affect the development of cardiovascular homeostasis.

9.3. Risk assessment of exposure at levels found in the Arctic

Epidemiological research should be used, if available, in the risk assessment of exposure to contaminants. However, few epidemiological studies exist and those that do cover few substances and only some of the possible clinical endpoints. In most cases risk assessment is based on animal studies. Of the contaminants in the Arctic, MeHg is the best researched using epidemiological methods; and of the several relevant endpoints, neurotoxic effects are the best described by epidemiological methods.

The neurobehavioral performance of an individual in response to contaminant exposure is affected by several factors. The outcome may depend on specific characteristics of the exposure, i.e., severity and chronicity, as well as the possibility of simultaneous exposure to other contaminants. Also, the effect depends on the vulnerability of the subject, as indicated by age, lifestyle, gender and premorbid status, etc. With prenatal exposure in particular, the time of the neurobehavioral assessment is of importance, as the effects may not become apparent until the nervous system has matured sufficiently to express the dysfunction. Epidemiological data are not a prerequisite for risk assessment. In fact, opportunities for epidemiological studies of neurotoxicity may arise only when prevention has failed, whether or not a risk assessment has been carried out, and whether or not the origin of the exposure is natural or anthropogenic. Given that neurotoxic exposures continue to occur, the best possible epidemiological studies should be undertaken to ensure that the unfortunate incidents will at least result in useful information that can provide a better basis for intervention. Frequently, several exposure factors must be determined, as the exposure under study is associated with other chemical exposures originating from the same source, e.g., in the Arctic, Hg and PCBs originating from consumption of marine mammals. Given that neurobehavioral function varies considerably within a population, even similar exposure circumstances may be associated with widely different performance results in a group of exposed subjects. Also, despite results of functional tests remaining well within the expected interval, differences can still be considerable between groups of individuals with different levels of exposure. Furthermore, although the individual may not be aware of any dysfunction, even minimal changes can, in some cases, have severe implications for daily life. These considerations are important when interpreting neurobehavioral data.

9.3.1. Methylmercury

By spring 2002 there was still no international agreement on the risk assessment of MeHg. According to the World Health Organization (WHO, 1990) a "prudent interpretation of the Iraqi data implies that a 5% risk may be associated with a peak mercury level of 10–20 µg/g in maternal hair." The WHO expert committee that drew up Environmental Health Criteria 101 on MeHg, stated: "There is a need for epidemiological studies on children exposed *in utero* to levels of methylmercury that result in peak maternal hair mercury levels below 20 µg/g, in order to screen for those effects only detectable by available psychological and behavioral tests."

Several major epidemiological studies have been performed since this recommendation. Scientific committees under the WHO and the U.S. National Research Council (NRC) recently reviewed the outcome of these studies. However, their conclusions differ, as can be seen in the following extracts from the conclusions.

In 2000, the fifty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives concluded on limit values to Hg exposure (WHO, 2000) as follows:

"The studies in the Faeroe Islands and the Seychelles that were evaluated by the Committee did not provide consistent evidence of neurodevelopmental effects in children of mothers whose intake of methylmercury yielded hair burdens of 20 µg/g or less. The Committee could not evaluate the risks for the complex and subtle neurological end-points used in these studies that would be associated with lower intakes. In the absence of any clear indication of a consistent risk in these recent studies, the Committee decided to maintain the PTWI of 3.3 µg/kg and recommended that methylmercury be re-evaluated in 2002, when the 96-month evaluation of the Seychelles cohort and other relevant data that may become available can be considered. The Committee noted that fish contribute importantly to nutrition, especially in certain regional and ethnic diets, and recommended that nutritional benefits be weighed against the possibility of harm when limits on the methylmercury concentrations in fish or on fish consumption are being considered."

