AMAP Assessment 2002:
Human Health in the Arctic

Arctic Monitoring and Assessment Programme (AMAP)

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Arctic Monitoring and Assessment Programme (AMAP), Oslo, 2003

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ISBN 82-7971-016-7

Published by
Arctic Monitoring and Assessment Programme (AMAP), P.O. Box 8100 Dep, N-0032 Oslo, Norway (www.amap.no)

Citation
AMAP, 2003. AMAP Assessment 2002: Human Health in the Arctic. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xiv + 137 pp.

Ordering
AMAP Secretariat, P.O. Box 8100 Dep, N-0032 Oslo, Norway

This report is also published as electronic documents, available from the AMAP website at www.amap.no

Production

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Design and production of computer graphics
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Printing
Nørhaven Book, Agerlandsvej 5, DK-8800 Viborg, Denmark

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The AMAP Working Group would like to thank the following persons for their work in preparing the AMAP 2002 Human Health Assessment.

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Special acknowledgements:

Chapter 3
The author would like to gratefully acknowledge the invaluable editorial assistance of Dr. Torbjørn Messner, Kiruna, Sweden.

Chapter 7
The author gratefully acknowledges the access to unpublished results and data published in local-language, national reports, which have generously been provided by the following local experts:
Poul Johansen, NERI, Roskilde, Denmark
Valery Klopov, RCMA, St. Petersburg, Russia
Helena Mussalo-Rauhamaa, Helsinki, Finland
Leena Soininen, Rovaniemi, Finland
Pál Weihe, Tórshavn, Faroe Islands
Harriet Kuhnlein, Centre for Indigenous Peoples' Nutrition and Environment, McGill University, Canada is also acknowledged for her detailed work on indigenous diets and her critical review of this chapter

Chapter 10
The author gratefully acknowledges the following individuals for the information they provided for the case studies and for their advice on the chapter: James Berner, Alaska; Eric Dewailly, Benoit Levesque and Jay Van Oostdam, Canada; Jens C. Hansen, Denmark; Valery Klopov, Russia; Torbjørn Messner, Sweden; Jon Øyvind Odland, Norway; Lena Soininen, Finland; and Pál Weihe, Faroe Islands. Several scientists and health policy makers also contributed by reviewing the chapter.

Preface

This assessment report details the results of the 2002 AMAP assessment of Human Health in the Arctic. It builds upon the previous AMAP human health assessment that was presented in 'AMAP Assessment Report: Arctic Pollution Issues' that was published in 1998.*

The Arctic Monitoring and Assessment Programme (AMAP) is a group working under the Arctic Council. The Arctic Council Ministers have requested AMAP to:

- *produce integrated assessment reports on the status and trends of the conditions of the Arctic ecosystems;*
- *identify possible causes for the changing conditions;*
- *detect emerging problems, their possible causes, and the potential risk to Arctic ecosystems including indigenous peoples and other Arctic residents; and to*
- *recommend actions required to reduce risks to Arctic ecosystems.*

The Ministers have placed special priority on the potential impacts of contaminants on the health of Arctic residents, including the combined effects of mixtures of contaminants acting together with other potential stressors.

*This report is one of five detailed assessment reports that provide the accessible scientific basis and validation for the statements and recommendations made in the second AMAP State of the Arctic Environment report, 'Arctic Pollution 2002' that was delivered to Arctic Council Ministers at their meeting in Inari, Finland in October 2002. It includes extensive background data and references to the scientific literature, and details the sources for figures reproduced in the 'Arctic Pollution 2002'** report. Whereas the 'Arctic Pollution 2002' report contains recommendations that specifically focus on actions aimed at improving the Arctic environment, the conclusions and recommendations presented in this report also cover issues of a more scientific nature, such as proposals for filling gaps in knowledge, and recommendations relevant to future monitoring and research work, etc.*

To allow readers of this report to see how AMAP interprets and developes its scientifically-based assessment product in terms of more action-orientated conclusions and recommendations, the 'Executive Summary of the Arctic Pollution 2002 Ministerial Report', which also covers other priority issues (Persistent Organic Pollutants, Heavy Metals, Radioactivity and Climate Change Effects on Contaminant Pathways), is reproduced in this report on pages ix to xiii.

The AMAP assessment is not a formal environmental risk assessment. Rather, it constitutes a compilation of current knowledge about the Arctic region, an evaluation of this information in relation to agreed criteria of environmental quality, and a statement of the prevailing conditions in the area. The assessment presented in this report was prepared in a systematic and uniform manner to provide a comparable knowledge base that builds on earlier work and can be extended through continuing work in the future.

The AMAP scientific assessments are prepared under the direction of the AMAP Assessment Steering Group. The product is the reponsibility of the scientific experts involved in the preparation of the assessment. Lead countries for the AMAP Human Health Assessment under AMAP Phase II were Canada and Denmark. The assessment is based on work conducted by a large number of scientists and experts from the Arctic countries (Canada, Denmark/Greenland/Faroe Islands, Finland, Iceland, Norway, Russia, Sweden, and the United States), together with contributions from indigenous peoples organizations, from other organizations, and from experts in other countries.

AMAP would like to express its appreciation to all of these experts, who have contributed their time, effort, and data; and especially to the lead experts who coordinated the production of this report, and to referees who provided valuable comments and helped ensure the quality of the report. A list of the main contributors is included in the acknowledgements on page vi of this report. The list is not comprehensive. Specifically, it does not include the many national institutes, laboratories and organizations, and their staff, which have been involved in the various countries. Apologies, and no lesser thanks, are given to any individuals unintentionally omitted from the list. Special thanks are due to the lead authors responsible for the preparation of the various chapters of this report.

The support of the Arctic countries is vital to the success of AMAP. AMAP work is essentially based on ongoing activities within the Arctic countries, and the countries also provide the necessary support for most of the experts involved in the preparation of the assessments. In particular, AMAP would like to express its appreciation to Canada and Denmark for undertaking a lead role in supporting the Human Health assessment. Special thanks are also offered to the Nordic Council of Ministers for their financial support to the work of AMAP, and to sponsors of the project on 'Persistent Toxic Substances (PTS) and Food Security of Indigenous Peoples of the Russian North' and other bilateral and multilateral projects that have delivered data for use in this assessment.

The AMAP Working Group that was established to oversee this work, and the AMAP human health assessment group are pleased to present its assessment.

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Oslo, January 2003

* AMAP, 1998. AMAP Assessment Report: Arctic Pollution Issues. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xii+859 pp.

** AMAP, 2002. Arctic Pollution 2002: Persistent Organic Pollutants, Heavy Metals, Radioactivity, Human Health, Changing Pathways. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xii+112 pp.

Executive Summary to the *Arctic Pollution 2002* Ministerial Report

The Arctic Monitoring and Assessment Programme (AMAP) was established in 1991 to monitor identified pollution risks and their impacts on Arctic ecosystems. In 1997 the first AMAP report, *Arctic Pollution Issues: A State of the Arctic Environment Report** was published.

The assessment showed that the Arctic is closely connected to the rest of the world, receiving contaminants from sources far outside the Arctic region. The report was welcomed by the Arctic Council Ministers, who agreed to increase their efforts to limit and reduce emissions of contaminants into the environment and to promote international cooperation in order to address the serious pollution risks reported by AMAP.

The AMAP information greatly assisted the negotation of the protocols on persistent organic pollutants (POPs) and heavy metals to the United Nations Economic Commission for Europe's Convention on Long-range Transboundary Air Pollution (LRTAP Convention). They also played an important role in establishing the need for a global agreement on POPs, which was concluded in 2001 as the Stockholm Convention. Persistence, long-range transport, and bioaccumulation are screening criteria under both the POPs protocol and the Stockholm Convention, to be applied to proposals to add substances to the agreements. Information from AMAP will be useful in this context in showing whether persistent substances are accumulating in the Arctic and are therefore candidates for control, and also in assessing the effectiveness of the agreements.

The Arctic Council also decided to take cooperative actions to reduce pollution of the Arctic. As a direct follow up of the AMAP reports, the Arctic Council Action Plan to Eliminate Pollution of the Arctic (ACAP) was created to address sources identified through AMAP. ACAP was approved in 2000 and several projects have begun. The AMAP information was also used in establishing priorities for the Arctic Regional Programme of Action to Prevent Pollution from Landbased Sources (RPA), developed by the working group on Protection of the Arctic Marine Environment (PAME), and adopted by the Arctic Council in 1998.

After the first assessment, AMAP was asked to continue its activities and provide an updated assessment on persistent organic pollutants (POPs), heavy metals, radioactivity, human health, and pathways in 2002. Five scientific reports and a plain-language report have been prepared. This Executive Summary provides the main conclusions and recommendations of the 2002 AMAP assessments.

International Agreements and Actions

As described above, the LRTAP Convention protocols and the Stockholm Convention are essential instruments for reducing contamination in the Arctic. However, they cannot have any effect until they are ratified and implemented.

It is therefore recommended that:

- **The UN ECE LRTAP Protocols on Heavy Metals and POPs be ratified and implemented.**
- **The Stockholm Convention on POPs be ratified and implemented.**

Specific recommendations for monitoring activities in support of these agreements are included in subsequent sections.

Persistent Organic Pollutants

The POPs assessment addresses several chemicals of concern, including both substances that have been studied for some time and chemicals that have only recently been found in the environment.

The 1997 AMAP assessment concluded that levels of POPs in the Arctic environment are generally lower than in more temperate regions. However, several biological and physical processes concentrate POPs in some species and at some locations, producing some high levels in the Arctic.

The present AMAP assessment has found that the conclusions and recommendations of the first assessment remain valid. In addition:

It has clearly been established that:

Certain Arctic species, particularly those at the upper end of the marine food chain as well as birds of prey, carry high levels of POPs. Marine mammals, such as polar bear, Arctic fox, long-finned pilot whale, killer whale, harbor porpoise, minke whale, narwhal, beluga, harp seal and northern fur seal, some marine birds including great skua, great black-backed gull and glaucous gull, and birds of prey such as peregrine falcon, tend to carry the highest body burdens.

Most of the total quantity of POPs found in the Arctic environment is derived from distant sources. The POPs are transported to the Arctic by regional and global physical processes, and are then subjected to biological mechanisms that lead to the high levels found in certain species. Several potential source regions have now been identified within and outside of the Arctic. A better understanding of local re-distribution mechanisms has also emphasized the important potential role of local processes and sources in determining observed geographical variability.

There is evidence that:

Adverse effects have been observed in some of the most highly exposed or sensitive species in some areas of the Arctic. Several studies have now been completed on a number of Arctic species, reporting the types of effects that have been associated in non-Arctic species with chronic exposure to POPs, of which there are several examples. Reduced immunological response in polar bears and northern fur seals has led to increased susceptibility

* AMAP, 1997. Arctic Pollution Issues: A State of the Arctic Environment Report. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway, xii+188 pp. *and*
AMAP, 1998. AMAP Assessment Report: Arctic Pollution Issues. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway, xii+859 pp.

to infection. Immunological, behavioral, and reproductive effects as well as reduced adult survival has been found in glaucous gulls. Peregrine falcons have suffered from eggshell thinning and reproductive effects. Reproductive effects in dogwhelks are associated with exposure to tributyltin.

It is therefore recommended that:

- **AMAP be asked to further enhance studies aimed at detecting effects in Arctic species relating to exposure to high levels of POPs and to integrate this information with an understanding of general population effects and health.** Without this understanding, it will not be possible to assess whether proposed and existing controls can be expected to afford the necessary protection (e.g., under the LRTAP and Stockholm agreements).

There is evidence that:

The levels of some POPs are decreasing in most species and media in the Arctic, but the rates vary in extent, location and media or species being studied. The decreases can be related to reduced release to the environment. For example, declines in alpha-HCH in air closely follow decreases in global usage, but declines in marine biota are much slower due to a huge reservoir of the substance in the global oceans.

For other POPs, declines are minimal and some levels are actually increasing, despite low current emissions. This illustrates the long period that may pass between the introduction of controls and the resulting decrease in levels in biota, as has been observed for PCBs, toxaphene, and beta-HCH.

It is therefore recommended that:

- **AMAP be asked to continue trend monitoring of POPs in key indicator media and biota.** This will enable assessment of whether the measures taken in the LRTAP Protocol and the Stockholm Convention are being effective in driving down POPs levels in the Arctic.

There is evidence that:

POPs substances other than those included in the LRTAP Protocol and Stockholm Convention may be at or approaching levels in the Arctic that could justify regional and global action. For example, levels of the brominated flame retardants such as polybrominated diphenyl ethers (PBDEs), polychlorinated naphthalenes (PCNs), and some current-use pesticides such as endosulfan have been monitored in Arctic air and biota. PBDEs are increasing in the Canadian Arctic.

It is therefore recommended that:

- **AMAP be asked to maintain a capacity to detect current-use POPs in the Arctic.** This will help ensure that Arctic States have an early opportunity to respond to a trend indicating Arctic accumulation, thus allowing a proactive approach to minimize the contamination rather than having to respond to a more serious situation later.

Heavy Metals

The heavy metals assessment focuses on mercury, lead, and cadmium.

It has clearly been established that:

In the Arctic, mercury is removed from the atmosphere and deposits on snow in a form that can become bioavailable. Enhanced deposition occurs in the Arctic. This recently discovered process is linked to polar sunrise, and is unique to high latitude areas. The resulting enhanced deposition may mean that the Arctic plays a previously unrecognized role as an important sink in the global mercury cycle.

There is evidence that:

Some of the deposited mercury is released to the environment at snowmelt, becoming bioavailable at the onset of animal and plant reproduction and rapid growth. Although poorly understood, this process may be the chief mechanism for transferring atmospheric mercury to Arctic food webs.

It is therefore recommended that:

- **The Arctic Council encourage expanded and accelerated research on critical aspects of the mercury cycle and budget in the Arctic.** Such research should include long-range transport, mercury deposition mechanisms, processes leading to biological exposure and effects, and the influence of climate variability and change on these processes.

There is evidence that:

Despite substantial mercury emission reductions in North America and Western Europe during the 1980s, global mercury emissions may, in fact, be increasing. Mercury emissions from waste incineration are likely underestimated. The burning of coal in small-scale power plants and residential heaters, principally in Asia, are major potential sources of current mercury emissions. These emissions are likely to increase significantly due to economic and population growth in this region.

It is therefore recommended that:

- **The Arctic Council promote efforts at global, regional, and national levels to quantify all sources of mercury and report results in a consistent and regular manner to improve emission inventories.** Particular efforts should focus on measuring contributions made by the burning of coal for residential heating and small-scale power plants as well as by waste incineration.

There is strong evidence that:

There is a trend of increasing mercury levels in marine birds and mammals in the Canadian Arctic, and some indications of increases in West Greenland. The effects of these levels are not well understood. However, there are also examples of stable or decreasing levels in other regions, perhaps indicating the importance of local or regional processes.

It is therefore recommended that:

- **AMAP be asked to continue temporal trend monitoring and the assessment of effects of mercury in key indicator media and biota.** This will enable assessment of whether the measures taken in the LRTAP Protocol are being effective in driving down mercury levels in the Arctic.

There is evidence that:
Current mercury exposures pose a health risk to some people and animals in the Arctic. These risks include subtle neurobehavioral effects.

It is therefore recommended that:
- **In view of the fact that reducing exposure to mercury can only be addressed by regional and global action to reduce worldwide emissions, and acknowledging the assessment for global action undertaken by UNEP and its resulting proposals, the Arctic Council take appropriate steps to ensure that Arctic concerns are adequately addressed and to promote the development of regional and global actions.**

It has clearly been established that:
Dramatic reduction in the deposition of atmospheric lead has occurred in Arctic regions where the use of leaded gasoline is banned. Arctic-wide elimination of leaded gasoline use will reduce lead exposure in other regions of the Arctic. Although levels in wildlife and fish have not measurably declined, likely reflecting continued uptake from the large reservoir of lead deposited in soils and sediments, lead levels in the environment are expected to diminish over time if current trends continue.

It is therefore recommended that:
- **The Arctic Council support continued efforts to eliminate the use of leaded gasoline in all Arctic regions.**

It has clearly been established that:
Certain regions of the Arctic contain elevated lead levels in the environment because of past or current use of lead shot by hunters. Even though lead shot is banned in Alaska, for example, lead blood levels in endangered US populations of Steller's eiders are above known avian toxicity thresholds for lead poisoning, which may be responsible for observed reduced breeding success. In Greenland, lead shot appears to be a significant source of human dietary exposure to lead.

It is therefore recommended that:
- **The Arctic Council encourage a complete ban on the use of lead shot in the Arctic, and that enforcement be improved.**

There is evidence that:
Cadmium levels in some seabirds is high enough to cause kidney damage. Monitoring data on cadmium in the abiotic and biotic environment to date provide no conclusive evidence of trends or effects. However, cadmium accumulates in birds and mammals and not enough is known about possible effects.

It is therefore recommended that:
- **The monitoring of cadmium in the Arctic be continued to support human exposure estimates.**

There is evidence that:
Levels of platinum, palladium, and rhodium have increased rapidly in Greenland snow and ice since the 1970s. These elements are used in automobile catalytic converters to reduce hydrocarbon pollution. The toxicity and bioaccumulation potential of these elements are largely unknown, which prevents assessment of their potential impact in the Arctic.

It is therefore recommended that:
- **AMAP be asked to consider the need to monitor trends of platinum, palladium, and rhodium in the Arctic.**

Radioactivity

The radioactivity assessment addresses man-made radionuclides and radiation exposures deriving from human activities.

It has clearly been established that:
In general, levels of anthropogenic radionuclides in the Arctic environment are declining. Most of the radioactive contamination in the Arctic land environment is from the fallout from nuclear weapons testing during the period 1945 to 1980. In some areas, the fallout from the Chernobyl accident in 1986 is a major source. For the Arctic marine environment, a major source of radionuclides is the releases from European reprocessing plants at Sellafield and Cap de la Hague.

However, releases from the reprocessing plants have resulted in increases in levels of some radionuclides in the European Arctic seas during recent years, in particular technetium-99 and iodine-129. The present doses to the population are low but the present levels of technetium in some marine foodstuffs marketed in Europe are above the EU intervention levels for food to infants and are close to the intervention level for adults.

The technetium information adds further weight to the recommendation made by AMAP to the Arctic Council in Barrow in 2000 that:
- **'The Arctic Council encourage the United Kingdom to reduce the releases from Sellafield to the marine environment of technetium, by implementing available technology.'**

There is evidence that:
Radionuclides in sediments are now a source of plutonium and cesium-137 to the Arctic. Earlier releases such as those from Sellafield that have deposited in sediments in the Irish Sea, especially cesium-137 and plutonium, have been observed to remobilize so that these deposits are now acting as sources to the Arctic. Thus, even if operational releases of these radionuclides from reprocessing plants are reduced, releases from environmental sources such as contaminated sediment in the Irish Sea and the Baltic Sea will be observed in the Arctic.

It is therefore recommended that:
- **The Arctic Council support a more detailed study on the remobilization of radionuclides from sediment and its potential effect on the Arctic.**

It is apparent that:
There is continuing uncertainty about the amount of radionuclides present at a number of sources and potential sources in the Arctic. Access to information about civilian and military sources continues to be a problem.

It is therefore recommended that:
- **The Arctic Council promote more openness of restricted information from any sources.**

It has clearly been established that:
Compared with other areas of the world, the Arctic contains large areas of high vulnerability to radionuclides. This is due to the characteristics of vegetation, animals, human diets, and land- and resource-use practices. On land in the AMAP area, there is considerable variation in vulnerability due to differences in these characteristics. In contrast, vulnerability associated with releases of radionuclides to the marine environment is relatively uniform and similar to that for other areas of the world. Maps of vulnerable areas, when combined with deposition maps, can be useful in an accident situation. The information on vulnerability is of importance for emergency planning.

It is therefore recommended that:
- **AMAP be asked to clarify the vulnerability and impact of radioactivity on the Arctic environment and its consequences for emergency preparedness planning.**

It is apparent that:
When performing risk reducing actions, close links to assessment programs are important and interventions should be prioritized in relation to the extent and magnitude of threats posed by nuclear activities, especially in respect to accidents. Interventions themselves can also have negative effects for humans and the environment, and careful judgments have to be made together with environmental impact assessments prior to carrying out a project. It is the view of AMAP that this has not always been done in interventions adopted to date.

It is therefore recommended that:
- **Risk and impact assessment programmes be performed prior to implementation of action to reduce risk.**
- **Risk and impact assessments, including accident scenarios, be performed with regard to the transport of nuclear waste and fuel within the Arctic and nearby areas and with regard to planned storage and reprocessing within the Arctic and nearby areas.**

It is apparent that:
The protection of the environment from the effects of radiation deserves specific attention. The current system of radiological protection is entirely based on the protection of human health. This approach can fail to address environmental damage in areas such as the Arctic that have low human population densities. Recently, an international consensus has emerged that the rapid development of a system and a framework for the protection of the environment needs further effort. The International Union of Radioecology (IUR), with support from AMAP, was one of the first international organizations to promote and present such a system and framework.

It is therefore recommended that:
- **AMAP be asked to take an active part in the continued efforts to address environmental protection, with special responsibility for the Arctic.** This should include the task of adding the need for protection of the environment into monitoring strategies and assessment tools.

It is noted that:
Since the previous AMAP assessment, nuclear safety programmes have been implemented in Russia at some nuclear power plants and other nuclear installations relevant to the Arctic.

It is therefore recommended that:
- **The Arctic Council continue its cooperation with Russia to improve the safety and safeguarding of nuclear installations and waste sites.**

Human Health

The human health assessment considered health risks associated with exposure to contaminants in relation to other lifestyle factors determining health. This assessment has extended geographical coverage and confirmed the conclusions and recommendations from the first assessment.

It has clearly been established that:
The highest Arctic exposures to several POPs and mercury are faced by Inuit populations in Greenland and Canada. These exposures are linked mainly to consumption of marine species as part of traditional diets. Temporal trends of human exposures to POPs have so far not been observed. Exposure to mercury has increased in many Arctic regions while exposure to lead has declined.

It is therefore recommended that:
- **The monitoring of human exposure to mercury, relevant POPs, including dioxins and dioxin-like compounds and other chemicals of concern, be continued in order to help estimate risk, further elaborate geographical trends, and begin to establish time trends of exposure.**

There is evidence that:
Subtle health effects are occurring in certain areas of the Arctic due to exposure to contaminants in traditional food, particularly for mercury and PCBs. The evidence suggests that the greatest concern is for fetal and neonatal development. In the Arctic, human intake of substances with dioxin-like effects is a matter of concern, confirmed by recent results from Greenland. Increasing human exposure to current-use chemicals has been documented, for example for brominated flame retardants. Others such as polychlorinated naphthalenes (PCN) are expected to be found in human tissues. Some of these compounds are expected to add to the total dioxin activity in humans. The AMAP human health monitoring program includes a number of measures of effects, ranging from biomarkers of effects at the molecular level to epidemiological outcomes.

It is therefore recommended that:
- **The human health effects program developed by AMAP be more extensively applied in order to provide a better base for human risk assessment especially concerning pre- and neonatal exposures.**

It has clearly been established that:
In the Arctic, diet is the main source of exposure to most contaminants. Dietary intake of mercury and PCBs ex-

ceeds established national guidelines in a number of communities in some areas of the Arctic, and there is evidence of neurobehavioral effects in children in some areas. In addition, life-style factors have been found to influence the body burden of some contaminants, for example cadmium exposure from smoking. In the Arctic region, a local public health intervention has successfully achieved a reduction of exposure to mercury by providing advice on the mercury content of available traditional foods. The physiological and nutritional benefits of traditional food support the need to base dietary recommendations on risk-benefit analyses. The health benefits of breast-feeding emphasize the importance of local programs that inform mothers how adjustments within their traditional diet can reduce contaminant levels in their milk without compromising the nutritional value of their diet.

It is therefore recommended that:

- **In locations where exposures are high, carefully considered and balanced dietary advice that takes risk and benefits into account be developed for children and men and women of reproductive age.** This advice should be developed by national and regional public health authorities in close consultation with affected communities.
- **Studies of the nutrient and contaminant content of traditional food items be promoted in order to assess their benefits and to estimate exposures as a basis for public health interventions.**
- **Breast-feeding continue to be recognized as a practice that benefits both mother and child.** Nonetheless, if contaminant levels increase or more information indicates increased risk, the potential need for restrictions should continue to be evaluated.

It is noted that:

From the Arctic human health perspective, it is of utmost importance that considerations for global actions against POPs and mercury take into account the concerns for Arctic human health. The Stockholm Convention and the LRTAP protocols should be properly monitored in the Arctic to determine whether their implementation is effective in protecting human health.

It is therefore recommended that:

- **AMAP participate in the global monitoring of human exposure to be established under the Stockholm Convention on POPs.**
- **The Arctic Council monitor proposals for global action on mercury being undertaken by UNEP, and contribute as necessary to ensure that Arctic concerns related to human health are adequately addressed.**

Changing pathways

The assessment of changing pathways provides an introduction to the types of changes on contaminants pathways to, within, and from the Arctic that might be expected as a result of global climate change and variability.

There is evidence that:

The routes and mechanisms by which POPs, heavy metals, and radionuclides are delivered to the Arctic are strongly influenced by climate variability and global climate change. These pathways are complex, interactive systems involving a number of factors, such as temperature, precipitation, winds, ocean currents, and snow and ice cover. Pathways within food webs and the effects on biota may also be modified by changes to climate. Studies using global change scenarios have indicated the potential for substantial changes in atmospheric and oceanographic pathways that carry contaminants to, within, and from the Arctic. These effects mean that climate-related variability in recent decades may be responsible at least in part for some of the trends observed in contaminant levels.

It is therefore recommended that:

- **AMAP be asked to further investigate how climate change and variability may influence the ways in which POPs, heavy metals, and radionuclides move with respect to the Arctic environment and accumulate in and affect biota.** This will enable Arctic States to better undertake strategic planning when considering the potential effectiveness of present and possible future national, regional, and global actions concerning contaminants.

Chapter 1

Introduction

Andrew Gilman, Jens C. Hansen, Valery Klopov, and Jon Øyvind Odland

1.1. Background for the Human Health Assessment

Since its establishment in 1991, the principal task for AMAP has been the preparation of assessments of the state of the Arctic environment with respect to a range of priority pollution issues including persistent organic pollutants (POPs), heavy metals (mercury, lead, and cadmium), radioactivity, and acidifying substances. The assessments have also covered pollution issues associated with petroleum hydrocarbons and the effects of climate change, ozone depletion, and ultraviolet-B (UV-B) radiation.

The AMAP assessments also address the implications of these pollution issues for the health of Arctic peoples including both indigenous and non-indigenous residents. The AMAP Human Health subprogramme is focused mainly on the potential health affects arising from exposure to POPs and heavy metals and, to a lesser degree, UV-B radiation. Radionuclides have been addressed in cooperation with the AMAP radioactivity assessment group (AMAP, 2003a). Acidification and petroleum hydrocarbons were regarded during the first phase of AMAP (1991–1996) as having no immediate impact on human health and were consequently not addressed in the health assessment that was prepared under AMAP Phase I.

The scope of the AMAP monitoring and assessment programme embraces sources of pollution, located both within the Arctic region and at lower latitudes, and the pathways of contaminant transport to and within the Arctic. The programme addresses concentration levels in abiotic and biotic compartments of the Arctic environment and ecosystems, temporal and spatial trends, the fate of pollutants in the environment, and their effects on Arctic ecosystems including effects of exposure on human populations in the Arctic. The information compiled during AMAP Phase I was published in the AMAP Assessment Report (AMAP, 1998). That assessment constitutes an invaluable documentation of the baseline situation during the 1990s, providing a basis for the continued activities under AMAP Phase II, which started in 1998.

1.1.1. Major conclusions from AMAP Phase I

The major conclusions from the first AMAP human health assessment (AMAP, 1997, 1998) were that several peoples or communities in the Arctic are highly exposed to environmental contaminants. Persistent contaminants derived from long-range transport or local sources accumulate in animals that are used as traditional foods. Thus, variation in human exposure depends on a combination of 1) varying environmental concentrations of contaminants, 2) local physical and biological pathways that make the contaminants available, and 3) the local dietary habits of the people.

- Exposure to POPs is the primary concern. People are most exposed to polychlorinated biphenyls (PCBs) and certain pesticides due to biomagnification of these contaminants in marine food webs, which results in high concentrations in some marine mammals, birds, and, to a lesser extent, fish. The use of different foods determines contaminant intake. Some indigenous peoples are exposed to levels that exceed established tolerable daily/weekly intake levels. Transfer to the fetus *in utero* or to infants through breast milk can result in levels in newborns, which are two to ten times higher than in regions further south.
- Exposure to radionuclides is mainly through atmospheric transfer and deposition to terrestrial ecosystems. Particular soil and vegetation characteristics concentrate some radionuclides, enabling high concentrations to develop in plants and animals (reindeer/caribou, game, lichens). Arctic peoples are generally exposed to higher levels of radionuclides than people in temperate zones.
- Of the heavy metals, both cadmium and mercury tend to accumulate in the long marine food chains. Methylmercury, partly because it is fat soluble, is efficiently taken up following consumption and therefore poses the main potential risk. Like POPs, methylmercury can be transferred to the fetus and to breast-fed children, and in certain areas and within certain populations levels are high enough to indicate a need for public health measures. Although mercury levels can be high, interactions with selenium and nutrients may reduce the toxicity of this contaminant and thus also the risk to people.
- Humans in the Arctic are exposed to enhanced UV-B radiation, resulting from the release of ozone-depleting substances at lower latitudes. The main health concern relates to possible ocular damage and additional immunosuppressive effects and dermatological disorders.
- Controls on emissions have resulted in measurable reductions in inputs of some contaminants (e.g., lead, radionuclides, atmospheric sulfur, and possibly PCBs and DDT). There is considerable variation across the Arctic, however, and recycling of accumulated pools of long-lived contaminants in ocean and lake water and in sediments, can result in continued exposure long after controls have been enforced.

1.1.2. Major gaps in knowledge identified under AMAP Phase I

In the AMAP Assessment Report (AMAP, 1998) a number of gaps in understanding were identified regarding sources, pathways, and transformations of pollutants in the environment. The following needs were identified specifically for the Human Health subprogramme:

- better understanding of physiological and toxicological effects of contaminants on human populations and species identified as most at risk, especially on devel-

opment of offspring, and/or immunosuppression and endocrine disrupting properties;

- detailed information on the diet and food consumption patterns of specific Arctic populations, including necessary information on other overall health factors (e.g., smoking) which can influence contaminant exposure, to allow better estimates of dietary intakes of contaminants and permit more reliable estimates of associated risks; and
- knowledge about combined effects of contaminants on biota and humans, both at the individual and ecosystem level.

In an interim report to Ministers delivered in 2000 (AMAP, 2000), the gaps in knowledge were discussed in more detail and recommendations for research were made, which also emphasized issues associated with the:

- identification of new POPs of concern; and
- the development of quantitative models for human exposure and health outcome.

1.1.3. Health related recommendations arising from AMAP Phase I

Weighing the well-known benefits of breast milk and traditional foods against the suspected, but not yet fully understood, effects of contaminants, the recommendations arising from AMAP Phase I were that:

- consumption of traditional/country food should continue to be encouraged, with recognition that there is a need for dietary advice to Arctic peoples so that they can make informed choices concerning the food they eat; and that
- breast feeding should continue to be promoted.

To ensure the interest and active involvement of Arctic indigenous peoples and other Arctic residents it was recommended that the Arctic countries should:

- ensure the use and integration of indigenous knowledge in environmental research and policy and should promote community participation in research and policy development;
- establish a long-term communication programme to provide public information about environmental contaminants studied by AMAP, to allow access to sound and regularly updated information in an understandable language; and
- provide contaminant information for population groups with different educational levels in order to raise general environmental and scientific literacy among Arctic residents, including indigenous peoples.

In the interim report to Ministers in 2000 (AMAP, 2000) the AMAP Human Health Expert Group reviewed the conclusions from its Phase I assessment (AMAP, 1997, 1998) and found them still to be valid. However, new data and significant progress in laboratory and population studies presented in the interim report gave rise to some additional conclusions and recommendations.

- Data on exposure sources of hexachlorocyclohexane (HCH) and DDT/DDE, in market foods, water supplies, air, and industrial/agricultural workplaces in Arctic Russia should be carefully examined to identify the primary cause of elevated levels of these contaminants in human tissues.
- Because lead shot, lead shot micro-fragments, and dissolved lead found in subsistence game can be a significant source of human lead exposure it was recommended that this problem should be extensively evaluated in regions where lead shot is used for subsistence hunting.
- All countries should undertake an evaluation of their current data on dioxins, furans and co-planar PCBs and should determine the relative contribution of these chemicals to the total TCDD toxic equivalencies.
- Levels of toxaphene in human tissues should be determined in all Arctic countries and reported utilizing compound-specific chemical analyses. Data showing levels of brominated flame retardants (e.g., PBDEs) equal to those of the dominant PCBs should be followed up.
- The relationship between immune system function and POPs exposure should be more fully evaluated.
- Existing studies on mercury exposure should be evaluated for subtle effects on infant neurodevelopment and blood pressure.
- The Phase II AMAP Human Health subprogramme, with its emphasis on human health effects and monitoring of spatial and temporal trends according a specified programme of activities, should be implemented in all the key sampling areas in order to improve the scientific background for local advice to Arctic peoples.

Increasingly strong evidence is found in the Arctic, as elsewhere in the world, concerning the positive benefits of breast feeding for infant development, especially for the psycho-social development of children and the development of their immune system. Nutritional studies also demonstrate the benefits of consuming traditional food. Consequently, the main recommendation from the AMAP Phase I assessment that traditional food consumption and breast feeding are to be encouraged in the circumpolar Arctic region was repeated.

1.1.4. Human health assessment under AMAP Phase II

At the fourth Arctic Environmental Protection Strategy (AEPS) Ministerial Conference in Alta, Norway, in June 1997 Ministers endorsed the continuation of activities under AMAP for monitoring, data collection, and exchange of data on the impacts and assessment of the effects of contaminants and their pathways, increased UV-B radiation due to stratospheric ozone depletion, and climate change on Arctic ecosystems. Ministers also agreed that special emphasis is required on human health impacts and the effects of multiple stressors (AEPS, 1997).

In order to address the updated requests from Ministers, the AMAP Human Health Expert Group reviewed

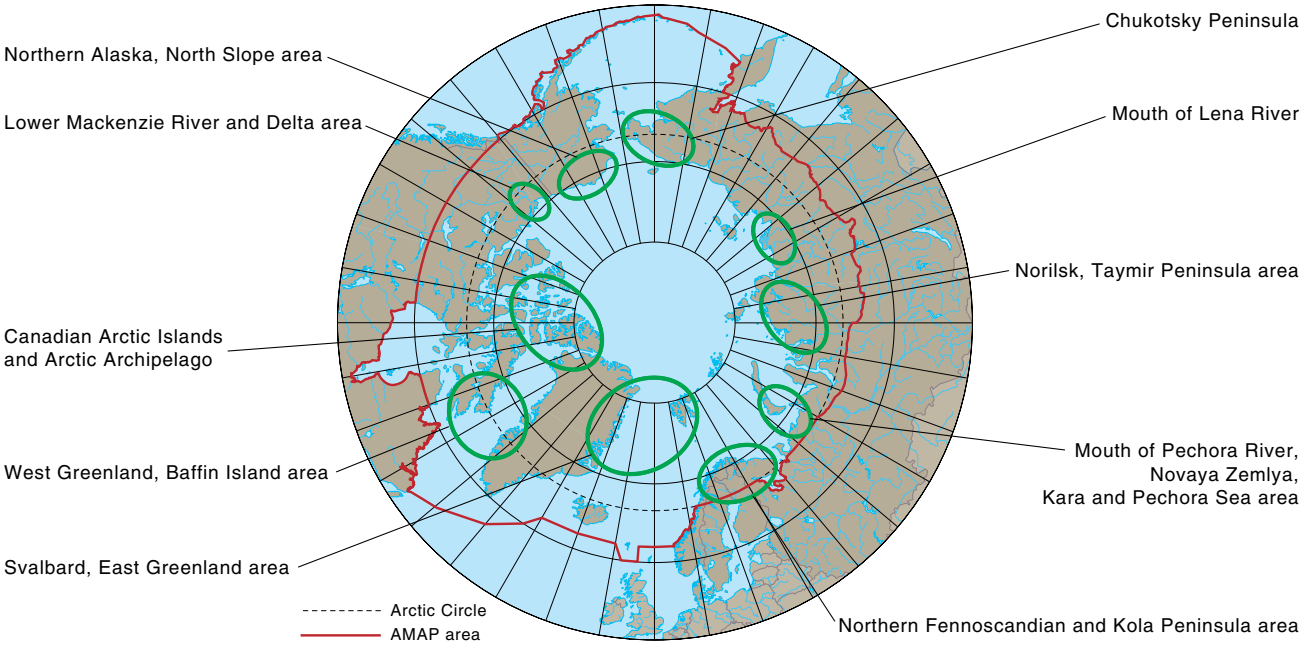

Figure 1·1. Map of 'key areas' for studies under AMAP Phase II.

and revised the original AMAP human health monitoring subprogramme that had been implemented between 1993 and 1997. An expanded core-programme of human health monitoring activities for temporal- and spatial-trend monitoring for AMAP Phase II was developed and agreed upon at the meeting of the AMAP Human Health Expert Group in Reykjavik in September 1998. A programme for human health effects monitoring was also discussed and finally agreed at the meeting of the AMAP Human Health Expert Group in Rovaniemi in January 2000. Details of the AMAP Phase II Human Health subprogramme are presented in sections B and C of the AMAP Trends and Effects Programme: 1998–2003 (AMAP, 1999).

The AMAP Human Health subprogramme focuses on exposure and the effects of different contaminants, both individually and in combination. In this context, the relevance of human exposure to new xenobiotic compounds being identified in the Arctic environment is of concern. The Human Health subprogramme is supported by information from other components of the AMAP Trends and Effects Programme, particularly those parts of the programme that are concerned with monitoring levels of POPs, metals and radioactivity in species consumed as food. To ensure effective integration between the human health studies and the other components, human health activities under AMAP Phase II have been concentrated in specified 'key areas' (Figure 1·1). In addition to the activities in these key areas, supplementary studies have been carried out in other settlement areas of indigenous and local populations of special interest.

Supporting studies are essential additional activities under the AMAP Trends and Effects Programme (see AMAP 1999, section D). These, largely research-based, activities provide detailed information that is necessary to allow a more meaningful interpretation of the results of the monitoring programme. Some of the main supporting studies of relevance to the human health assessment concern dietary surveys. These studies help to provide the basis for contaminant intake estimation and for dietary advice to Arctic peoples so that they can make informed choices concerning the food they eat. Supporting research is needed to provide local health authorities with scientifically documented indications concerning possible needs for regulatory intervention.

1.2. The concept of combined effects

Environmental exposure of human populations to a single chemical pollutant is rare (generally only occurring in accidental or occupational scenarios); environmental exposures are almost always to mixtures of substances. As a result, the interactive toxicity of the combined exposure is of utmost importance from a public health point of view. While the effects of individual pollutants and mixtures can be studied in controlled tests in research laboratories, it is very difficult to examine the effects of single substances on human populations. Epidemiological studies usually provide information on combined effects. This is true even where it is intended to study single compound effects by eliminating confounding factors. As the overall exposure situation usually varies from one population to another, this mix of contaminants may explain the often-contradictory findings from epidemiological studies endeavoring to report on effects of single components.

Animal studies and *in vitro* tests have demonstrated that exposure to a mixture of chemicals can produce additive, synergistic, or antagonistic effects. This is most likely also to be the case with humans. The sum effect of exposure to chemicals is also influenced and modified by genetics, nutritional status, and lifestyle.