In 2000, the Board on Environmental Studies and Toxicology of the U.S. NRC Committee on the Toxicological Effects of Methylmercury concluded as follows (NRC, 2000):

"On the basis of its evaluation, the committee's consensus is that the value of US-EPA's current Reference Dose (RfD) for MeHg, 0.1 µg/kg per day, is a scientifi-

cally justifiable level for the protection of public health. However, the committee recommends that the Iraqi study no longer be used as the scientific basis of the RfD. The RfD should still be based on the developmental neurotoxic effects of MeHg, but the Faeroe Islands study should be used as the critical study for the derivation of the RfD. Based on cord blood analyses from the Faeroe Islands study, the lowest BMD (Benchmark Dose) for a neurobehavioral end point the committee considered to be sufficiently reliable is for the Boston Naming Test. For that end point, dose-response data based on Hg concentrations in cord blood should be modeled using the K-power model (K≥1). This approach estimates a BMDL (BMD lower confidence limit) of 58 µg/L of Hg in cord blood (corresponding to a BMDL of 12µg/g of Hg in hair) as a reasonable point of departure for deriving a RfD. To calculate the RfD, the BMDL should be divided by uncertainty factors that take into consideration biological variability when estimating dose and MeHg database insufficiencies. As stated earlier, given those considerations, an uncertainty factor of at least 10 is supported by the committee."

It is noted that the 'reasonable point of departure' for deriving a reference dose is 12 µg/g in hair, which is within the range of the 1990 WHO recommendations (10–20 µg/g in hair). It is the chosen uncertainty factor of 10 that leads to a limit value in hair of only 1.2 µg/g. Not only will some of the Arctic populations exceed this value, e.g., in Greenland and the Faroe Islands, but even some non-Arctic populations in the United States (NRC, 2000).

From food consumption surveys, the U.S. EPA has estimated that 7% of women nationally exceeded the U.S. EPA Reference Dose (corresponding to hair Hg levels of around 1.2 µg/g and a maternal blood concentration of 4.4 µg/L). From a food consumption survey in New Jersey it was estimated that 21% of women of reproductive age exceed the Reference Dose. In general, the concentration in hair is 250 to 300 times the simultaneous concentration in blood. Methylmercury is around 25% higher in cord blood than maternal blood. Hence 4.4 µg/L in maternal blood corresponds to 5.8 µg/L in cord blood, which is the limit, when the lowest Benchmark Dose found by the U.S. NRC is divided by an uncertainty factor of 10.

In the 1970s, Health Canada developed blood guidelines for Hg and indicated that <20 µg/L was the normal range, 20 to 100 µg/L the increasing-risk range, and >100 µg/L the at-risk range. Figure 9·1 also compares Hg levels reported in the Arctic with the new U.S. EPA level of 4.4 µg/L for maternal blood (comparable to a cord blood level of 5.8 µg/L). Figure 9·1 is in fact based on exceedance of 5.8 mg/L, which results in slightly lower levels of exceedance than would have been the case using the 4.4 mg/L value.

In Greenland, only 3% of mothers in the Nuuk Region exceeded the 20 µg/L blood Hg guideline, compared with 31% of mothers in Ilullissat and 45% of non-pregnant women in Ittoqqortoormiit (the corresponding value for pregnant women from this region was 13%). Non-pregnant Ittoqqortoormiit women also had the highest percentage exceedance of the 5.8 µg/L blood Hg guideline – 93% – followed by mothers from Ilullissat (80%) and Ittoqqortoormiit women (both pregnant and non-pregnant) (68%). Although Nuuk women showed the lowest percentage exceedance of the 5.8 µg/L guideline – 27% – this is still a substantial proportion (Figure 9·1).

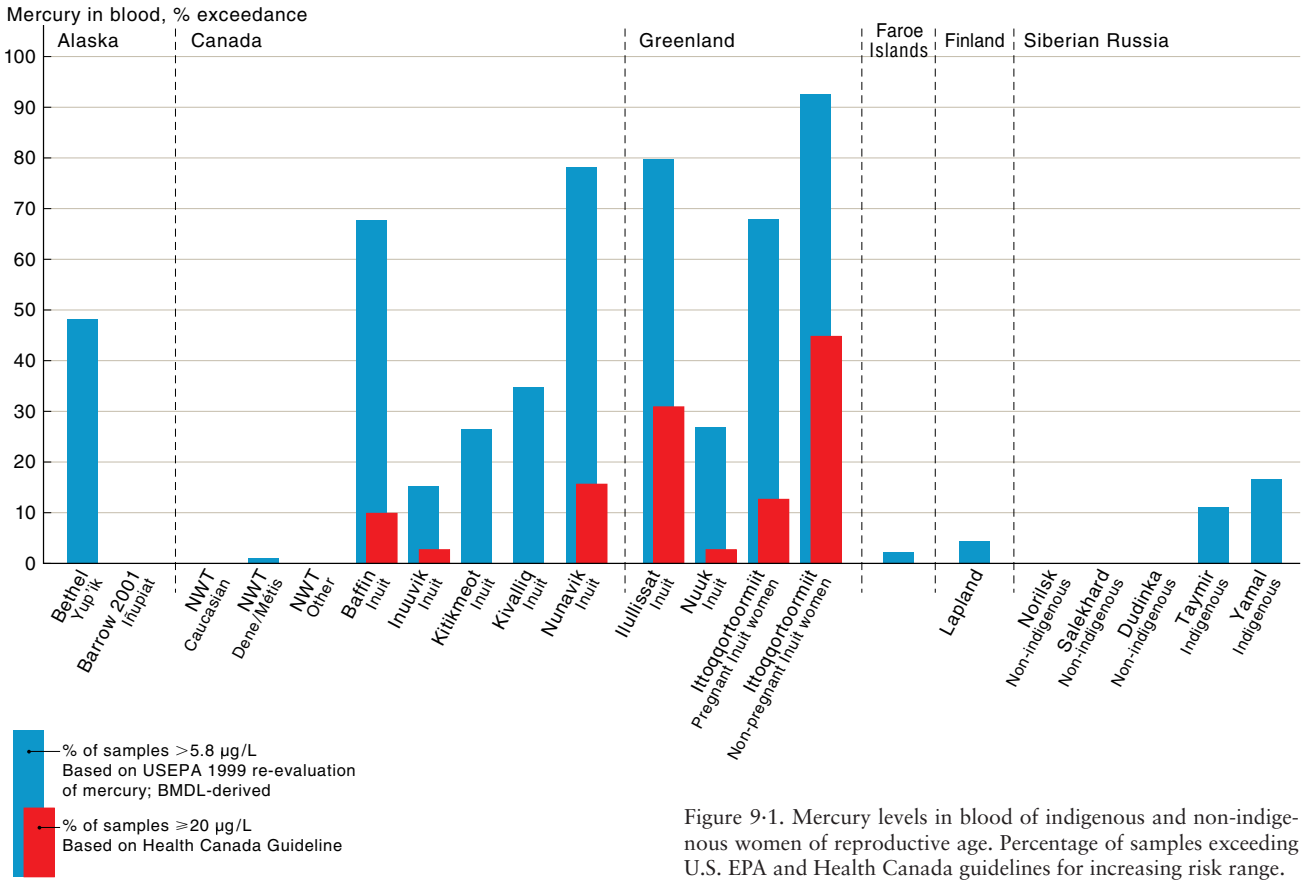

Figure 9·1. Mercury levels in blood of indigenous and non-indigenous women of reproductive age. Percentage of samples exceeding U.S. EPA and Health Canada guidelines for increasing risk range.

In Qaanaaq, in the Thule district of northern Greenland, 43 children were examined in 1995. Their age ranged from 6.2 to 12.0 years, with a median of 8.4. The children's hair Hg concentrations varied up to 18.4 µg/g (geometric mean, 5.5 µg/g). Maternal hair samples (n=31) showed a maximum Hg concentration of 32.9 µg/g and geometric mean of 15.5 µg/g (Weihe *et al.*, 2002).

The Canadian data show that among the Inuit women from NWT/Nunavut, 3% exceeded 20 µg/L, the Canadian Level of Concern for MeHg, and 34% exceeded the lower 5.8 µg/L U.S.-based guideline; Nunavik and Baffin Inuit women had the highest percentage exceedance (16 and 9.7%, respectively). The percentage exceedance of the 5.8 µg/L guideline among Canadian Inuit women overall was 34%, and ranged from 16% in Inuvik to 68% in Baffin. Among non-Inuit women (i.e., Caucasian, Dene/Métis, Others), none exceeded the 20 µg/L guideline and only 1%, all Dene/Métis, exceeded the 5.8 µg/L guideline.

None of the blood Hg levels for women from the five regions of Siberian Russia exceeded the 20 µg/L guideline, but 11% and 17% of those from Taymir and Yamal, respectively – both indigenous regions – exceeded the 5.8 µg/L guideline.