Environmental factors may influence health in both a positive and a negative way. From a public health perspective, a major toxicological issue is the possibility of unusual toxicity due to interactions of a multitude of toxic chemicals and physical stressors at levels that are

normally considered harmless for individuals. In this connection, the occurrence of chemically induced hormesis should be mentioned. Chemical hormesis refers to the occurrence of a biphasic dose-response relationship in which higher doses cause an inhibitory effect and lower doses cause a stimulatory effect (Calabrese *et al.*, 1987). The phenomenon has been reported widely in the biological literature during the last twenty years, but has in general been neglected in toxicology. Hormesis has been reported in both plants and animals, with a wide variety of exposures, e.g., to radionuclides, heavy metals and POPs. Of great interest is the finding that the hormetic mechanisms that determine the threshold for physical or chemical toxicity can be mitigated by other chemical and physical agents, resulting in highly accentuated toxicity. This should be taken into account especially when making risk assessments at low levels of exposure to combinations of chemicals. Recognition of the existence of cellular and tissue hormesis provides a mechanistic basis to evaluate thresholds of toxic effects, enabling consideration of specific identifiable adverse health effects of low levels of exposure to chemicals in the environment (Mehendale, 1994).

The combined effect of the actual chemical mixture is a result of interactive processes between the chemical and physical stressors and biological receptors. Interactions can be anticipated between:

- individual contaminants in a mixture
- a mixture of contaminants and radiation (ionizing and UV)
- a mixture of contaminants and nutrients
- radiation and nutrients

The sum effect of these interactions may be observed at different levels:

- molecular
- cellular
- organ
- individual
- population

Prerequisites for understanding the combined effects of environmental stressors are the development of mechanistic effect models for individual contaminants and for the mixtures of contaminants prevalent in the environment, and the conduct of studies of genetic polymorphism in populations in order to describe individual genetic susceptibility to adverse effects from contaminants.

Some individuals are more sensitive to xenobiotic compounds than others, and this may in part be due to differences in metabolic capacity. Based upon *in vitro* and *in vivo* studies, e.g., transgenic animal studies on the pharmacokinetic properties of various contaminants, a risk profile for a particular exposure situation may be designed for both high and low exposure scenarios.

In addition, identification of reliable and applicable biomarkers of effects is needed in order to estimate the validity of assumptions of effect. Although toxicology and biomarker research provide the theoretical background for the understanding of combined effects, their applicability for actual exposure situations among Arctic populations requires additional information. Evaluation of the combined effect of pollutants in the Arctic must be based on extensive environmental and biological monitoring, and on nutritional, epidemiological, and socio-economic data.

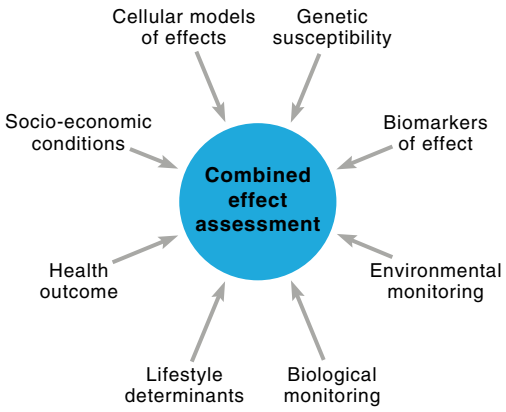

Figure 1·2. Disciplines involved in combined effects studies.

The disciplines needed for a thorough evaluation of combined effects are represented in Figure 1·2.

1.2.1. Combined effect assessment

Assessment of combined effects requires information from a range of different types of study.

1. **Cellular models of effect**. Toxicological studies of single compounds and mixtures at the molecular and cellular level.

2. **Genetic susceptibility**. Genetic polymorphism in relation to genetic epidemiology.

3. **Biomarkers of effect**. Identification of relevant and validated biomarkers of exposure and their *in vivo* relation to effects at specific exposure levels (effects monitoring).

4. **Environmental monitoring**. Identification and ranking of sources of exposure and geographical variation. Identification of risk areas, temporal trends, and estimation of possible (daily intake) exposures.

5. **Biological monitoring**. Repeated determination of contaminant concentrations in biological index media to determine individual and population exposure level and internal dose. Identification of risk groups, and establishment of time trends.

6. **Lifestyle determinants**. Identification of lifestyle factors that may influence contaminant effects, e.g., nutrition, obesity, smoking, alcohol/drug consumption and occupation.

7. **Health outcome**. Surveillance of health outcomes in priority categories such as: birth defects, reproductive disorders, cancer, immune function disorders, kidney function disorders, liver function disorders, lung and respiratory diseases, and neurological disorders.

8. **Socio-economic conditions**. Description of general living conditions in countries, regions, and ethnic groups. Nutritional status, sanitary conditions, drinking water quality, air quality, housing conditions, use of traditional and imported foods, community integrity, availability of health care and education, and economic status, etc.

1.3. The scope of the AMAP Phase II Human Health Assessment Report

From a public health perspective, the human environment is the sum of physical, chemical, biological, social, and cultural factors that influence people's health.

This report concentrates on the concept of the combined effects of environmental contaminants, as requested in the AMAP Ministerial mandate. It addresses the modifying influences, both positive and negative, of other environmental factors that affect the human condition and underline the need for a global assessment of the linkages between health and the environment. This approach to a holistic assessment of the health–environment interaction is a huge task.

From both a scientific and ethical perspective, the following issues need to be considered:

- the sum effect of environmental contaminants on human health;
- the possibilities for examination of health impacts from the environment;
- the relevance of existing tolerable daily intake (TDI) values for Arctic peoples;
- the adequacy of existing information on the populations most at risk; and
- mitigation, the ways people can reduce their exposures.

This report re-evaluates the relationship between environmental contaminants and health status for people in the Arctic by integrating what is currently known about multiple stressors. The assessment builds on data generated and experience gained during AMAP Phase I, but is mainly based on new data from studies conducted during AMAP Phase II, and other recent scientific work.

Within the limitations imposed by the (understandably) inadequate information base and still significant gaps in knowledge, this report will attempt to summarize the present state of knowledge in the field of environmental medicine in the Arctic. Hopefully it will constitute a further step toward a better understanding of the relationship and linkages between health and environment in the Arctic, and provide an improved background/baseline for further information gathering. The key objective of the AMAP human health assessments is improved health status among Arctic peoples (Figure 1·3).

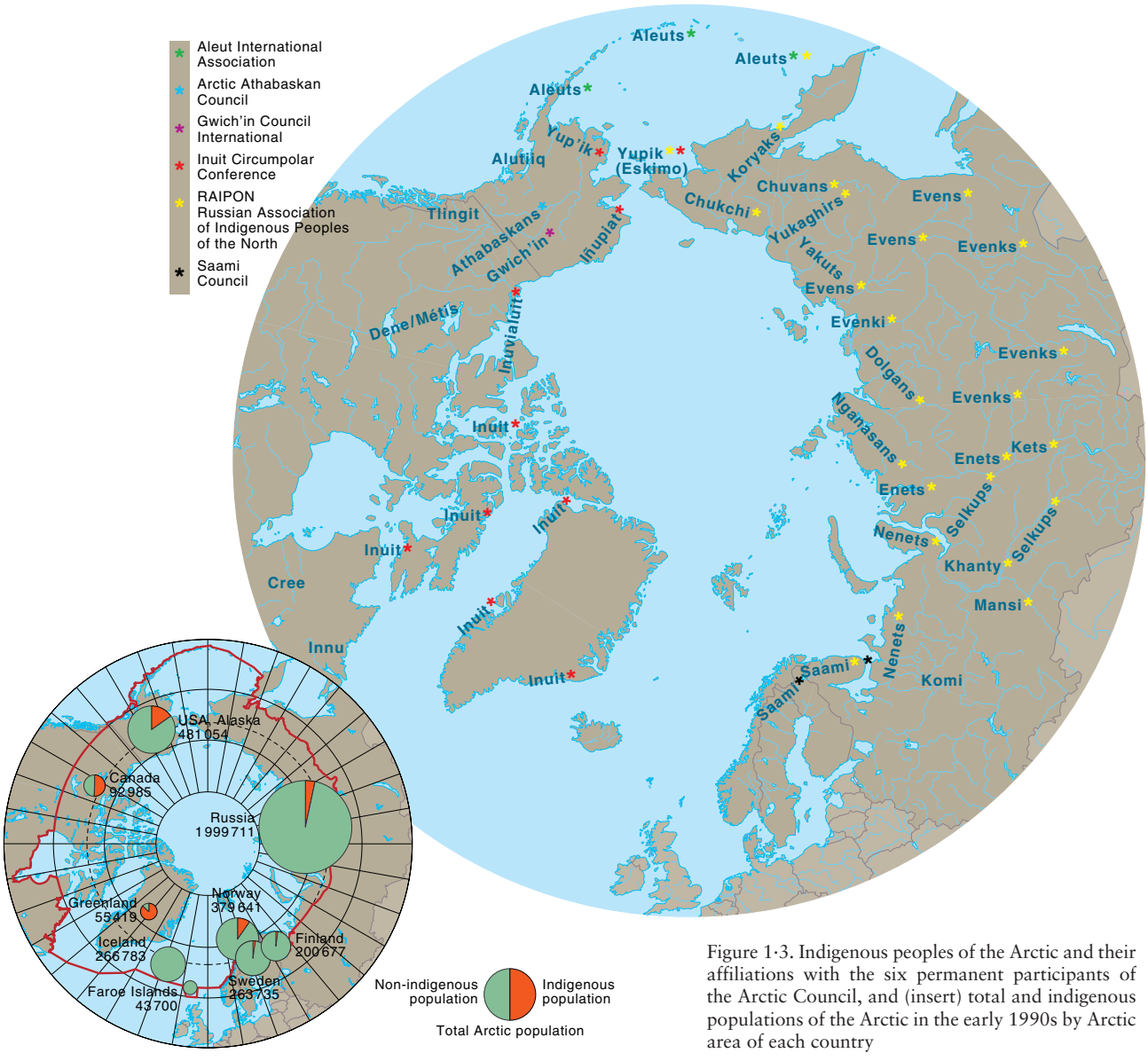

Figure 1·3. Indigenous peoples of the Arctic and their affiliations with the six permanent participants of the Arctic Council, and (insert) total and indigenous populations of the Arctic in the early 1990s by Arctic area of each country

Chapter 2

Ethno-cultural Adaptation of the Peoples of the Arctic Region

Peter Bjerregaard

Summary

The Arctic regions of the world share many common characteristics but there are significant social, cultural, and political differences. The indigenous peoples of the Arctic include the Inuit and Iñupiat who inhabit the northern part of the North American continent, and Greenland; the Saami of northern Scandinavia, Finland, and the Kola Peninsula; in northern Russia the Yakuts together with some sixteen indigenous minorities, ranging from the Saami and Nenets in the west to the Chukchi and Eskimo (or Yupik) in the east; the Aleuts, Yup'ik, Athabaskans and other indigenous groups of Alaska; and in Canada the Dene and Yukon First Nations Indians, who occupy the northwest Arctic and subarctic regions along with the Métis (Figure 1·3). The indigenous peoples of the Arctic are estimated to comprise nearly 650 000 individuals, most of whom live in northern Russia. Past colonization and the resulting contact with outsiders had a major negative impact on the health of these peoples causing devastating epidemics, which resulted in severe depopulation. After a period of stabilization and recuperation, societal changes during the last 50 years have had both positive and negative impacts on health. Life expectancy has increased, infant mortality and the importance of infectious diseases have decreased dramatically, and health care has improved, while psycho-social health has generally deteriorated. Chronic diseases such as cardiovascular disease and diabetes have increased due to changing lifestyles. In some areas, the indigenous peoples enjoy the same level of health as the non-indigenous populations, but in most areas their health is significantly poorer.

2.1. Population overview

The Arctic regions of the world share common characteristics such as sparse population, a hostile climate, similar geographic features, and characteristic seasonal extremes of daylight hours. Within the Arctic, however, there are significant differences in political systems, languages and culture, and economic and service infrastructure.

The inhabitants of the Arctic include a diverse group of indigenous peoples, located near the Arctic Circle in Norway, Sweden and Finland, and in the Russian Federation from the Norwegian border to the Chukotka region, from Alaska to Canada, and eastward to Greenland. The lives of the indigenous peoples and other Arctic inhabitants are closely linked to natural resources that provide food for nourishment, and spiritual and cultural connections to the land (AMAP, 1997). Arctic indigenous peoples rely on the food that they hunt and harvest from the land, as it provides for much of their nutritional intake and their cultural identity. These natural resources may also be important for economic reasons.

Over the last 50 years, the population of most regions of the Arctic has dramatically increased. Much of this increase is due to the reduction in infant mortality, and the reduction in mortality from infectious diseases, particularly tuberculosis and the vaccine preventable diseases of childhood. Safe water supplies and improved sewage disposal have also contributed to the reduction in disease, and the development of rural hospitals, and in some regions, community-based medical services have provided improved care in the event of injuries or illness. All regions have developed greatly improved transportation infrastructure, with the resulting availability of western food items, tobacco, and alcohol on a scale not previously possible. In addition, communication technology has made western culture visible in even the most remote settlements. To facilitate the provision of services and economic opportunities Arctic indigenous populations are, in most regions, encouraged to live in fixed settlements. Survival often depends on a complex mix of government-funded economic support, combined with primarily service-based employment in schools, sanitation facilities, and transportation infrastructure. In this setting, the local culture, including related subsistence food gathering, is frequently the primary source of psycho-social support for a community. The local culture is subject to stress by competing western culture and, in some areas, commercial resource exploitation. Concerns for the security of traditional food resources due to contaminants and the presence of zoonotic and parasitic diseases associated with some traditional food species and preparations (e.g., trichinosis, echinococcosis or botulism) also increase this stress on indigenous culture. As a result, erosion of cultural support, decrease in traditional activities, and substitution of western foods for traditional foods have resulted in changes in causes of morbidity and mortality of Arctic populations. In some respects, the morbidity and mortality rates now more closely resemble western populations. However, differences between countries, and differences between cultural groups within each country, make generalizations concerning social and health changes in the Arctic indigenous peoples difficult.

The peoples of the Arctic were described in detail in previous AMAP assessments (AMAP, 1997, 1998). Sections 2.1.1. to 2.1.3. provide brief descriptions based mainly on these sources.

2.1.1. Arctic North America and Greenland

There are three groups of Alaska Natives, commonly called the Aleuts, Inuit (or Eskimo), and Indians. About 73 000 individuals belonging to these groups live in Arctic Alaska, where they make up 15% of the total population. In Canada, three groups of indigenous peoples

are recognized: the Inuit, the Métis, and the First Nations, who in the Arctic include the Dene, Gwich'in and Athabaskans. Together, the indigenous groups make up 47 500 people or about half the population of Canada north of 60º N. The total population of Greenland is 56 000 of which 90% are Inuit.

Life expectancy at birth is consistently lower among the indigenous peoples of North America and Greenland than in the general populations of Denmark, Canada, and the United States. Although the incidence of and mortality from infectious diseases have decreased substantially, they remain considerably higher than in the general populations of the three countries. Mortality from accidents and suicide is high, particularly among men, and this contributes to the low life expectancy (see chapter 3).

2.1.2. Scandinavia, Finland, and the Kola Peninsula

The Saami live in northern Norway, Sweden, Finland and the Kola Peninsula of northwest Russia. The Saami population is estimated to total some 50 000 to 70 000 persons; they constitute a minority in all four areas. The Saami make up about 2.5% of the population in the Arctic areas of Norway, Sweden, Finland, and the Kola Peninsula.

There are no socio-medical differences between the Saami in Finland, Norway and Sweden and the non-indigenous population. Access to health care is identical for both population groups and life expectancy is the same.

2.1.3. Northern Russia

According to the 1989 census, the total population of Arctic Russia is approximately 2 million people, of whom approximately 67 000 are indigenous minorities: the Dolgans, Nganasans, Nenets, Saami, Khanty, Chukchi, Evenks, Evens, Enets, Yupik, Yukaghirs, Selkups, Chuvans, Mansi, Kets, and Koryaks. The Yakuts, who number approximately 350 000 people, are too numerous to be considered a minority, but their traditional way of life is similar to that of the other indigenous groups in the area.

Mortality and morbidity statistics indicate a poor health situation relative to both the general population of Russia and in comparison with other indigenous peoples of the Arctic. Life expectancy is 10 to 20 years lower than the Russian average. Injuries, infectious diseases, especially tuberculosis, cardiovascular disease, parasites, and respiratory disease are common causes of death. Many health problems are related to alcoholism. Infant mortality is very high.

2.2. Health and socio-cultural changes in the Arctic: A case study of the Inuit

This chapter cannot adequately describe all the social and cultural changes that have occurred among the Arctic indigenous peoples, but rather will use as an example the situation of the Inuit to describe briefly the effects of social and cultural change on health.

Among the indigenous North Americans, the Inuit were the first to encounter Europeans, and also the last. The first Europeans to come into contact with the Inuit were the Vikings who established a colony in Greenland toward the end of the tenth century. At its height, in the twelfth century, the population of the Norse colonies in Greenland reached as many as 5000 to 7000 inhabitants. However, for a variety of reasons, including climate change, the Viking settlements were vacated, or had died out by the late fifteenth century. By that time, European whalers had already been hunting in the Baffin Bay area off the coast of Labrador and Greenland for more than a hundred years. The exploration of the Arctic started in the sixteenth century and colonization followed. However, areas of the central Canadian Arctic and northern Greenland remained unexplored until the early part of the twentieth century.

Contact and colonization were accompanied by cultural change, which proceeded at a different pace across the circumpolar region. The Inuit adopted some items of European material culture and Christianity replaced traditional beliefs, but the hunting lifestyle remained largely intact well into the twentieth century in most regions. The population expanded rapidly during and after the Second World War, when economic development and military activities in Alaska, northern Canada and Greenland greatly increased the influence of western culture on the indigenous Inuit populations.

The social changes that resulted from contact with non-Inuit people have followed the same general outline in all Inuit communities. The changes can generally be divided into three phases: 1) an initial period of profound and disruptive transformation, 2) a period of relative stability and, 3) a second period of intense transformation and adaptation (Bjerregaard and Young, 1998). The initial phase was the period from the first contact until essentially the whole Inuit society had adopted Christianity. This took place at different times, in West Greenland from the mid-seventeenth to the mid-nineteenth century, but much later in other regions. The third phase started in the 1950s and is still ongoing. Over a very short period, the subsistence-oriented traditional way of life has given way to wage earning and a western lifestyle.

2.2.1. Phase 1 and 2

The size of the Inuit population in North America, including Greenland, was estimated to be about 74 000 during the sixteenth to eighteenth centuries. The population declined throughout the nineteenth century and by 1900 it is believed to have reached its nadir at 35 000. The population slowly recovered during the twentieth century, reaching 52 000 by 1950 and reaching the pre-contact level by 1970 (Ubelaker, 1992). Introduced diseases, especially infectious diseases, played a major role in the post-contact depopulation. Influenza, smallpox, and measles spread rapidly through populations that had no prior immunity.

Specific information is available from a few locations. Before contact, approximately 4000 people inhabited St. Lawrence Island. In 1878, a combination of famine and epidemic struck the island and two thirds of the population perished. The population decline continued, to 222 in 1917, since when the population has still not recovered to its pre-contact size. In Canada, the Inuvialuit suffered severe depopulation due to diseases introduced by American whalers in the late nineteenth century.

The first epidemic (of smallpox) was reported in Greenland in 1734 only a few years after the coloniza-

tion. It was followed by the epidemic of 1800 in which the population of entire districts perished. During the following centuries recurrent epidemics of respiratory infections, influenza, smallpox and typhoid fever killed a substantial proportion of the population. The last epidemic of smallpox took place in 1852 although a few isolated cases were seen later (Gad, 1974; Bertelsen, 1943).

A number of major epidemics swept through most Inuit communities of Alaska. The indigenous people of Alaska have borne an exceptionally heavy burden of disease and disability since early contact (Fortuine, 1975). With the arrival in Alaska of the Russians and other European explorers, beginning in the mid-eighteenth century, new factors began to influence the traditional way of life.

In Alaska syphilis was the first major disease to spread, reaching epidemic proportions in the Aleutian Islands and in southeastern Alaska during the Russian period. Two epidemics rank among the most significant single events in the history of the peoples they affected. The first was the smallpox epidemic of 1835 to 1840, and the second was the influenza epidemic, 'The Great Sickness' of 1900. Thousands of people died, and entire villages were wiped out. Another influenza epidemic struck in 1918 to 1919 (Fortuine, 1975).

When exactly tuberculosis was introduced is uncertain, but by the late eighteenth century it was well established in the general population and remained active for the next 150 years. The tuberculosis epidemic reached its peak after the end of the Second World War, and was associated with one of the highest death rates from tuberculosis recorded worldwide. Gonorrhea and alcohol abuse were also prominent causes of major ill health in Alaska during the nineteenth century (Fortuine, 1989).

The disruptive first phase of social change was followed by some years of relative tranquility. During this second phase of development, epidemics of respiratory infections, diarrhea, whooping cough, diphtheria, rubella, mumps, and poliomyelitis, to name but a few, continued to be common. For several epidemic diseases the Arctic populations were too small to act as reservoirs for the infectious agent and the diseases were reintroduced from outside at different times. Typhoid fever, dysentery, hepatitis, and meningitis were endemic. Starvation and chronic malnutrition were still common but tuberculosis was the most serious threat to public health. Nevertheless, despite all this, fertility increased while mortality decreased, resulting in a general growth of the population during the second period.

2.2.2. **Phase 3**

By the end of the Second World War, the regions inhabited by the Inuit differed considerably with respect to their degree of integration into modern western society. However, in all Inuit communities it is the last 50 years that have completed the change from the relatively isolated, self-reliant communities based on hunting and fishing that existed at the time of the first contact with Europeans to communities that are integrated within their respective national states.

Among the most important changes that have affected health are the transition from subsistence hunting and fishing to an economy based on wage earning, a comprehensive change of infrastructure and housing, generally brought about with the Inuit as spectators, and increased contact with the rest of the world through travel, radio and television, plus an unprecedented population growth and relocation to larger communities. Last but not least, non-Inuit people have poured into the Inuit communities and taken over many of the well-paid jobs and influential positions that were created in the modernization process. Through self-government and Home Rule the Inuit are gradually redressing the balance and taking charge of their present and future. Other changes with more direct effects on health and disease are dietary changes, along with an increased reliance on store bought food, a more sedentary lifestyle, increased access to alcohol and tobacco, and improvements in comprehensive health care.

During the first few years after the Second World War, mortality decreased dramatically while fertility continued to increase resulting in a sharp increase in population size. This was a period of receding epidemics. However, measles epidemics occurred for the first time in many places and caused numerous deaths. During the 1950s tuberculosis and acute infections lost their importance as causes of death. Mortality decreased until around 1970, first rapidly, then later at a relatively steady rate (Bjerregaard and Young, 1998).

Since the 1970s, suicide rates have increased. Suicide rates are exceptionally high in the circumpolar indigenous populations and are higher among the Greenlanders than among the Inuit of Alaska and Canada (see chapter 3). Contrary to the pattern in most western countries, where the suicide rates increase with age, it is predominantly young people, and more often men than women, who commit suicide in the circumpolar populations. The temporal association of the rising suicide rate with rapid societal development in many communities lends itself to a causal relationship, but it is not clear what specific aspects of the modernization process increase suicidal behavior in young people.

2.2.3. **Consequences of recent societal development on health**

In much of the literature, rapid socio-cultural change is invariably seen as detrimental to physical and mental health. Change, however, is in itself not necessarily stressful (Bjerregaard and Curtis, 2002). In the recent history of indigenous peoples change has often been associated with powerlessness and frustration, but it has also offered increased opportunities for survival and economic as well as cultural development. This section describes some examples of recent changes in Inuit societies resulting in negative health consequences and some resulting in positive health consequences (Bjerregaard and Young, 1998).

The change from an economy based on hunting to modern wage earning has resulted in a decreased mortality from accidents. The traditional Inuit life was extremely perilous and many hunters died at an early age leaving wives and children in poor social conditions. With modern hunting methods and weaponry, combined with traditional methods, the hunter-gatherer role is overall more successful than in previous centuries. However, an increase in accidental deaths from all-terrain vehicles and snow machines is seen in Alaska (Smith and

Middaugh, 1986; Landen *et al.*, 1999). Alcohol plays a major role in overall accident causation.

Housing conditions, sanitation, and food security have generally improved. Household sizes are smaller and houses are larger with more rooms, thus decreasing the transmission of infectious diseases, in particular tuberculosis and other respiratory infections. Sanitation has improved in towns and most villages, thereby decreasing exposure to several microorganisms. Nutrition has generally improved, if not qualitatively then at least with respect to reliability. Seasonal starvation has disappeared from all Inuit communities thus increasing general resistance to infections.

Increased contact with the rest of the world through travel and migration has brought a number of infectious diseases to the Inuit communities that had previously been relatively spared; these include measles, gonorrhea, syphilis, and HIV/AIDS.

The influx of non-Inuit people, rapid growth of the Inuit populations, and increasing population concentration in larger communities of up to several thousand inhabitants have profoundly altered the social structure of Inuit communities. Together with other socio-cultural changes this has resulted in acculturative stress and increased prevalence of mental health problems, including suicide.

Dietary changes leading to an increased reliance on store bought food, an increasingly sedentary lifestyle, and increased access to tobacco have resulted in the emergence of chronic diseases well known in western societies, e.g., obesity, diabetes, atherosclerotic heart disease, and dental caries.

Increased access to alcohol and tobacco has led to an excessive use of these substances in most Inuit communities. Although in some regions alcohol importation to villages is not allowed, alcohol abuse is, in general, a major contributing factor to the high prevalence of violence, suicide and social pathologies among the Inuit. In some communities, alcohol addiction is considered to be the main health problem.

Last but not least, along with infrastructural and socio-cultural changes, the Inuit have achieved general access to modern health care systems. Although accessibility to health care services is less for Inuit living in villages than for the predominantly urban populations in the southern regions of Arctic countries, and although tertiary level care usually involves travel to hospitals in the south, the health care services have been important in reducing morbidity and mortality from tuberculosis and several other infectious diseases, in reducing perinatal mortality, and in improving dental health. The health care services have also played a substantial role in improving the quality of life for many people due to early treatment of disabling diseases.

2.2.4. Lifestyle changes, cardiovascular disease, and diabetes

Traditionally, the Inuit appear to have been protected from atherosclerotic diseases and diabetes. This may have been the result of a lifestyle and diet which had been characterized by a high intake of marine mammals and fish, a high level of physical activity, and low tobacco consumption, all of which contribute to a low cardiovascular risk profile. Recent studies indicate that, like certain other indigenous populations, the Inuit may be genetically predisposed to atherosclerosis thus supporting the idea that the low prevalence of disease must be caused by a protective lifestyle (Bjerregaard and Young, 1998; Hegele *et al.*, 1997).

Recently conducted dietary surveys indicate that consumption of marine mammals and fish is greater among the older members of the population, and considerably less among some of the younger members of the same population. Nevertheless, young Inuit still consume more marine food than the average westerner (see chapter 7).

It is reasonable to believe that the mechanization of many tasks and the change to sedentary occupations have not been sufficiently counterbalanced by physical activities during leisure time. The widespread use of tobacco is another factor with a significant impact on the disease and mortality pattern. Cigarette smoking is a major contributory factor in several cancers. It is also an important contributing factor to cardiovascular disease and chronic lung disease, both of which are emerging health problems among the Inuit.

The traditional diet is nutritious and is believed to reduce the risk of developing atherosclerosis and diabetes. From this perspective it is disturbing to note a decreasing preference for traditional food items among the younger adults. Further details of this transition from traditional to non-traditional diets can be found in chapter 7.

Furthermore, as a result of global pollution by polychlorinated biphenyls, pesticides and mercury, the marine mammals that make up a substantial proportion of the traditional diet of the Inuit have become contaminated. Blood concentrations of several organochlorine compounds and mercury are often above established levels of concern for Inuit in Greenland and eastern Canada (see chapter 5). Potential health consequences include sex hormonal effects, damage to the immune system, and transgenerational effects (see chapter 6). Clinical overt damage to health, however, has not yet been demonstrated (AMAP, 1998).

2.3. Conclusions

The indigenous peoples in the Arctic are in most countries a minority of the population. Their living conditions, dietary habits, employment, subsistence activities, and access to health care often differ from those of southern populations. In most regions of the Arctic, the health of the indigenous peoples is worse than that of the general population of the countries in which they live, although the gap has narrowed considerably in recent years.

During the last 50 years the indigenous peoples in the Arctic have experienced large increases in life expectancy as a result of decreasing infant mortality and the successful prevention and treatment of many infectious diseases, among other things. Whether health in general has improved or declined due to the recent societal changes depends on whether the positive or negative is emphasized; a simple answer is impossible to give. It is undeniable that physical survival has increased in all age groups, but it has probably been at the expense of mental and social health. The disease pattern of the future will depend on whether the current lifestyle trends can be shifted in a more healthy direction. The rapid changes in culture and disease spectrum require a major change in health care for those indigenous peoples concerned.

Chapter 3

Health Status of the Arctic Residents

James Berner

Summary

In recent years there has been significant improvement in the general health of the indigenous peoples of the North. However, significant health disparities remain between indigenous residents and majority populations. For instance, shorter life expectancy and mortality related to suicide and injuries are still more frequent. Lifestyle related conditions, such as obesity, diabetes mellitus, and circulatory disease have become more frequent. Since the age structure in the indigenous populations includes a large number of young persons, preventive measures are very important in reducing the burden of these diseases.

3.1. Introduction

The health status of Arctic residents, as it is for all people, is the result of the complex interaction between environment, genetics, nutrition, psychological factors, and economic conditions.

The Arctic is not a homogeneous region, and Arctic residents, while fewer in number than in temperate regions, are extremely diverse, with very few features in common except latitude of residence and hours of daylight. Some Arctic regions are economically depressed, such as much of Arctic Russia, while most others do provide at least adequate economic opportunities and support for residents. Some regions do not keep ethnic-specific health data, while others separate health data by ethnic group. Some countries combine the sparse Arctic population data with that of the remainder of the country so that regional differences in health status are not discernible. In some regions, data are difficult or impossible to obtain.

Despite these limitations, examination of available health status information can provide useful insights into major public health problems, and can suggest where, over time, useful information on the possible health impact of contaminants might be obtained. As this chapter will show, there are significant differences in the age structure of the various Arctic populations. Indigenous (or largely aboriginal) populations such as those found in Alaska, Greenland, and Canada (the Yukon, the Northwest Territories, Nunavut, and northern Quebec and Labrador – referred to collectively as Arctic Canada) have a larger percentage of younger persons and fewer elderly persons than the non-indigenous populations of Iceland, Sweden, Norway, Finland, and the Faroe Islands. For this reason, most population data are age-adjusted to compensate for these differences. Data for Greenland are presumed to represent the dominant (90%) Inuit population.

This chapter does not include information on the current health care system in each country, nor on access to health care, as these are both outside the scope of AMAP. Rather, it reviews current population structure, current population health indicators and selects indicators of maternal and child health morbidity and mortality for the populations of Arctic countries. A section highlighting the differences in health status of Arctic indigenous residents is included to focus attention on the most vulnerable Arctic populations.

Among Arctic populations, advances in acute care, in public health practices, such as childhood immunization, prenatal care, safe water supplies and sewage disposal, family planning, antibiotics, and in improved transportation and communication have considerably changed the likelihood of survival to an older age, and have improved basic health for Arctic children and adults. As an example, by the mid-1990s, the infant mortality rate in Alaska Native infants was approaching that for the United States as a whole (Figure 3·1).

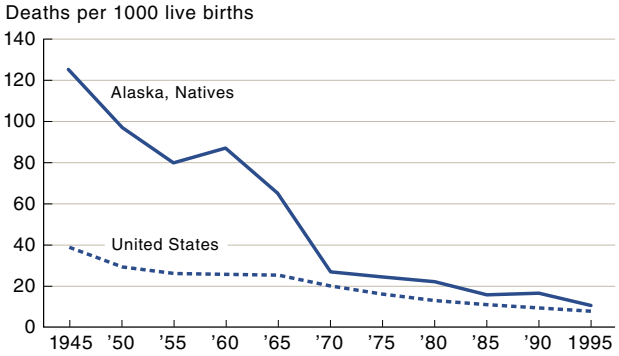

Figure 3·1. Infant (under 1 year) mortality rates in the United States general population and in Alaska Natives, 1945 to 1995. Source: Alaska Area Profile FY2000.

This improvement in the infant mortality rate is related to safe water supply, sanitation improvements, and on-site village primary health care providers, which were all steadily improved in the period 1960 to 1970. These, along with improvements in transportation, infant immunizations, and medical care have lowered the infant mortality rate to present levels.

3.1.1. Data sources

The primary data sources utilized in this section include NOMESCO (2001), NWT (1999), the World Health Organization, the State of Alaska, and other cited literature.

A series of basic health status indicators are utilized, as well as trend data, where available. Data used in this section for Canadian Arctic residents are labeled 'Northwest Territories (NWT)'. During the period reflected by the data, the Northwest Territories contained virtually all of Arctic Canada (excluding the Yukon). In 1999, a large part of the Northwest Territories (some 60%, or one fifth of the Canadian landmass, including most of the Canadian Arctic islands) became the new territory of Nunavut.

Data from sources such as published studies of Arctic populations, which usually focus on single conditions or a narrow set of risk factors, are also utilized. Such data are usually representative of a single period of time, and are often not directly comparable in all respects with other populations. Often, however, such data may represent the only information available.

3.2. Population demographics

3.2.1. Population structure

The age composition of the residents of Arctic countries varies greatly, as can be seen in Figure 3·2. Due to their shape, these representations are often referred to as population pyramids.

A population pyramid is influenced at its base by the number of women in the 15 to 45 year age ranges, the most common ages at which women bear children, and the number of children each woman bears. The base is also affected by infant mortality. The middle portion of the pyramid can be decreased by any major source of mortality in the early and middle adult years. The narrowing of the pyramid for the elderly ages reflects the incidence of chronic disease, access to medical care, and the quality of medical care. A stable population, reproducing at a replacement rate, with no major sources of unusual premature mortality, would have a population pyramid tapering only slightly from its base to the fifth decade, when it would more rapidly attenuate to the eighth decade. A population pyramid can effectively predict numbers of population in certain age groups, aiding in planning the infrastructure for the country or area concerned.

From these figures, for the population of Alaska Natives, the Canadian Arctic, and Greenland, the average

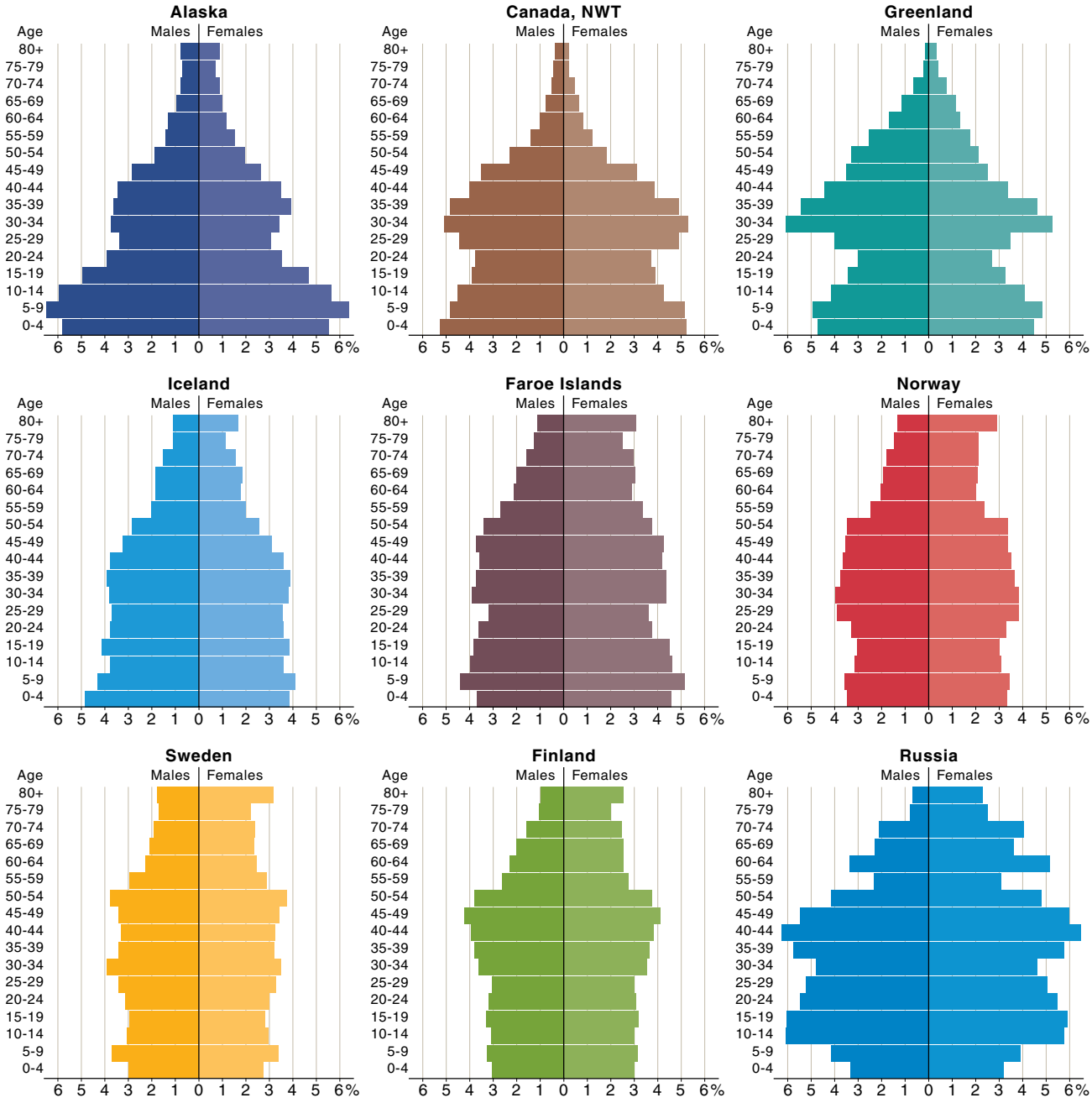

Figure 3·2. Population pyramids for Alaska (1998), Canada (NWT, 1996), and Arctic countries (1999). Source: Alaska Area Profile FY2000 (Alaska); NWT, 1999 (Canada); NOMESCO, 2001 (Faroe Islands, Finland, Greenland, Iceland, Norway, and Sweden).

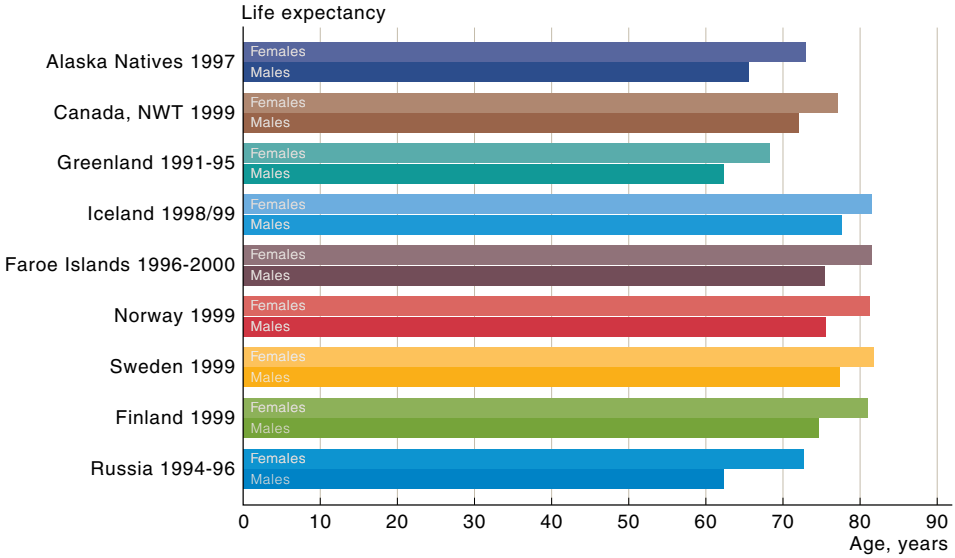

Figure 3·3. Life expectancy in the 1990s of Alaska Natives, residents of NWT/Nunavut in Canada, and general populations of other Arctic countries. Source: WHO Statistical Database; US IHS, 2000; NWT, 1999; NOMESCO, 2001.

age is younger, the proportion of children greater, and the proportion of elderly less than the reference population statistics for the other countries shown. The population structure for Russia is unique in this dataset and shows a lower proportion of both children and the elderly, the highest average age, and a smaller man to woman ratio, this is primarily due to the absence of older men, one effect of devastating wars, where several million young men were killed. The fertility rate and infant mortality rate graphs show how these factors influence the base of the Russian population pyramid (see sections 3.3.3. and 3.3.5.).