In Alaska, 48% of women from Bethel had blood Hg levels greater than or equal to the 5.8 µg/L guideline, while all those from Barrow were below. Neither group exceeded the 20 µg/L guideline.

In Finland, none of the maternal blood Hg levels exceeded the 20 µg/L guideline (no information was available on exceedance of the 5.8 µg/L guideline, but a population mean and range of 1.4 and 0. to 6.0 respectively, suggests few individuals would exceed this level).

In the Faroe Islands the geometric mean hair Hg concentration at parturition in 1986/87 was 4.27 µg/g; in 1994, 4.0 µg/g; and in 1998/99, 2.1 µg/g. Public health authority warnings about the consumption of pilot whale meat by pregnant women have reduced hair Hg levels significantly, but the concentration for the majority of the Faroe Islands population is still above the 1.2 µg/g limit. In 1986/87, 13% exceeded 10 µg/g, but by 1998/99 this had reduced to 3%. In other words, less than 3% now exceed the Benchmark Dose Limit of 12 µg/g in hair.

In order to understand and be able to mediate the evaluation of risk, the implications of the results from the research described in section 9.2.1.1. must be explained in generally understandable terms using the study from the Faroe Islands as an example (Grandjean *et al.*, 1997). In this respect, it is important to note that the children clinically do not differ from that expected. There are no children showing any physical signs of Hg poisoning. Nevertheless, the Hg exposure is not negligible, as illustrated by the calculations of delayed development using regression analyses. A more differentiated interpretation could be obtained by including the regression coefficient for known factors, e.g., age, which also influence the result. When the regression coefficients are compared, it seems that a doubling of the Hg exposure corresponds to a delay in development of 1 to 2 months for most test results. Even if the regression coefficients are small, the influence is nevertheless considerable, when it is related to the importance of age in a period where there is very fast development. A supplementary interpretation can be based on comparing intelligence quotients (IQ).

Risk management in the Faroe Islands community has now become a matter of finding an appropriate uncertainty factor. There is no consistent approach in the application of uncertainty factors. The adoption of an uncertainty factor represents a scientific policy judgment that has a major influence on what is acceptable to eat, e.g., what types of marine food. An uncertainty factor of 10 is considered adequate by most risk assessment agencies to address the variation in response between different population groups.

The responsible public health authorities must find the magnitude of this factor appropriate for the communities in the Arctic. They must evaluate whether the populations they are responsible for are more or less sensitive than the populations in the benchmark epidemiological studies. The uncertainty comprises many contributors: nutritional status, levels of beneficial nutrients (such as Se and fatty acids from seafood), general health, genetic background, inter-individual variability in sensitivity, exposure to other neurotoxins found in the Arctic, e.g., PCBs, and peak exposures in critical periods of susceptibility for the developing fetal brain.

However, other health endpoints more sensitive than neurotoxicity could be of greater relevance in some areas. For example, the low incidence of coronary heart disease in Greenland Inuit, possibly due to the fatty acid composition of their diet, could be attenuated by high Hg exposure, since recent studies indicate that Hg can have a negative effect on the cardiovascular system (Rissanen *et al.*, 2000). The reason for this is still unknown, but Hg could inhibit important antioxidative mechanisms in humans. Mercury could promote the peroxidation of unsaturated fatty acids such as docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA). Regarding cardiovascular toxicity at low level MeHg exposures, the first Faroe Islands cohort showed that blood pressure tended to increase and heart rate variability tended to decrease when prenatal Hg exposure increased in the low-dose range (Sorensen *et al.*, 1999). Alkylmercury poisoning is associated with increased blood pressure (Höök *et al.*, 1954) and children with Hg poisoning often have increased heart rates and blood pressure (Warkany and Hubbard, 1953). Experimental evidence shows that MeHg toxicity results in irreversible hypertension that remains many months after the cessation of exposure (Wakita *et al.*, 1987). Although insufficient for risk assessment purposes, this evidence suggests that the cardiovascular system should be considered a potential target for MeHg. Even a slight negative impact on the cardiovascular system could be of greater public health relevance than a slight impact on the central nervous system.

9.3.2. **Persistent organic pollutants**

Over the years, a number of biological guidelines have been issued by Health Canada through its Medical Services Branch. In 1979, Health Canada issued a 'Level of Concern' for PCBs in blood of 5 µg/L for pregnant women, 20 µg/L for the general population, and 100 µg/L as an 'Action Level'. These guidelines are expressed as Aroclor 1254 concentrations, rather than Aroclor 1260 concentrations. Because PCB concentrations derived from the AMAP datasets are expressed as Aroclor 1260 equivalents (as calculated from CB138 and CB153

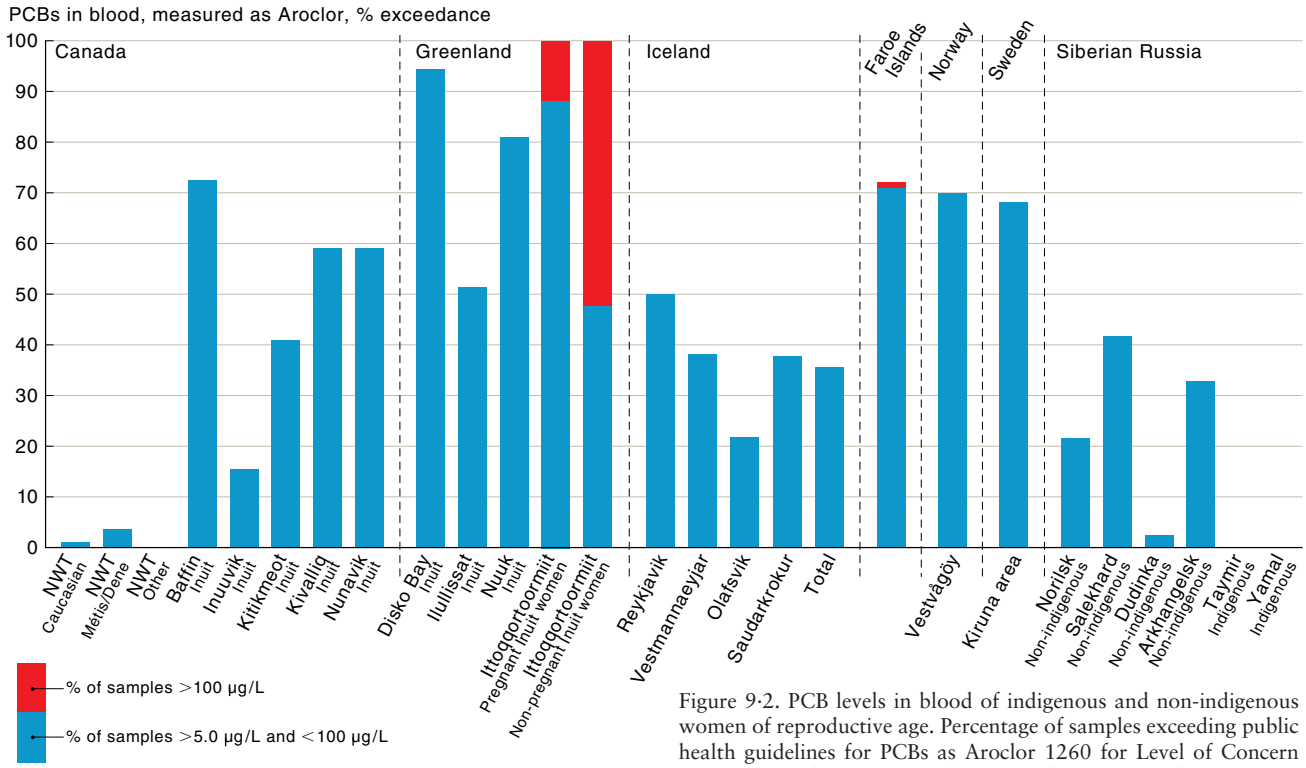

Figure 9·2. PCB levels in blood of indigenous and non-indigenous women of reproductive age. Percentage of samples exceeding public health guidelines for PCBs as Aroclor 1260 for Level of Concern (LOC, >5 and <100 µg/L plasma) and Action Level (>100 µg/L plasma).

levels), the Health Canada guidelines may not be directly applicable, however, they are adequate for the purposes of the general comparisons made below.