3.3. Health status indicators

3.3.1. Life expectancy

In most countries, the largest single contributor to an improvement in life expectancy is a decrease in infant mortality. Other factors include population diet, tobacco and alcohol use, lifestyle choices, access to medical care, and socio-economic factors. In Figure 3·3, the Nordic countries have a stable life expectancy for women, exceeding 80 years, with that for men about four years less. The life expectancies for the indigenous Arctic populations in other countries are considerably lower for men and women alike, one cause being higher infant mortality rates (see section 3.3.5.).

3.3.2. Maternal and infant indicators

Many persistent organic pollutants, and certain toxic metal contaminants, have the ability to act as agonists or antagonists of steroid hormones. Chronic low-level exposure to these compounds in fetuses, pregnant women, and young infants is being investigated for possible association with adverse health effects. Effects under investigation include decreased fertility, an increased likelihood of spontaneous abortion, abnormal intrauterine growth, and abnormal neurodevelopment in infancy, increased susceptibility to infection in infancy, and blood pressure elevation in children (see chapters 6 and 9). Regularly gathered health status indicators that reflect maternal and/or infant health do not provide specific data for most of these impacts, and subtle effects may be difficult to separate from the impact of confounding factors, such as prenatal use of alcohol and tobacco, breast feeding, maternal nutrition, and poverty.

In Greenland, the ratio of male to female live births has changed from 1.05 (the usual ratio for humans) to 1.02 over the past 30 years (Bjerregaard and Young, 1998). If this ratio persists it may reflect, among other influences, prenatal exposure to endocrine disrupting persistent organic chemical compounds (Bjerregaard and Young, 1998).

In western Arctic Russia, occupational stress, tobacco use, and heavy metal exposure have all been associated with adverse pregnancy outcome (see section 8.4.2.) (Odland *et al.*,1999b).

3.3.3. Fertility rates

Fertility rates are highest in Russia, Arctic Canada (NWT/Nunavut), Greenland, and Alaska (Natives) between the ages of 20 and 24, whereas in the other locations the peak fertility rates occur in the 25 to 29 year age group (Figure 3·4). A large number of factors affect fertility, especially socio-economic conditions and access to family planning. One such factor is the increasing

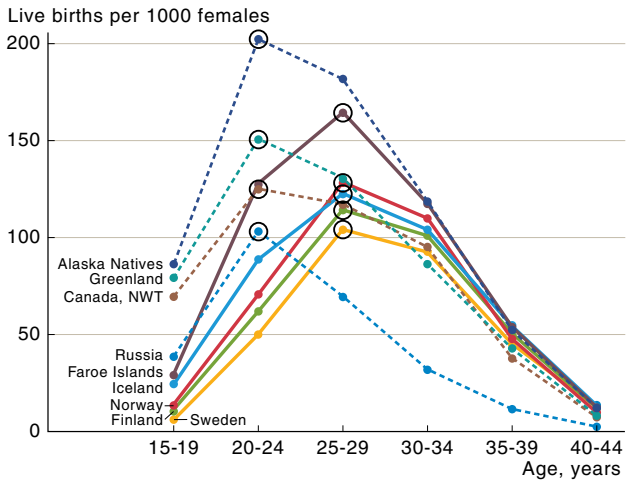

Figure 3·4. Fertility rates for Alaska Natives (1998–1999), residents of NWT in Canada (1992–1996), and populations of other Arctic countries (Faroe Islands/Greenland, 1991–1995; Iceland/Norway/Sweden, 1999; Russia, 1994–1997); circles indicate peaks. Source: WHO Statistical Database; US IHS, 2000; NWT, 1999; NOMESCO, 2001.

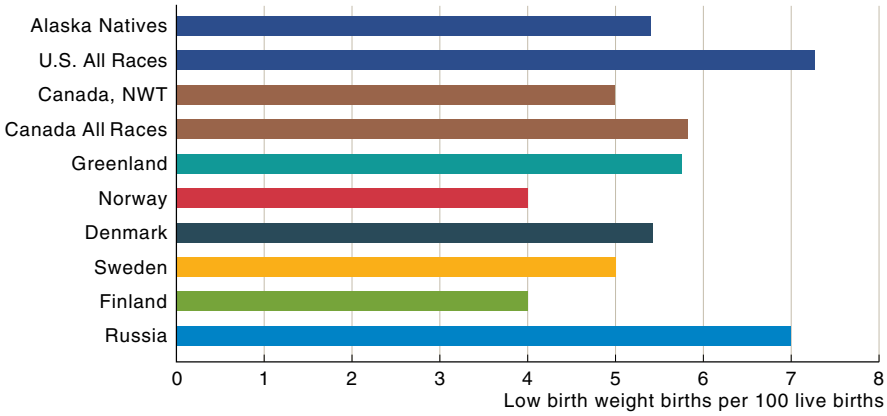

Figure 3·5. Low birth weight rates in Arctic countries (general populations: Canada All Races, 1996; Russia, 1994–1997; Sweden/Norway/Iceland/Finland/Greenland/Faroe Islands/Denmark, 1998; U.S. All Races, 1995) and some indigenous populations (Alaska Natives, 1994–1996; Canada NWT/Nunavut 1996). Source: US IHS, 2000; Health Canada, 1999; WHO Statistical Database; NOMESCO, 2001.

proportion of women in the work force, which delays child bearing and is reflected in the older age of mothers in the Nordic countries.

3.3.4. Low birth weight

In general, low birth weights (less than 2500 grams) may reflect shortened duration of pregnancy, poor maternal nutrition, maternal use of alcohol and/or tobacco, hypertensive complications of pregnancy, and prenatal maternal/infant infection. There is a possibility that a low birth weight predisposes to certain chronic diseases in older age, like high blood pressure, cardiovascular disease, and asthma (Forsdahl, 1977; Barker, 1990). It is thus desirable to reduce the proportion of babies with a low birth weight. Methods to bring this about include improving the socio-economic conditions for the fertile population together with early access to high quality prenatal care. In the Naryan-Mar region of Arctic Russia, prenatal exposure to polychlorinated biphenyls (PCBs), DDE, and DDT have shown a weak, but significant correlation with lower birth weight (Polder *et al.*, 2002b), suggesting that environmental factors may significantly affect health status.

The incidence of low birth weight in circumpolar populations, with the exception of Russia (at 7%), is between 4% and 5.8%, similar to the Nordic countries (Figure 3·5). This may reflect the increase in efforts to provide early access to high quality prenatal care.

3.3.5. Infant mortality and morbidity

Infant mortality is generally subdivided into deaths in days 0 to 28 of age (neonatal mortality) and deaths in days 29 to 365 (post-neonatal mortality) (Figure 3·6).

Neonatal mortality reflects prenatal care and the availability of intensive perinatal care. The most important contributor to this indicator is pre-term delivery; before 37 weeks gestation.

Post-neonatal deaths are influenced by the rate of Sudden Infant Death Syndrome (SIDS) in a population, as well as by infection, congenital anomalies in fetal development, and socio-economic conditions such as poverty.

In Greenland, Arctic Canada (NWT/Nunavut), and Alaska, infant mortality among the indigenous populations, particularly post-neonatal mortality, is higher than for the other Arctic countries shown. In Alaska Natives, the excess post-neonatal mortality above the U.S. All Races rate is due to the higher incidence of SIDS.

Serious morbidity in indigenous infants in the first year of life usually reflects their predilection to infection, and, for each region, is usually dominated by types of infection that reflect environmental conditions. Rate of respiratory infection often reflect crowded housing. Gastrointestinal illness may reflect the quality of the water supply (Berman, 1991; Maynard and Harmmes, 1970).

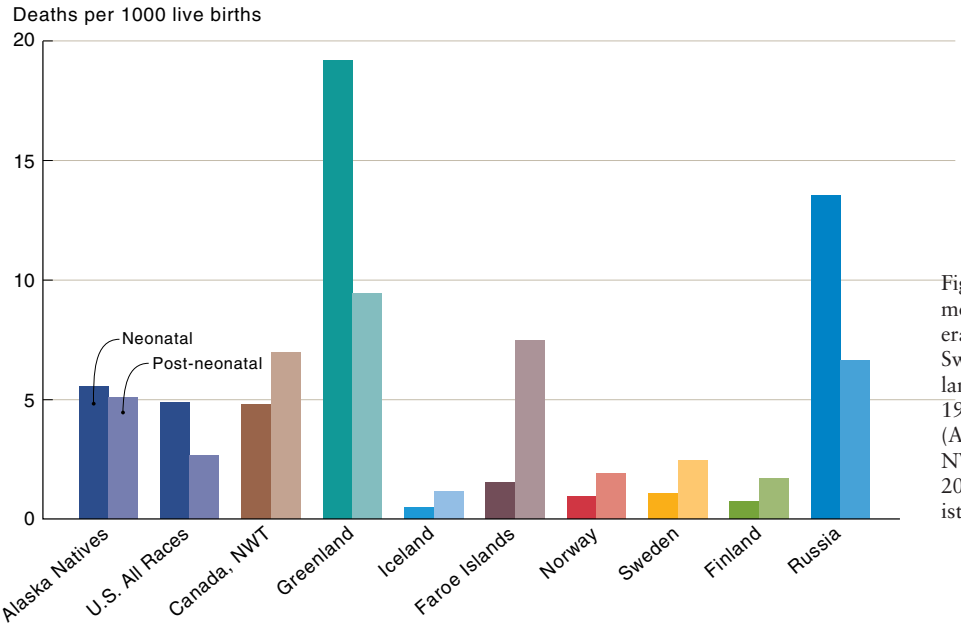

Figure 3·6. Neonatal and post-neonatal mortality rates in Arctic countries (general populations: Russia 1994–1997; Sweden/Norway/Iceland/Finland/Greenland/Faroe Islands 1998; U.S. All Races, 1995) and some indigenous populations (Alaska Natives, 1994–1996; Canada NWT/Nunavut, 1994). Source: US IHS, 2000; Health Canada, 1999; WHO Statistical Database; NOMESCO, 2001.

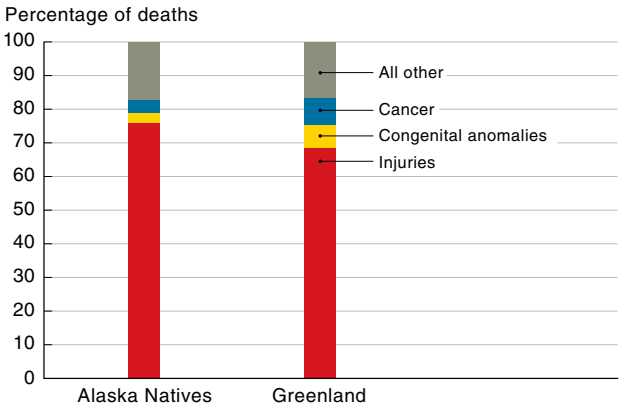

Figure 3·7. Percentage distribution of causes of child mortality (age 1 to 16 years) in Alaska Natives (1994–1996) and Greenland (1998). Source: US IHS, 2000; Annual Report from the Chief Medical Officer in Greenland 1999.

3.3.6. Child mortality and morbidity

Among Alaska Natives and Greenland Inuit, about 70% of all deaths between 1 year and 16 years are related to injury, either intentional or unintentional. Less than 10% are attributed to cancer and congenital anomalies, respectively (Figure 3·7).

3.3.7. Adult mortality and morbidity

Causes of adult mortality and morbidity vary with age and sex. Mortality in the young adult age range is largely related to injury, both intentional and unintentional. Among Arctic men, suicide is a major cause of injury mortality, and injury mortality from all causes is greater for men than for women. In general, morbidity tends to be related to injury and infections. Morbidity for certain infectious diseases and for diabetes is discussed in section 3.4.

Wide variation between populations/cultures exists, especially in intentional injury mortality, and may reflect differences in cultural stress, economy, or rates of depressive illness (Bjerregaard and Young, 1998).

In both sexes, over age 45 years, chronic disease becomes increasingly prominent in both mortality and morbidity indicators. Atherosclerotic heart disease, strokes, and cancer are the primary causes of mortality in this age range, partly reflecting an increasingly western lifestyle (Figure 3·8). In many countries, strokes and heart disease are combined in a single category called circulatory disease. As use of tobacco, a sedentary lifestyle, and a western diet have become more common, cancer, heart disease, obesity, and diabetes mellitus have become more frequent in indigenous Arctic residents. In certain Arctic regions environmental factors have been shown to be associated with health status. Studies of the Republic of Karelia residents in western Russia, where naturally low levels of calcium and magnesium are found in the water supply, indicate that these residents are associated with a high risk of hypertension, and strokes (Dorshakova and Karapetian, 2002).

3.4. Health status of indigenous Arctic residents

Disparities in health status of indigenous Arctic residents are presented in sections 3.2. and 3.3. Limited data availability restricts the possibilities for a detailed examination of health status differences among Arctic residents, especially among indigenous peoples. The most useful datasets exist for Alaska Natives, Canadian First Nations peoples, and the Inuit of Greenland. Nowhere are the datasets for Arctic populations as continuous or as comprehensive as the health data for the majority national populations of the relevant countries (United States, Canada, and Denmark). The reasons for the differences described in this section are multi-factorial and,

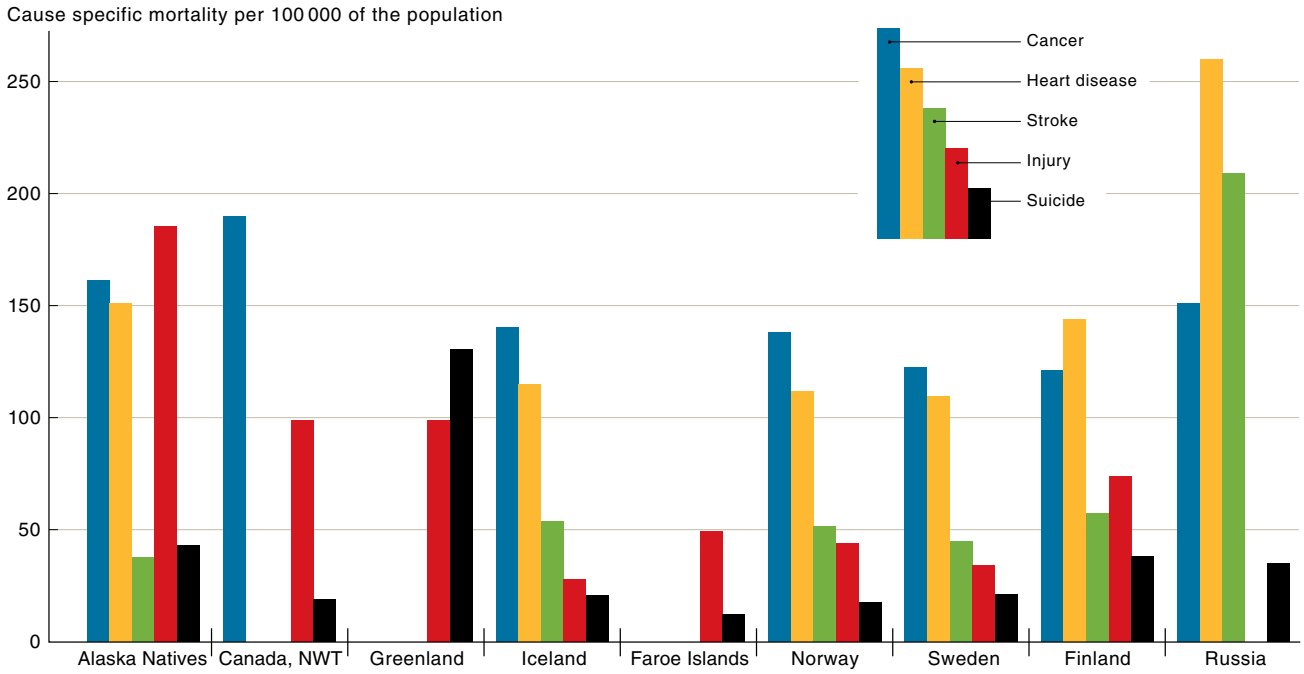

Figure 3·8. Adult age-standardized population mortality rates for cancer, heart disease, strokes, injury, and suicide within the Arctic countries (general populations: Greenland/Faroe Islands, 1991–95; Iceland/Norway, 1995; Russia, 1997; Sweden/Finland, 1996) and some indigenous populations (Alaska Natives 1994–1996; Canada NWT/Nunavut 1991–1996). Source: WHO Statistical Database; US IHS, 2000; NWT, 1999; NOMESCO, 2001.

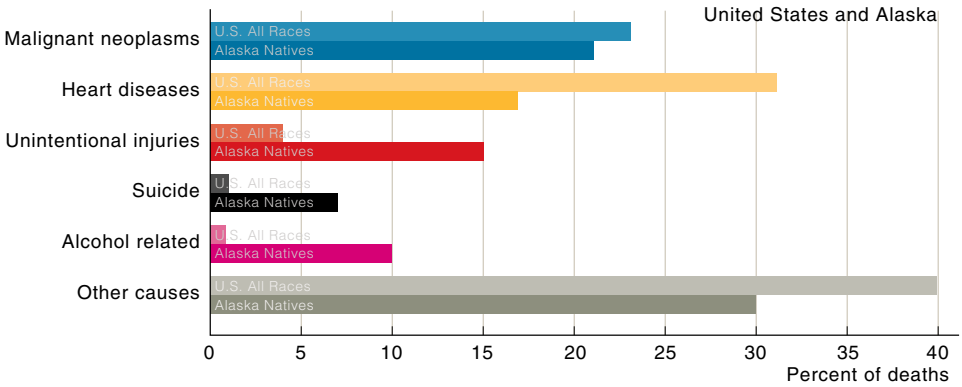

Figure 3·9. Percentage comparison of causes of death in U.S. All Races (1998) and Alaska Natives (1996–98). Source: Alaska Native Tribal Health Consortium (ANTHC) Statistics.

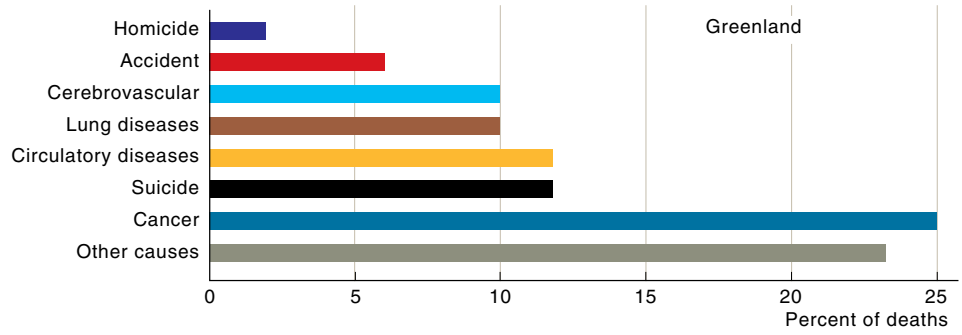

Figure 3·10. Percentage distribution of causes of death in Greenland in 1996. Source: Report from the Chief Medical Officer in Greenland 1999.

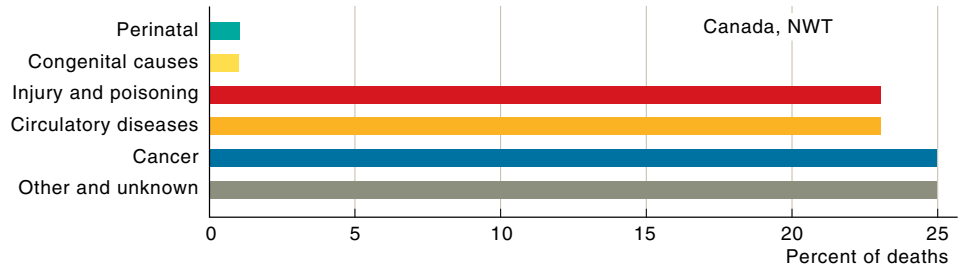

Figure 3·11. Percentage distribution of causes of death in Canada NWT/Nunavut, 1991 to 1996. Source: NWT, 1999.

in some cases, poorly understood. Major differences exist in the categories of injury, infant mortality, infectious disease, cancer, cardiovascular disease, and child health that are described in the compiled national/regional statistics. The population age structure is generally quite similar among various groups of indigenous Arctic residents, with more children, and fewer elderly (see section 3.2.1). For this reason, it is useful to compare causes of death by percentage of cause with the corresponding data for a non-indigenous population to better understand the way indigenous communities perceive the most common causes of death in their communities. From Figure 3·9 it is apparent that the main difference between Alaska Natives and U.S. All Races causes of death is due to suicide, unintentional injuries and alcohol-related deaths. A somewhat smaller proportion of Alaska Natives die from heart disease. Also, in Greenland (Figure 3·10) and Arctic Canada (Figure 3·11), violent death by homicide, suicide, and accidents is common and accounts for about 20% of all deaths.

3.4.1. Cancer

The incidence of invasive cancer has risen steadily from the mid-1970s in most populations studied (Nielsen *et al.*, 1996; Lanier *et al.*, 2001).

Although comparison data since 1988 from other Arctic countries are not available, the incidence of all invasive cancers in Alaska Natives from 1969 until 1998 is shown in Figure 3·12, for males and females, compared to U.S. Caucasians.

The incidence of all invasive cancers has increased significantly for both sexes, with the major statistically significant increases for Alaska Native men in lung, colorectal, and prostate cancer. In Alaska Native women, significant increases were seen in lung and breast cancer (Lanier *et al.*, 2001). Lung cancer increases are probably

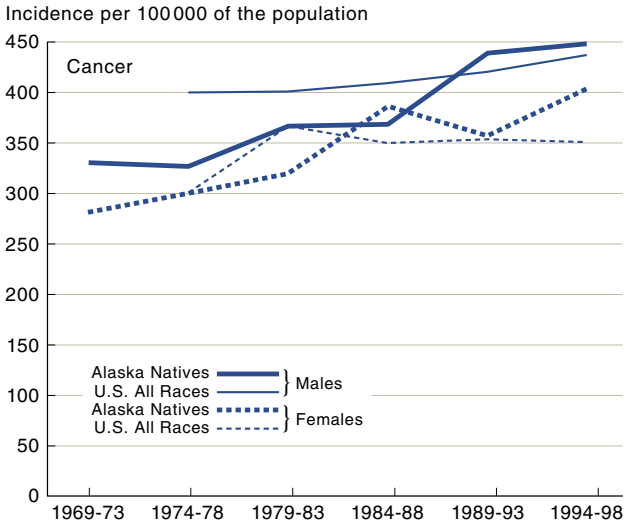

Figure 3·12. Trends in age-adjusted invasive cancer incidence rates in Alaska Natives (1969–1998) and U.S. All Races (1974–98). Source: Lanier *et al.*, 2001.

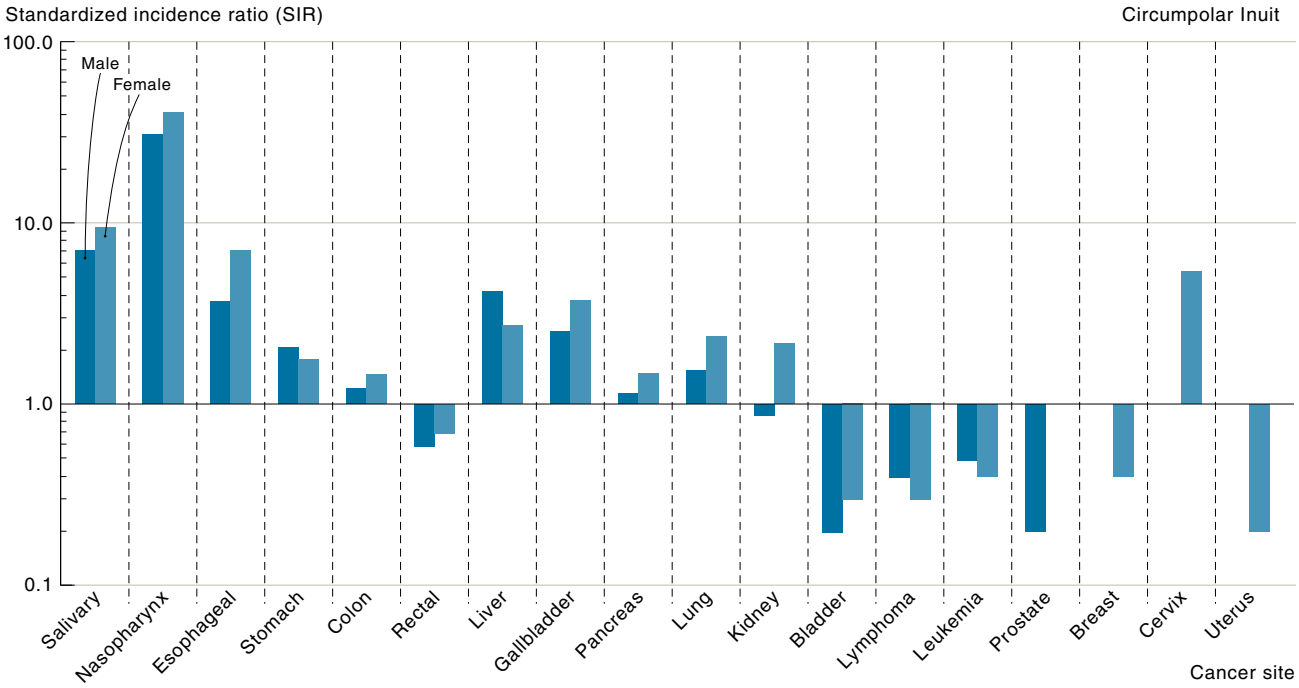

Figure 3·13. Standardized incidence ratio for selected cancer sites among male and female circumpolar Inuit, 1969 to 1988. Source: Bjerregaard and Young, 1998.

related to tobacco use, with tobacco becoming readily available throughout rural Alaska in the years following the Second World War. Changes in diet, and other relevant factors, along with the increase in the number of elderly probably contribute to the overall rise in cancer incidence (Nielsen *et al.*, 1996). Although tobacco is the major risk factor for lung cancer, the rise in colorectal cancer may be related to genetics, increased use of western foods, and other factors.

The incidence of various types of cancer differs in pattern from that apparent in non-indigenous residents, as seen in Figure 3·13, which shows relative risk for Inuit men and women for developing certain cancers, over the period 1966 to 1988, compared to the risk experienced by the majority populations, which is expressed as 1.0.

Certain cancers, notably prostate for men and breast for women, appear to be less common in indigenous populations (Nielsen *et al.*, 1996). In Alaska Natives, prostate and breast cancers remain less frequent than in the U.S. reference population, however comparable data for the Greenlandic and Canadian indigenous populations are not available (Lanier *et al.*, 2001). Figure 3·13 represents a compilation of all cancer incidence data for western hemisphere Inuit men and women, between 1969 and 1988, expressed as a 'standardized incidence ratio' (SIR). This is compared to national populations in Canada, Denmark, and the United States. Thus, a malignancy with an SIR of 1.0 occurs with equal frequency in Inuit and the majority populations used for comparison. A malignancy with an SIR of 7.0 occurs seven times more frequently in the age-adjusted Inuit population, while a malignancy with an SIR of less than 1.0 occurs less frequently in the age-adjusted Inuit population.

Other malignancies related to known risk factors, such as lung cancer (tobacco) are at least as frequent as in other populations, and liver cancer related to previously endemic hepatitis B infection is greatly increased. Other well established malignancies with increased frequencies, such as nasopharyngeal cancer, might well be related to other infectious agents such as the Epstein-Barr Virus, as well as other unidentified genetic or environmental factors (Nielsen *et al.*, 1996).

3.4.2. Infectious diseases

Immunizations, antibiotics, and basic sanitation have greatly lessened mortality from infectious diseases, but the burden of infectious disease continues to be a major

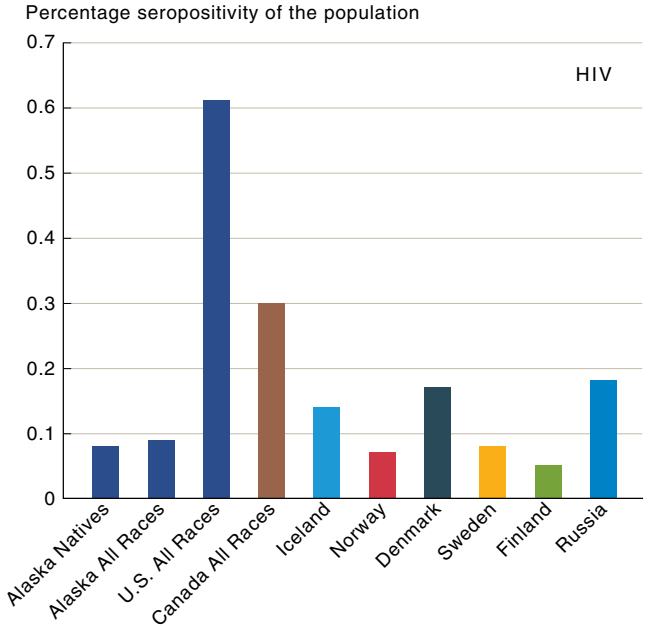

Figure 3·14. Percentage of population living with HIV/AIDS in Arctic countries (general populations: Alaska All Races/U.S. All Races, 1998–99; Canada All Races, 1999; Denmark/Finland/Iceland/Norway/Sweden, 1999), and among Alaska Natives (1998–99). Source: US IHS, 2000; Health Canada, 1999; NOMESCO, 2001.

source of disproportionate morbidity for Arctic indigenous residents. The majority of serious morbidity falls in the 0 to 4 year age range, and the over 50 years age groups. The exceptions are sexually transmitted diseases (STDs), and Human Immunodeficiency Virus (HIV) infections, which are predominantly seen in the 15 to 45 year age range. The prevalence of people living with HIV/AIDS is fairly low in most Arctic populations with the exception of Canada (0.30%) and the United States (0.61%) (Figure 3·14).

3.4.2.1. **Bacterial diseases**

Streptococcus pneumoniae and ***Hemophilus influenza*, type B**, cause diseases most frequently seen in infants and the elderly. The incidence of invasive disease from both these bacteria were 10 to 20 times higher in Arctic indigenous infants compared to Caucasian infants, with frequent severe illness leading to mental retardation, hearing loss, and death (Singleton *et al.*, 1994). The recent availability of vaccines for these organisms has begun to lessen the frequency of disease dramatically.

Tuberculosis is no longer a significant cause of mortality, but infection is more frequent among indigenous residents, primarily due to re-activation of tuberculosis in elderly people previously infected during the 1920 to 1960 period. Notable is the incidence in NWT/Nunavut Canada (over 50 per 100 000 population) and Greenland (110 per 100 000 population) (Figure 3·15).

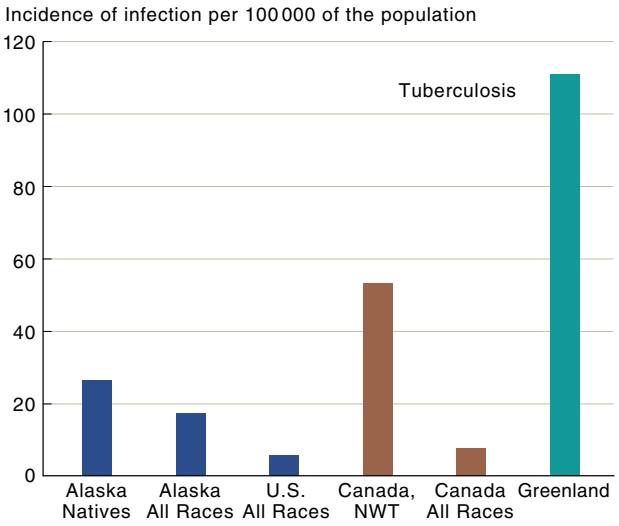

Figure 3·15. Crude incidence rate of tuberculosis infection, 1998 to 2000. Source: US IHS, 2000; Tuberculosis Control in Alaska, July 2001, State of Alaska; NWT, 1999; Annual Report from the Chief Medical Officer in Greenland 1999.

In settings of small, crowded housing and with high smoking prevalence, early symptoms, such as coughing, are often not seen as alarming or significant and as a result disease spread by airborne droplets is very efficient and effective.

Helicobacter pylori is a relatively recently discovered bacterium infecting the stomach, and capable of causing ulcers, stomach inflammation and bleeding. It has also been associated with increased risk for certain types of stomach malignant disease. The risk factors for infection

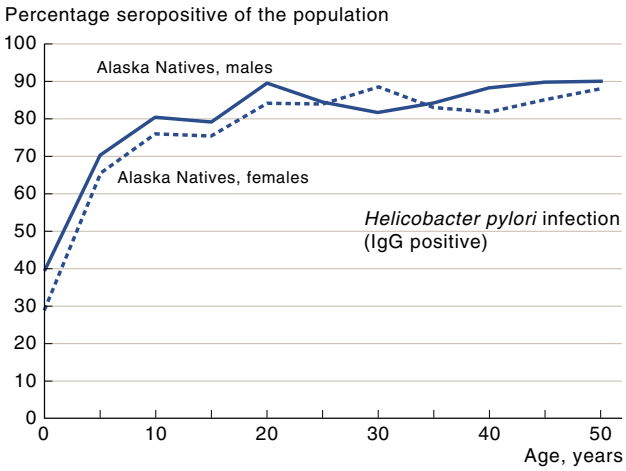

Figure 3·16. Rates of *Helicobacter pylori* infection among Alaska Natives by age and gender, 1980 to 1986. Source: Alaska Native Tribal Health Consortium (ANTHC) Statistics.

are not all known, but could include crowded housing and poor sanitation. The infection is common in the developing world, and is endemic among Alaska Natives, who begin to acquire the infection in early childhood (Figure 3·16) (Parkinson *et al.*, 2000).

Whether other Arctic peoples are endemically infected is not known, but the similarity of environmental conditions suggests that it is possible. Alaska Natives have the highest prevalence of *Helicobacter pylori* infection of any U.S. population.

3.4.2.2. **Sexually transmitted diseases**

There are many different organisms, both bacterial and viral, which cause disease and are transmitted by sexual contact. There are four for which comparable data exist: HIV, gonorrhea, syphilis, and *Chlamydia trachomatis*. HIV has not shown penetration into the Arctic indigenous populations in amounts greater than (and is in most places less than) in the Caucasian population (Figure 3·14). Syphilis has, in recent times, not been detected in amounts exceeding that in the Caucasian population (Bjerregaard and Young, 1998).

The rates of gonorrhea and chlamydia infection in Alaska Natives, however, are regularly reported to be two to four times the rate for Caucasians in Alaska. Among Canadian and Greenland Inuit, rates range from ten to 100 times the rates seen in Canada and Denmark (Bjerregaard and Young, 1998).

3.4.2.3. **Viral diseases**

Arctic residents, including indigenous residents, are connected by air transportation to the rest of the world, and experience regular seasonal viral epidemics of respiratory illness such as influenza, at the same times as cities in the subarctic and northern temperate zone.

Conditions of crowding and poor sanitation contributed to endemic hepatitis B in Alaska, Arctic Canada and Greenland, although universal immunization, beginning at birth, has virtually eliminated new hepatitis B infections (Bjerregaard and Young, 1998).

Hepatitis A swept the rural Arctic populations in epidemics on a 10 to 20 year cycle, infecting up to 90% of village populations in some regions (Bjerregaard and

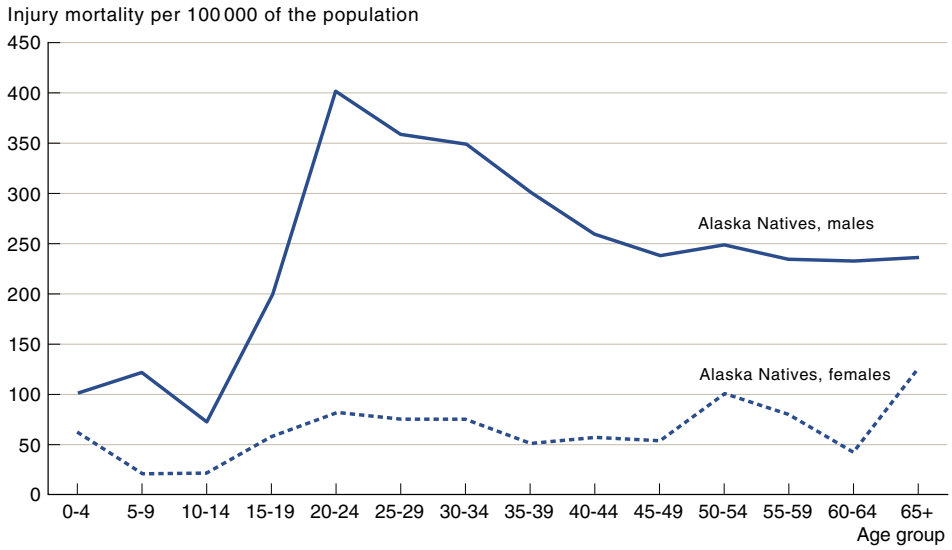

Figure 3·17. Injury mortality rates for Alaska Natives, 1991, by age-group and gender. Source: Bjerregaard and Young, 1998.

Young, 1998). Using an aggressive hepatitis A immunization effort, in the year 2000, no new hepatitis A infection was clinically recognized in the State of Alaska, demonstrating the potential of this vaccine (Middaugh, pers. comm., 2001).

Among Alaska Native infants, the Respiratory Syncytial Virus (RSV) causes far more severe lower respiratory illness than in other populations studied (Karron *et al.*, 1999), at rates from ten to 25 times higher. In studies of risk factors for severe RSV disease in Alaska Natives, premature birth, smoking in the home, and congenital heart disease increased risk, while breast feeding was found to decrease risk. Even so, 50% of severely ill infants did not have identified risk factors.

3.4.3. Unintentional injury

National injury data was previously presented in section 3.3.7. All indigenous Arctic residents have higher rates of mortality for unintentional injury, related to multiple factors, including the severe climate and weather, and substance abuse. The excess mortality is seen in all age groups with a dominance in the 20 to 24 year age group, also with an increase in the rates among the 65+ age group (Figure 3·17).

3.4.4. Intentional injury

Suicide is more common in young men and women among Arctic indigenous peoples, than the All Races data from the United States, Canada, and Denmark (Figure 3·18). The rates for Alaska Native men in the 15 to 24 year age group is four times the rate for women.

Cultural stress, erosion of traditional lifestyles, and substance abuse are all considered to be contributory factors (Bjerregaard and Young, 1998). In a Greenland study of risk factors, for both men and women, the presence of alcohol problems in the parental home and sexual abuse as a child were strong independent risk factors for serious suicidal thoughts (Bjerregaard and Young, 1998).

3.4.5. Diabetes mellitus

Diabetes has historically been thought to be absent from Arctic indigenous peoples, but recent data suggest that rates of type II diabetes among some indigenous popula-

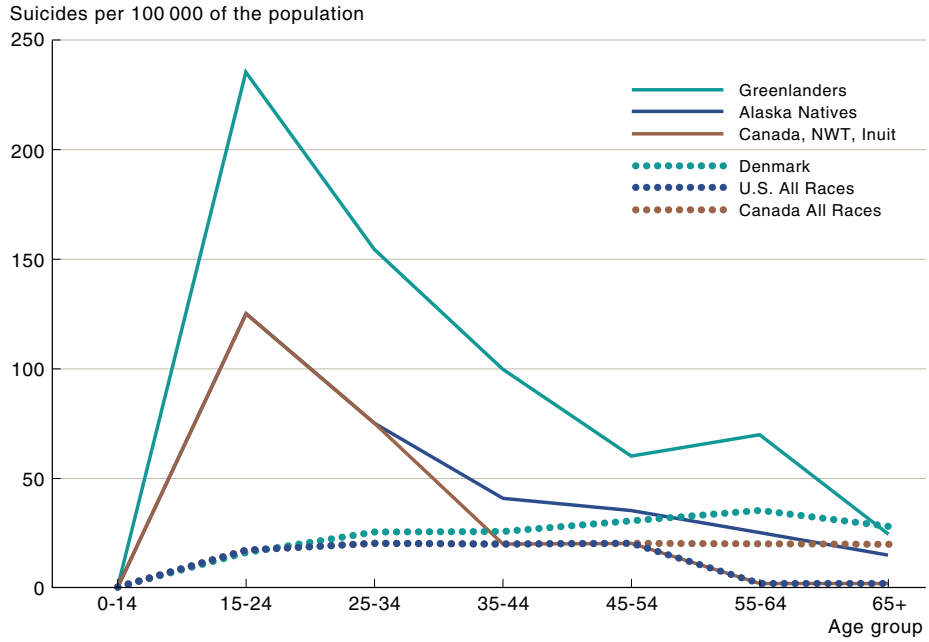

Figure 3·18. Suicide mortality rates in different age-groups of Greenlanders, Alaska Natives, and Inuit in Canada NWT/Nunavut compared to general populations in Denmark, Canada, and the United States, 1980 to 1989. Source: Bjerregaard and Young, 1998.