The guideline proposed by Health Canada for PCBs in breast milk is 50 µg/kg (whole milk) (Information letter DD24 - March 1978). Assuming a 3.5% fat concentration in whole milk and an average lipid content of 10 g/L in plasma, this guideline corresponds to a concentration of 1.43 mg/kg in milk fat and a plasma concentration of 14.3 µg/L in pregnant women.

It is also possible to use a guideline based on the dose/response assessment of Jacobson's data from the Michigan cohort (see section 9.2.1.2.) developed by Tilson *et al.* (1990). The proposed NOAEL (no observed adverse effects level) for visual recognition memory was estimated at 1 mg/kg of PCBs in milk fat. By extension this 1 mg/kg threshold concentration, expressed on a lipid basis, can be applied to all tissues and biological fluids, including plasma.

The analytical and quantification methods are crucial in elaborating sound biological guidelines. For example, the 1 mg/kg lipid threshold for neurobehavioral effects identified in Jacobson's studies (Jacobson *et al.*, 1985, 1990a, 1992) corresponds to a 2 mg/kg lipid NOAEL, using the quantification scheme developed in laboratories involved in the AMAP database. This threshold corresponds to the following plasma concentrations (whole weight): umbilical cord, 5 µg/L; pregnant women, 20 µg/L.

Jacobson and Jacobson (1996) followed-up their assessment of the Michigan cohort at 11 years of age. They reported a 1.25 mg/kg threshold PCB concentration in lipids for full scale IQ, based on the prenatal exposure assessment, and rounded this to 1 mg/kg for general use. This threshold concentration, derived using PCBs as measured by the packed column/Webb-McCall method, corresponds to concentrations of 2.5 mg/kg and 2 mg/kg (or 10 µg/L) respectively, using the capillary column method to determine PCBs (for an explanation of the calculation of the correction factor used to compare the two methods, see Rhainds *et al.*, 1999). For interpretation purposes the Health Canada guidelines are used.

In the Canadian Arctic, 43% of blood samples from Inuit women from NWT and Nunavut had blood PCBs at a 'Level of Concern' (i.e., above 5 µg/L); of these, 87% were less than 20 µg/L, and none exceeded 100 µg/L (Figure 9·1). The extent of concentrations above the 5 µg/L blood guideline varied widely, with higher percentages in Baffin (73%), Kivalliq (59%), and Nunavik (59%), where higher levels of PCBs were observed. The corresponding values for Dene/Métis and Caucasians were 3.2% and 0.7%, respectively (Van Oostdam *et al.*, 1999).

Among women of reproductive age in the Greenland Disko Bay, Ilullissat, Nuuk, and Ittoqqortoormiit districts, the >5 µg/L 'Level of Concern' for PCBs as Aroclor 1254 was exceeded by 95%, 52%, 81% and 81% of the women, respectively (Deutch and Hansen, 2000). In Ittoqqortoormiit, 12% of pregnant women exceeded the 'Action Level' (100 µg/L) for PCBs as Aroclor 1254, relative to 52% of non-pregnant women. These markedly higher proportions of the populations exceeding the 'Level of Concern' reflect the considerably higher PCB levels in Greenland Inuit.

The four Icelandic regions for which maternal blood samples were analyzed for PCBs as Aroclor 1260 showed percentage exceedance of the 'Level of Concern' (5 µg/L) ranging from 22% to 50%, with Reykjavik having the highest value. The corresponding values for the Vestvågøy region of Norway, Sweden and Finland were 70%, 68%, and 7.7% respectively. The higher percentages among the Icelandic, Norwegian and Swedish women may be due to higher fish intakes and thus higher PCB levels.