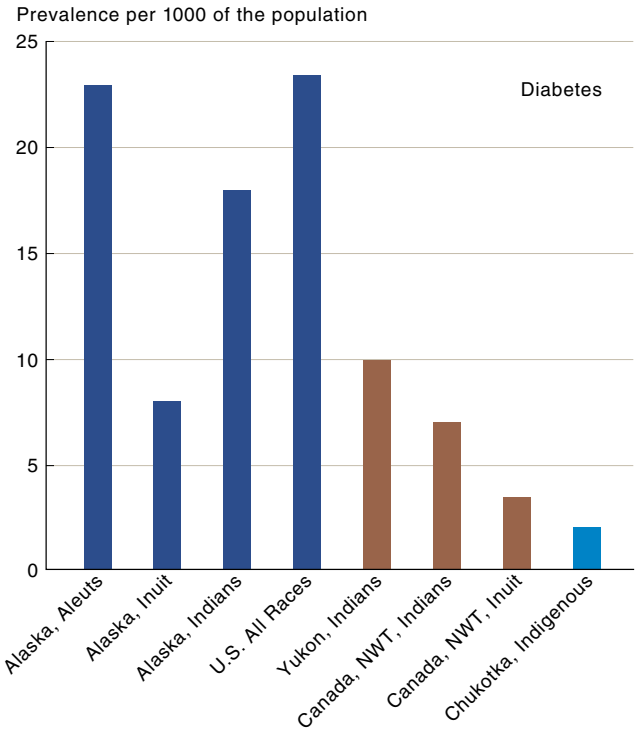

Figure 3·19. Age-standardized prevalence of diabetes mellitus in indigenous populations of Chukotka, Alaska, Yukon, and NWT/Nunavut, and in U.S. All Races in the late 1980s. Source: Bjerregaard and Young, 1998.

tions have increased to levels approaching those of other developed countries (Figure 3·19) (Bjerregaard and Young, 1998).

Rates of obesity have also increased which may be one explanation for the increase in type II diabetes, and for the increase in gestational diabetes which has also occurred. Increased rates of obesity may be partly related to the increased consumption of western foods, lower consumption of traditional foods, and lifestyle factors, such as decreased exercise.

3.4.6. Substance abuse

The data sources for use of alcohol and illegal drugs, such as marijuana, cocaine, opiates, amphetamines, and solvents abused by inhalation, are incomplete, and rarely comparable across groups (see section 8.2.3).

A survey of Greenland residents showed that 39% of men and 12% of women meet criteria for 'binge drinking' or 'high consumer.' Among Inuit residents in Arctic Canada, the results of the Indigenous Peoples Survey indicate that the prevalence of problems with alcohol (self-reported for at least one incident of an alcohol-related problem, such as missed days of work, arrest related to driving a vehicle while under the influence of alcohol, etc.) in the population range from 13% to 29%, and are highest in the 20 to 24 year age range, with only slight differences between men and women (Bjerregaard and Young, 1998).

The results of the Alaska Behavioral Risk Factor Survey indicated that for Alaska Natives 34% of men and 21% of women practised binge drinking (5 or more drinks on at least one occasion within the last month) compared to the U.S. rate of 14% for men and women together (Bjerregaard and Young, 1998). Inhalant abuse, often involving gasoline or glue sniffing, is a problem in many Arctic communities, usually among children and adolescents, with rates of adolescents stating that they had inhaled solvents at least once ranging from 7% to 26%, and with current rates of between 1% and 8% (Bjerregaard and Young, 1998). Data for Alaska Natives reveal that solvent inhalation in childhood is a strong predictor of alcohol and illegal drug use in later life (Prinz, pers. comm. 2001).

Consumption of alcohol during pregnancy can result in damage to the developing fetus, including cognitive impairment, small stature, poor growth, and altered development of facial bones. In its most severe form, the combination of poor prenatal or postnatal growth, poorly developed mid-facial bone structure, and a variety of brain function impairments is referred to as Fetal Alcohol Syndrome (FAS). Lesser degrees of prenatal alcohol exposure can result in brain dysfunction without growth impairment or altered development of facial features (Egeland *et al.*, 1998b).

Active surveillance for FAS carried out in the Alaska Native health care system from 1988 to 1994 indicated a rate of 4.2 per 1000 live births, compared to rates of 0.3 to 1.0 per 1000 live births in the U.S. population. Among Alaska Natives, FAS is the most common cause of preventable congenital mental retardation (Egeland *et al.*, 1998b).

It is quite possible that rates of FAS are also elevated in other Arctic populations, but active surveillance has not regularly taken place.

3.4.7. Indigenous infant and child health

3.4.7.1. Infant mortality

Infant mortality steadily decreased between 1950 and 1995 for all Arctic indigenous residents, but remains elevated above the rates for the United States, Canada, and Denmark (see section 3.3.5.). Anecdotal evidence about adverse trends in, e.g., infant mortality rates among Russian Arctic indigenous populations in the late 1990s, is a matter of concern. Disruption to essential services (food supply, fuel, employment opportunities, and health care services, etc.) following the change to a market economy is proposed as a major contributary factor in these negative developments. There is an urgent need for reliable statistics to confirm these indications and to document recent trends.

When neonatal (age 0–28 days) and post-neonatal mortality are examined separately, larger disparities are present in indigenous post-neonatal mortality rates with much smaller differences seen in neonatal mortality. SIDS is a major contributor to post-neonatal mortality among all indigenous residents in the Arctic. The cause of SIDS is unknown, but smoking in the home is a major risk factor.

Injury deaths in infancy are also elevated among indigenous peoples, as in all other age groups.

3.4.7.2. Oral health

Oral health status in children is recorded as the number of teeth which are decayed, missing, or filled (DMF) at certain ages. Although the ages and time periods represented are somewhat different, the rates of DMF teeth,

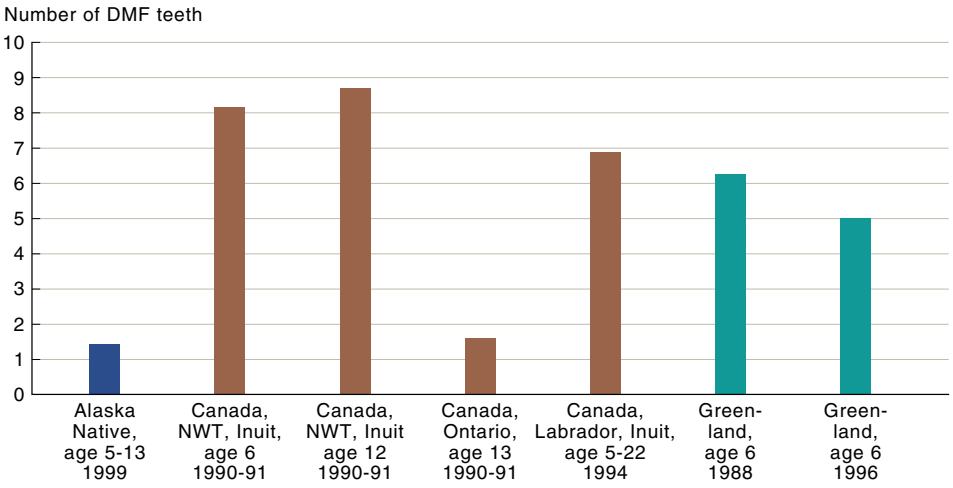

Figure 3·20. Oral health, measured as the number of Decayed, Missing and Filled (DMF) teeth in indigenous children in Alaska, Canada (NWT/Nunavut and Labrador) and Greenland, and children from Ontario, Canada, 1988 to 1999. Source: Bjerregaard and Young, 1998.

compared to majority populations, is higher among indigenous populations (Figure 3·20).

Tooth decay is greatly enhanced by simple sugars in foods, and, in Greenland was virtually unknown until the twentieth century (Bjerregaard and Young, 1998). The bacterium *Streptococcus mutans* is the causative agent of common childhood tooth decay and is often passed from mother to child during infancy. Measures such as fluoridation of water supplies and other public health dental practices can also reduce the DMF rates in childhood, but access to these measures is limited in many rural Arctic communities, as is restorative dental care.

3.5. Conclusions and recommendations

Arctic regions, in general, have much smaller, more isolated, younger populations, with fewer elderly people and larger families. Their mortality patterns are changing as increasing life expectancy and western influences on diet, lifestyle, and culture alter health status. As is the case in the more populated temperate regions of Arctic countries, cancer, strokes, and heart disease have become leading causes of death.

The younger age structure of the population in the Arctic regions provides an opportunity for effective emphasis on preventive measures for cardiovascular disease and general health promotion. Availability and access to comparable data for the different populations in the circumpolar region is still a problem and hampers the development of detailed comparisons and evaluations. This lack of data should be addressed by the health ministries of the Arctic countries.

Injury remains a disproportionately prominent cause of death and the suicide rate appears strikingly different in some regions. Crude indicators, such as suicide and homicide rates, would seem to point to a need to better identify prevalence and trends in behavioral risk factors, in order to better target early interventions and prevention efforts. Data on behavioral risk factors, such as alcohol consumption, or domestic violence, are inconsistently gathered among rural, isolated Arctic populations.

Illness associated with infections, especially infant respiratory disease, and sexually transmitted diseases (STDs), are far more frequent among some Arctic residents. Better housing, less crowding and advice aimed at increasing the proportion of breast-feeding mothers would lead to a reduced burden of infectious disease among infants. Innovative STD prevention programmes currently in use in some Arctic countries should be considered as models for those Arctic regions with high incidence rates.

Among certain Arctic peoples, the incidence of obesity and type II diabetes have increased to rates equal to those in most developed western countries. This may, in part, reflect an intake of more western foods, with a shift away from the traditional diet, sometimes as a result of community concern about the safety of traditional food sources.

Data on cultural factors, such as regular subsistence diet information, traditional harvests and celebrations, use of native language in the home, and traditional health practices are infrequently gathered, and would be useful in planning prevention programmes for a variety of medical and behavioral health problems.

The net effect of medical and public health advances has been to increase life expectancy. However, as the impact of western influences on indigenous cultures becomes more apparent, lifestyle changes have made chronic diseases a negative factor in the lives of Arctic residents.

As well as improving living conditions for the population in the reproductive age range, it is also important to improve the quality and number of 'healthy mother and baby programmes' to reduce pre- and postnatal morbidity and mortality, and possibly also to decrease the burden of adult chronic disease.

Chapter 4

Priority Contaminants, 'New' Toxic Substances, and Analytical Issues

Ivan C. Burkow and Jean-Philippe Weber

Summary

Ongoing monitoring of persistent toxic substances (PTSs) in the Arctic has focused on three well-known groups of contaminants: industrial compounds and by-products, chlorinated pesticides, and heavy metals. However, increasing levels of several 'new' contaminants and metabolites are a cause for concern. Brominated flame retardants, polychlorinated paraffins, and perfluoroorganic compounds have recently received international attention, but more data on their presence and possible effects are needed to evaluate their environmental impact.

Interpretation of monitoring results requires reliable and comparable data, a condition not always met. Therefore all laboratories producing human PTS data for AMAP are required to participate in relevant intercalibration programmes and to achieve acceptable results. Where relevant, measurements should be congener-specific and the data lipid-normalized for the organic pollutants, and speciated for the heavy metals to distinguish toxic and non-toxic forms.

4.1. Persistent toxic substances

Most research and ongoing monitoring work on PTSs in the Arctic have focused on three groups of contaminants: industrial compounds and by-products (e.g., polychlorinated biphenyls – PCBs, and dioxins), pesticides (e.g., lindane, the DDT-group, and cyclodiene analogues), and heavy metals (e.g., mercury – Hg, lead – Pb, and cadmium – Cd) (AMAP, 1998; Hansen *et al.*, 1996; Jensen *et al.*, 1997; Lønne *et al.*, 1997). The Stockholm Convention on Persistent Organic Pollutants (POPs) facilitated by the United Nations Environment Programme (UNEP), and the U.N. Economic Commission for Europe (UN ECE) Protocols for Heavy Metals and POPs also reflect the global concern associated with these contaminants. The UNEP POPs list includes aldrin, chlordane, DDT, dieldrin, dioxins and furans, endrin, heptachlor, hexachlorobenzene (HCB), mirex, PCBs, and toxaphene. The UN ECE POPs Protocol includes the UNEP 12 plus chlordecone, hexachlorocyclohexane (HCH), hexabromobiphenyl and polycyclic aromatic hydrocarbons (PAHs). The UN ECE Heavy Metals Protocol initially focuses on Cd, Pb, and Hg. During the last few years, however, there has been an increasing interest in 'new' toxic substances and metabolites.

The 'new' environmental toxins cover a range of organic compounds and compound classes. These include some of the more persistent polar pesticides currently in use. 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 (PCNs), polybrominated diphenylethers (PBDEs), polychlorinated paraffins, and perfluoroorganic compounds (e.g., perfluorooctane sulfonate – PFOS) are identified as 'new' toxic substances. Of these, PBDEs, polychlorinated paraffins, and PFOS have recently received particular attention. Due to their distribution and accumulation pattern, the synthetic musks, phthalates and new generation pesticides are generally not considered a particular problem in the Arctic. None of these 'new' compounds are on the current UNEP list of most unwanted POPs.

Increasing interest in the metabolites or halogenated phenolic compounds is partly caused by their structural similarity to natural hormones (see Figure 4·1) and possible action as hormonal mimics (Connor *et al.*, 1997; Hovander *et al.*, 2002). In addition, many of the well-known toxins are chiral (exist in mirror image forms) and hence exist in enantiomeric pairs (Kallenborn and Hühnerfuss, 2001), which have the potential to cause different biological effects. An enantio-selective accumulation has been reported for several organochlorine compounds (Karlsson *et al.*, 2000; Wiberg *et al.*, 2000). That the enantiomers may have different biological effects has in most cases been overlooked when assessing the possible environmental impact of these compounds.

Long-range transport allows many PTSs to reach remote areas such as the Arctic, where few, if any, local sources of these contaminants exist. Depending on the geographic location of sources, weather conditions, and the physico-chemical properties of the contaminants,

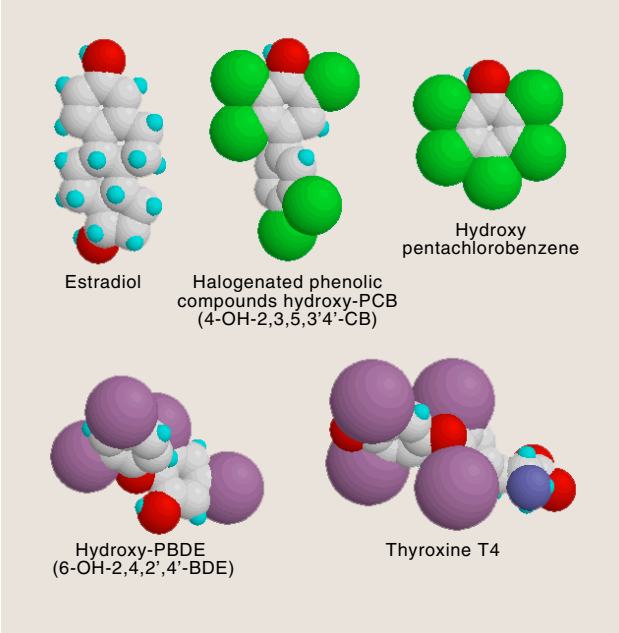

Figure 4·1. Structural similarities between the natural hormones estradiol and thyroxine T4, and the halogenated phenolic compounds hydroxy-PCB, hydroxy pentachlorobenzene and hydroxy-PBDE.

transport to and within the Arctic can occur via the atmosphere, ocean currents, sea ice drift, and river systems (AMAP, 1998; Burkow and Kallenborn, 2000). Due to their persistence and high lipophilicity, several of these compounds bioaccumulate, presenting a possible risk to humans, particularly those who depend on the lipid-rich marine mammals (whale, seal and walrus) for food. Among the many thousands of synthetic bulk chemicals in use today, only a limited number have been tested or evaluated for their hazard potential. To understand the possible consequences for human health and the Arctic environment extensive evaluations are needed. It should be kept in mind that the consequences may only become apparent decades after emissions to the environment have occurred, and thus after wildlife and people have already been exposed. Evaluation criteria must therefore include propensity for long-range transport, persistence, bioaccumulation potential, and hazards for human health and the environment (toxicity). Section 4.2 presents some key information for the most common and most debated PTSs from non-occupational exposure in the Arctic. More information about sources and environmental levels of contaminants in the Arctic can be found in two related assessment reports: the AMAP 2002 assessments of heavy metals (AMAP, 2003b) and POPs (AMAP, 2003c).

4.2. Industrial chemicals and by-products

4.2.1. Dibenzo-*p*-dioxins and dibenzofurans

Commonly known as dioxins and furans, polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are two structurally similar families of, respectively, 75 and 135 congeners. Dioxins and furans are mainly released through relatively low temperature (below 800°C) domestic and industrial incineration processes, with chlorine present, as well as during the manufacture of industrial chemicals including PCBs and pesticides (Alcock and Jones, 1996; Fiedler, 1996). A significant reduction in the emissions of dioxins and furans to the environment has been achieved through the implementation of pollution control measures.

Dioxins and furans are insoluble in water, lipophilic, persistent in the environment, and toxic. In particular, the 2,3,7,8-tetrachlorinated dioxins are known to bioaccumulate, while the more predominant congeners from combustion processes are known to biodegrade. Because they bind to particulate matter, dioxins are normally regarded as a major problem close to the source. In addition to a few local sources, these compounds enter the Arctic ecosystem via long-range atmospheric transport, but not to the same extent as for the other chlorinated PTSs. Diet is the main route of human exposure in the Arctic. Typical ΣPCDD/F values reported in human milk from the Arctic are in the range 10 to 40 pg/g lw (lipid weight) (AMAP, 1998); data on levels in human plasma from the Arctic are, however, sparse.

New methods for sample extraction and clean-up have improved the analytical capability for dioxin/furan trace analysis and pooled blood samples are no longer needed when using the most modern clean-up and quantitative techniques.

Chloracne is a well documented effect following dioxin/furan exposure. Other possible effects include effects on the immune system, cancer, reproductive disturbances, and acute toxic reactions (Fiedler, 1996; Whysner and Williams, 1996).

4.2.2. Polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) are a group of 209 congeners, several of which are atropisomers (i.e., exist as enantiomeric pairs due to restricted rotation of the bond between the two phenyl rings). PCBs were commercially produced and sold mainly as Aroclor and Clophen mixtures (Safe, 1994). Worldwide PCB production is estimated at 1.3 million tonnes (Breivik *et al.*, 2002). PCBs have been used extensively since the 1930s for a variety of industrial and commercial purposes, but their manufacture and new uses have now been phased out in many western countries. PCBs have widespread applications, including as dielectric fluids in transformers and large capacitors, as heat exchange fluids, in lubricating oils, as paint additives, in plastics, and in sealants. At present, the major source of PCB exposure seems to be environmental recycling of PCBs from former usage. PCBs are still present in older electrical transformers and at a number of contaminated industrial and waste sites throughout the Arctic. Like most POPs, PCBs have primarily contaminated the Arctic ecosystem through long-range transport from more southern regions.