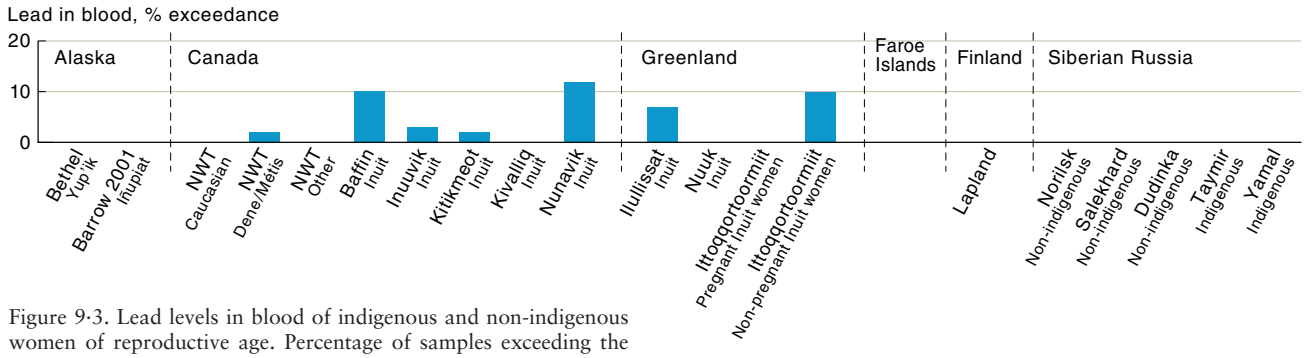

Figure 9·3. Lead levels in blood of indigenous and non-indigenous women of reproductive age. Percentage of samples exceeding the blood guideline Action Level of 100 µg/L.

9.3.3. Lead

Blood guidelines have also been developed for Pb. Figure 9·3 shows that levels of exceedance of the guideline value of 100 µg/L are low throughout the Arctic. The low levels of exceedance found in some populations in Canada and Greenland are thought to be related to local Pb contamination from the lead shot used by hunters, rather than environmental Pb from long-range transport.

9.4. Combined effects

9.4.1. Mixtures

Arctic residents are exposed to a variety of contaminants present in the food chain. POPs are composed of numerous compounds; most of which are capable of accumulating both in the food chain and in humans. Similarly, concomitant exposure to MeHg and POPs is often observed. It is thus difficult to determine which compound is responsible for any particular observed effect. Any single substance risk assessment is therefore of limited relevance for regulatory purposes.

In the Faroe Islands, prenatal exposure to PCBs was examined by analyses of cord tissue from 435 children from a birth cohort established in 1986/87 (Grandjean *et al.*, 1992, 1997, 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. 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 neurotoxins. PCB-associated increased thresholds were seen at two of eight frequencies in audiometric tests. No deficits occurred on evoked potentials or contrast sensitivity. The limited PCB-related neurotoxicity group in this cohort appears to be affected by concomitant MeHg exposure.

The neurotoxic effects of MeHg may be attenuated by protective effects of Se and n-3 polyunsaturated fatty acids. Increased intake of Se and n-3 fatty acids would be expected in peoples 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 (NRC, 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; Whanger, 1992). n-3 polyunsaturated fatty acids especially 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 n-3 polyunsaturated fatty acid supplements can enhance visual acuity and brain development in preterm infants (Bjerve *et al.*, 1992; Uauy *et al.*, 1990), but it is not clear whether increased levels during the fetal period can protect full-term infants against neurotoxicity associated with prenatal exposure to environmental contaminants.

Many health endpoints are multi-factorial and environmental stressors contribute to a various extent to the etiology of these diseases. Compared to the importance of lifestyle and genetic factors in the etiology of most diseases, contaminants are likely to play a modest role. However, exposure to many persistent organic contaminants is preventable, and their presence in the remote Arctic is unethical.

In risk assessment based on epidemiological studies there are many confounding factors that should be considered. Epidemiological studies on children should include information on, at least: maternal and paternal age at childbirth, parity, smoking, education, mothers and if possible fathers intelligence, employment status, migration, risk factors in past medical history, weight, height, breast feeding, age at examination, gestational age, number and age of siblings, day care, home environment, and type of delivery.

9.5. Conclusions

Except for Hg- and OC-induced neurodevelopmental effects in the Faroe Islands, POPs and links with the immune system in Nunavik (Canada), and links between pregnancy outcome and metals on the Kola Peninsula, very few major environmental epidemiological studies have been conducted in the Arctic. This is because Arctic studies are extremely difficult to undertake, owing to the remoteness of communities, the cultural context, climatic factors, small population sizes, and confounding social and behavioral factors etc. The special characteristics of the Arctic raises the question as to how far results and conclusions from epidemiological studies conducted outside the Arctic can apply to this region. Mixtures of contaminants are also different. Due to the properties of contaminants that lead to their distribution throughout the Arctic, and their concentration in certain food webs, the exposure profiles for the Arctic are likely to differ from those reported at mid-latitudes where local sources are more likely to contribute to the mix-

ture. Patterns of exposure in the Artic can be influenced by hunting and fishing seasons, and resulting occasional high exposures, as opposed to constant exposure, may have different toxic consequences. Arctic residents consume wild animals and plants. This country food contains specific components, which may influence or counteract the toxicity of contaminants. For example, Inuit are exposed to similar amounts of Hg as people from the Faroe Islands, but their Se intake is much higher. Finally, indigenous peoples may have specific genetic backgrounds that influence their susceptibility to toxic agents.

The highest proportions of exceedance of blood guidelines for contaminants parallel the patterns for the concentrations of contaminants in blood. The Inuit from the east coast of Greenland, who consume large numbers of marine mammals, have the highest proportion of blood concentrations exceeding the Canadian PCB guidelines, thereafter followed by west coast Greenland Inuit populations and Inuit populations from the Baffin and Nunavik regions of eastern Canada. A similar pattern occurs for exceedance of the blood Hg guidelines (used by Canada and the United States), but the data are more limited. When the new U.S. EPA mercury guidelines are applied it is evident 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 guidelines for Pb concentration in blood. Most of the Pb contamination in these communities is a local problem associated with lead shot used for hunting game, as opposed to Pb from long-range atmospheric transport. Northern Europeans from Norway, Sweden, the Faroe Islands, and Iceland have higher levels of PCBs and markedly higher proportions exceeding the PCB blood guideline than Caucasians from Arctic Canada.

Exposures in many risk assessment studies are not 'pure' and most include more than one neurotoxin. The Faroe Islands studies offer some potential for separating the effects of different contaminants because PCBs and Hg showed only moderate association and because Pb exposures are very low (Grandjean *et al.*, 1992). However, the most serious problem in this regard is that environmental PCBs do not comprise one well-defined chemical but consist of 209 congeners. Several of these are considered neurotoxic (Sauer *et al.*, 1994), but few are included in routine analyses, and as a result are not included in risk assessments of persistent congeners. Furthermore, PCBs occur in conjunction with other OCs, 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 comparisons 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 outcome, as well as in statistical power, must be taken into account. For marine food-mediated exposure, confounding influences of, for example, n-3 polyunsaturated fatty acids must be considered, because these nutrients are also essential for the development of the nervous system. Thus, birth weight and fatty acid status are important cofactors for consideration.

Whenever possible, risk assessment of contaminants should be based on epidemiological evidence, however Arctic epidemiological studies are few in number, and are difficult to perform. Serious consideration should be given to the cohort study on neurological disorders associated with prenatal MeHg (in the Faroe Islands) and the study of immune dysfunction in children exposed prenatally to POPs (in Nunavik). As human exposure to contaminants is to a mixture of many different substances simultaneously, as indicated by the exposure data in this report, it is not appropriate and currently not even possible to establish the risk from single substances using epidemiological studies. The Faroe Islands study shows there are negative effects related to Hg and PCBs and perhaps DDT, DDE and other OCs. Similar exposure levels have been found in other areas of the Arctic, e.g., Greenland. It is likely that the negative effects, although small in the Faroe Islands, can be found at other places with similar exposures. It is the future responsibility of the public health authorities to decide on suitable undertakings to reduce the human exposure levels. Consideration should also be given to the possible negative effects on public health that could be caused by changes in lifestyle.

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.

9.6. Recommendations

The following recommendations are made in order to improve the understanding of health effects associated with contaminant exposure in the Arctic.

1. Circumpolar epidemiological studies should be implemented.
2. MeHg- and POPs-related effects are still the key issues. However the role of new contaminants (polybrominated diphenylethers, polychlorinated naphthalenes, etc.) should be investigated.
3. For exposure assessment, epidemiological studies should consider mixtures and confounding factors such as the interaction of nutritional components.
4. Epidemiological studies on the nutritional benefits of traditional food should be included in the risk assessment profile.
5. Tissue banking for samples collected in the course of epidemiological studies should be carefully organized to allow subsequent assessment of new contaminants and time trend studies.