The physico-chemical properties of PCBs, including low water solubility, high stability (particularly those lacking unsubstituted positions on the biphenyl rings), and semi-volatility, favor long-range atmospheric transport and accumulation in lipid-rich media. Thus, the main source of human exposure is through diet; however, inhalation and dermal routes are likely under occupational exposure scenarios. Typical ΣPCB values in plasma are in the range 1 to 60 μg/L (AMAP, 1998).

Historical levels are not always easy to compare with contemporary measurements due to changing trace analytical techniques and quantitative methods. ΣPCB values are often reported based on different quantitative methods (e.g., as Aroclor 1260 or a selected number of congeners), making comparisons difficult. Co-elution with other chlorinated compounds like chlorobornanes and cyclodiene pesticides has previously made reliable analytical interpretation difficult.

The most persistent congeners in lipid media are CB99, CB118, CB138, CB153, CB170, and CB180. Although regarded as persistent, some PCBs, depending on chlorine substitution, are transformed in the environment by biotic and abiotic processes. Naturally occurring microorganisms are capable of degrading the low chlorinated PCBs with vicinal hydrogen atoms. The presence of PCB metabolites in animals and humans formed by the action of CYP (cytochrome P450) and phase-II enzymes is recognized (Boon *et al.*, 1989), but to date these have not been included in environmental monitoring programmes. Reports have shown that the most abundant hydroxy-PCBs in human blood samples equal the presence of some abundant PCB congeners with sum values in the range 0.1 to 10 μg/L (Bergman *et al.*, 1994; Hovander *et al.*, 2002; Sandau *et al.*, 2000a). Metabolism also includes the formation of diols, phenolic conjugates and glutathione conjugates.

Methyl sulfone metabolites are also reported to bioaccumulate (Letcher *et al.*, 1998), but are present in substantially lower amounts compared to the hydroxy compounds.

Several possible adverse human health effects to PCB exposure have been suggested, including effects on the immune system, cancer, effects on the reproductive system, and cognitive development (Safe, 1994). Some of their toxicity may be linked to the biotransformation products. Due to structural similarities (with hydroxy group in *para-* or *meta*-position), the hydroxy metabolites are assumed to be able to mimic hormonal activities (Connor *et al.*, 1997; Kester *et al.*, 2000). The non-*ortho* and mono-*ortho* substituted PCBs are planar with toxic properties similar to the dioxins.

4.2.3. Chlorinated naphthalenes

Polychlorinated naphthalenes (PCNs) exist as 75 congeners that are structurally similar to the PCBs with comparable chemical and thermal stability (Falandysz, 1998). PCNs were first used commercially in the early 1900s for wood, paper, and textile impregnation, but were shortly thereafter replaced by PCBs. The numerous industrial applications also include usage in electrical equipment (e.g., capacitors and cables), lubricants, solvents, dyes, and sealants. Technical PCN formulations have been found under the names Halowaxes, Seekay waxes and Nibren waxes depending on manufacture. Other sources of PCNs in the environment are technical PCB formulations (up to 0.09% PCN) and thermal processes (e.g., combustion, roasting, metal reclaiming, and the chlor-alkali industry). PCNs are also believed to be formed during combustion of PAHs. In the 1920s, worldwide annual production was approximately 9000 tonnes. One of the largest PCN producers voluntarily ceased production in the late 1970s. However, general information about world production volumes and history is limited. Although the use of PCNs has declined in the past few decades, they are not prohibited in most countries and still occur in many PCB-like applications.

PCNs are transported to the Arctic mainly via long-range atmospheric transport. Partitioning to aerosols is especially important, governing both transport pathways to remote areas and depositional patterns. PCNs are lipophilic and, as for PCBs, the chlorine substitution pattern governs their persistence (Falandysz, 1998). Knowledge of the actual levels and distribution of specific congeners in humans is very limited. Data on human liver and adipose tissue indicate PCN levels 200 to 500 times lower than the total PCB burden (Weistrand and Norén, 1998). Hydroxylated metabolites of PCN have also been reported.

The analytical challenges associated with PCN analysis are the same as those for non-*ortho* substituted PCBs and dioxins; highly sensitive and specific trace-analytical techniques are required. Although all 75 congeners have been synthesized, full congener separation is not yet possible due to co-elution.

Some of the PCN congeners appear to exhibit dioxin-like toxicity of a similar magnitude to some of the co-planar PCBs (Falandysz, 1998; Villeneuve *et al.*, 2000).

4.2.4. Polychlorinated paraffins

Short-chain chlorinated paraffins (SCCPs) are part of the group of polychlorinated-*n*-alkanes (PCAs) with up to 30 carbon atoms and a chlorine content of 30 to 70% by mass (Tomy *et al.*, 1998). PCAs are used as additives to improve water repellent and flame retardant properties in metal working fluids and lubricants, plastics, adhesives, paints, and sealants. The SCCPs have carbon lengths of 10 to 13 and are of particular interest because they have the greatest potential for environmental release and the highest toxicity of the PCAs. Information on historical production volumes of PCAs is difficult to find but annual global production during the 1990s was estimated at 300 000 tonnes, of which 50 000 tonnes were SCCPs (Muir *et al.*, 2001). Due to concerns about their possible environmental impact the use of SCCPs is declining.

SCCPs are relatively mobile, subject to long-range transport, and are found in the Arctic. Studies indicate that SCCPs are less persistent and bioaccumulative than PCBs hence levels in the environment are low compared to PCBs (Fisk *et al.*, 2000). Medium- and long-chain chlorinated paraffins are not yet reported in the Arctic.

In contrast to most other environmental toxins, the number of SCCP congeners is extremely high, and this has resulted in a substantial analytical challenge. No congener-specific analysis exists, as this inability to resolve the individual components causes major problems for quantitation. A high degree of variability has also been reported in the quantitation depending on the analytical technique used.

SCCPs appear to elicit fewer acute and chronic toxic effects when compared to PCBs, but information is very limited. Risk assessments of SCCPs are inconsistent with respect to their conclusions regarding ecological risk, including carcinogenicity, clearly indicating the need for more data (Muir *et al.*, 2001).

4.2.5. Brominated flame retardants

Polybrominated diphenylethers (PBDEs), polybrominated biphenyls (PBBs), and tetrabromobisphenol A (TBBPA) are the three main classes of brominated compounds used as flame retardants (Renner, 2000). Brominated flame retardants (BFRs) are used extensively in a variety of consumer products such as in thermoplastics for televisions and personal computers, building materials, foams for furniture and insulation materials, as well as in textiles. BFRs are either chemically incorporated (covalently bound) in materials or applied as an additive to the material; BFRs from the latter group can more easily migrate into the environment. The major commercial products include the covalently bound TBBPA and its derivatives (representing a third of production), the additive PBDEs (representing a third of production), and a number of other compounds. PBBs for use as an additive flame retardant are no longer produced. The annual usage and variety of compounds manufactured have drastically increased during the last few years, with an annual world production of over 150 000 tonnes in 1998 (Larsen *et al.*, 1999).

The physical properties of BFRs encourage long-range transport and accumulation. That BFRs are found

in air and biological samples from remote areas of the Arctic supports the indications that these substances are globally distributed in the environment. Although decabromodiphenyl ether (BDE 209) accounts for most PBDE use, the most commonly found congeners are the *tetra* and *penta* derivatives. Typical values of ΣPBDEs (mainly BDE 47 and BDE 99) in plasma are in the range 5 to 40 ng/L (about 0.5% of levels of ΣPCBs) (Darnerud *et al.*, 2001). Recent findings of increasing PBDE levels in temporal trend studies, and the general lack of data on these substances, underline the importance of further investigations on these compounds (Norén and Meironyté, 2000).

With increasing availability of reference compounds, quantitation of the major congeners can be achieved. However, a complete identification and quantitation of all BFRs is not yet possible, and BDE 209 is often omitted when the PBDEs are reported. Studies indicate effective uptake from the gastrointestinal tract and substantial breast milk transfer to offspring. The formation of metabolites is also reported.

Although little information is available, data on possible effects suggest that PBDEs are likely to be carcinogens, endocrine disrupters, and neurodevelopmental toxicants (Hooper and McDonald, 2000).

4.2.6. Perfluorooctane sulfonate

With the possible exception of chlorofluorocarbons (CFCs), fluorinated organics have traditionally received less attention than chlorinated and brominated organics, partly because they are believed to be relatively inert and therefore less likely to have an impact on human health and the environment. A number of different chemical classes belong to this group (e.g., CFCs, aromatics, sulfonamides, acids and sulfonates). Perfluorooctane sulfonate (PFOS), which belongs to the important class of fluorinated surfactants, has, however, received more attention recently (Giesy and Kannan, 2001; Kannan *et al.*, 2001; Moody and Field, 2000). PFOS is used as a refrigerant, a surfactant, and as a component of pharmaceuticals, flame retardants, lubricants, paints, adhesives, cosmetics, paper coatings, and insecticides. PFOS has been manufactured for over 50 years and its many useful properties have steadily increased its use, making PFOS a high volume product with an estimated U.S. production of 3000 tonnes in 2000. As a result of the 3M Company's phase out, U.S. production is anticipated to decline.

The strong C–F bond makes fluorinated organics more inert, both chemically and biologically, than the corresponding chlorine or bromine analogues, and hence they are expected to have an environmental persistence greater than the more well-known organic contaminants (Key *et al.*, 1997). In general, however, little is known about their biodegradation and accumulation characteristics. PFOS has been detected in marine mammals from the Arctic, but no data exist on levels in humans from this area. The physical properties of fluorinated organics encourage long-range transport, as they are more volatile than chlorine or bromine analogues.

Part of the reason why PFOS received less attention in the past was because its measurement is complicated. Due to its surface-active properties, extraction is difficult and there is a need for sophisticated LC–MS methods for proper quantitation.

PFOS has been shown to affect cell–cell communication, membrane transport, energy generation, and proxisome proliferation (Sohlenius *et al.*, 1993; Upham *et al.*, 1998), but concentrations in wildlife are believed to be lower than those required to cause adverse effects.

4.2.7. Octachlorostyrene

Octachlorostyrene (OCS) is an industrial by-product formed during electrolysis of salt solutions to produce chlorine and magnesium, and when purifying aluminum (Deutscher and Cathro, 2001; Selden *et al.*, 1997). Maximum releases probably occurred in the 1960s, but little is known about global emissions.

Although found in high levels close to industrial sites, OCS has not been regarded as a major contaminant in the Arctic. However, the metabolite 4-hydroxy heptachlorostyrene has recently been identified as one of the major metabolites in human plasma in the Arctic (Hovander *et al.*, 2002).

No particular problems are associated with OCS analysis.

The potential human health concern with OCS is because it has a binding affinity for both the androgen and estrogen receptor (Satoh *et al.*, 2001). The metabolite is believed to have an influence on thyroid hormone and retinol homeostasis (Sandau *et al.*, 2000b).

4.2.8. Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) constitute a large class of compounds, which comprise hundreds of individual substances. They are produced as a result of incomplete combustion (pyrolysis) of organic matter. Sources are ubiquitous and include notably the burning and coking of coal, wood burning (including forest fires), production of aluminum, emissions from internal combustion engines (particularly diesel), cooking over fire or hot coals, and cigarette smoking. The main sources of non-occupational exposure are cigarette smoke, smoke from wood combustion, and smoked or broiled (over charcoal or fire) food (IARC, 1983).

PAHs released into the atmosphere by these combustion processes are rapidly adsorbed onto particulate matter and distributed into the different environmental compartments. PAHs are hydrophobic and insoluble in water and are readily taken up in lipid deposits of aquatic organisms. PAHs are photooxidized by sunlight in air and water. Since PAHs are biodegraded by microorganisms and metabolized by higher organisms, they show little tendency to bioaccumulate. Levels in humans are affected by smoking status, occupational exposure and consumption of PAH-containing foods. In nonsmokers, the levels of the metabolite 2-naphthol are below 2 μmol/mol creatinine, whereas smokers exhibit average levels of 4 μmol/mol creatinine. Higher levels are encountered in occupationally exposed individuals (ATSDR, 1995).

PAHs may be detected and measured by a number of methods, based on their UV absorption, fluorescence, or molecular mass. Analysis is performed using a separation technique such as high performance liquid chro-

matography (HPLC) or gas chromatography (GC) to enable identification of individual members. Evaluation of human exposure is performed through the measurement of hydroxylated metabolites in the urine (including 1-hydroxypyrene and 2-naphthol) using GC–MS.

Usually PAHs with two to six fused aromatic rings are those of toxicological interest. PAHs are not acutely toxic to humans. However, many PAHs have been shown to be potentially carcinogenic as well as genotoxic. Metabolites (e.g., hydroxides, epoxides, and nitro-PAH) appear to be responsible for these effects (Angerer *et al.*, 1997).

4.3. Chlorinated pesticides

4.3.1. Hexachlorocyclohexanes

Hexachlorocyclohexanes (HCHs) are a group of organochlorine compounds existing in eight isomeric forms including the often-reported α, β- and γ-HCH, the last more commonly known as the pesticide lindane. α-HCH is chiral and hence exists as an enantiomeric pair. The gamma isomer lindane is used as an insecticide on fruit, vegetables, and forest crops. Many countries still use large amounts of lindane and there are some registered uses of lindane in some circumpolar countries. Technical grade HCH, mainly containing the alpha isomer and only 15% γ-HCH, was once used as an insecticide. Total world production is estimated at 0.7 million tonnes of lindane and 10 million tonnes of technical HCH (Li, 1999).

Owing to their physico-chemical properties, HCHs are readily transported to the Arctic, via both atmospheric and aquatic pathways. HCHs partition into all environmental media in the Arctic. Biodegradation seems to be the dominant decomposition pathway in soil and water. Like other POPs, most human exposure to HCHs comes from food consumption. HCHs are not a major contaminant in drinking water. HCHs, especially β-HCH, accumulate readily in fatty tissues and are excreted slowly via feces, breast milk, and urine. Because of its persistence, β-HCH exhibits the highest concentration of the isomers normally reported in human samples. Typical plasma levels are in the range 0.1 to 2 μg/L (AMAP, 1998).

Except for the general difficulties in separating enantiomers, no problems are associated with HCH analysis.

High HCH exposure can affect the liver, the nervous system, the kidney, the reproductive system, and the immune system. HCH is regarded as a possible carcinogen (ATSDR, 1994; Coosen and van Velsen, 1989).

4.3.2. Hexachlorobenzene

Hexachlorobenzene (HCB) was introduced in 1945 as a fungicide for seed treatment. HCB is also an industrial by-product associated with the manufacture of chlorinated solvents, and several metallurgical industrial processes. It is a known impurity in several pesticide formulations that are currently in use. HCB is banned in many countries or its use has been severely restricted. The estimated current global annual emission is 23 tonnes (Bailey, 2001).

HCB is very persistent and bioaccumulates in animals. Dietary intake is the major route of human exposure, with highest concentrations found in oils and fats, meat, poultry, and fish. Exposure via inhalation or through drinking water is considered to be low. Typical plasma levels in Arctic populations are in the range 0.3 to 2 μg/L (AMAP, 1998). HCB is transformed into both pentachlorophenol (PeCP) and conjugates; however, elimination appears to be small compared to adipose deposits (To-Figueras *et al.*, 2000).

In addition to inducing porphyria, HCB has a broad range of toxic effects in experimental animals including immunotoxicity, endocrine effects, and cancer (Fisher, 1999).

4.3.3. DDT group

The use of 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (*p,p'*-DDT) as a pesticide has been declining in the temperate regions of the Northern Hemisphere since the 1960s and especially since the mid-1970s when its production and use were banned by many western nations (Mellanby, 1992). DDT was commonly used as a pesticide on a variety of agricultural crops and is still in use for the control of mosquitoes that spread malaria (vector control). Total global usage was estimated at 2.6 million tonnes up until 1992 (Voldner and Li, 1995). *p,p'*-DDT is easily metabolized to 1,1-dichloro-2,2-bis (*p*-chlorophenyl)ethene (*p,p'*-DDE) and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane (*p,p'*-DDD). The DDE/DDT ratio indicates age since release, or closeness to the source of a release. Two minor isomers of the DDT group, *o,p'*-DDT and *o,p'*-DDD, are chiral.

The persistence of the DDT group in the environment and its continued entry into the Arctic region via long-range atmospheric transport has meant that DDT is detectable in almost all compartments of the ecosystem and in human tissues. Levels of total DDT in human tissue in the Arctic are considerably higher than those in most southern populations, reflecting biomagnification in Arctic food chains and the higher consumption of high trophic level species for food in the Arctic. Typical plasma levels are in the range 1 to 9 μg/L (AMAP, 1998). DDT and its metabolites are stored in fatty tissue and excreted very slowly. Due to its lipophilicity, DDT and its metabolites are found in breast milk and can readily cross the placental barrier.

Except for the possibility of decomposition during analysis, there are no general limitations connected to DDT analysis.

Some evidence suggests that the DDT group may suppress the immune system, mimic hormones and be a possible human carcinogen (Fisher, 1999).

4.3.4. Cyclodiene pesticides

The cyclodiene pesticides are a diverse group of compounds including the chlordanes, heptachlor, aldrin, dieldrin, and endrin.

Technical chlordane is a mixture of *cis*- and *trans*-chlordane, *cis*- and *trans*-nonachlor, heptachlor and other chlordane isomers (Dearth and Hites, 1991). The total number of compounds is at least 147, of which 10 are major ones. Most chlordanes are chiral and hence found as racemates (mixture of mirror images) in the technical product. Chlordane was manufactured from

the late 1940s as a broad-spectrum insecticide used on agricultural crops and for termite control. Total global usage has been estimated at 78 000 tonnes (Barrie *et al.*, 1992), and action to ban chlordane has been taken in many countries. It is not registered for use in circumpolar jurisdictions and enters the Arctic ecosystem primarily via long-range transport. The chlordanes are highly volatile, lipid soluble and hence readily accumulate in fatty tissues in the marine food web. In general, only small amounts of chlordane are found in human tissues. However, relatively larger amounts of *trans*-nonachlor and the metabolites oxychlordane and heptachlor epoxide are found. The chlordanes are one of the most abundant environmental pollutants. Typical values (sum of chlordanes) in human plasma are in the range 0.2 to 2 μg/L (AMAP, 1998). No analytical limitations, except for the separation of the chlordane enantiomers, are reported. The compound class is a possible carcinogen and is believed to affect the immune system (Fisher, 1999).

Heptachlor, also used as an insecticide against termites, grasshoppers, and malaria mosquitoes, is now banned in several countries and severely restricted in others. Heptachlor is metabolized in animals to heptachlorepoxide. Typical plasma levels are in the range 0.05 to 0.15 μg/L (AMAP, 1998). As for chlordane, heptachlor is highly volatile, lipid soluble, and bioaccumulates. The compound and its metabolite are classified as carcinogens (Fisher, 1999).

Aldrin is a pesticide used to protect crops such as corn and potatoes from grasshoppers and worms, and to protect wooden structures from termites. Total global production has been estimated at 500 000 tonnes (Barrie *et al.*, 1992). Aldrin is readily metabolized in plants and animals to dieldrin. Dieldrin was traditionally used in agriculture to control soil insects, with a worldwide total production of 34 000 tonnes. Today, primary uses include controlling termites, woodborers, and textile pests. Endrin has been used as an insecticide on cotton and grain, and as a rodenticide to control mice and voles. Aldrin and endrin have been banned or severely restricted in most countries. Action has also been taken to ban or restrict the use of dieldrin, one of the most common pesticides. Due to the persistence and lipophilicity of aldrin and dieldrin, these compounds readily bioaccumulate. Endrin is rapidly metabolized by animals and does not accumulate in fatty tissues to the same extent as the other compounds. The main source of human exposure is through food. Adverse effects include toxicity, immune system depression, and carcinogenic action (Fisher, 1999).

4.3.5. Mirex

Mirex is an insecticide primarily used to control fire ants and other insects. Mirex has also been used as a flame retardant in plastics, rubber, and paint. The compound has never been used in any of the circumpolar jurisdictions and is now banned in many countries. It has been manufactured and applied extensively in the United States and has reached the Arctic via long-range atmospheric transport.

Mirex is one of the most stable and persistent pesticides with an environmental half-life of up to 10 years. Mirex is readily absorbed and stored in fatty tissues. It bioaccumulates, and is now found at low levels in human tissue. The primary source of exposure is food, especially meat, fish, and game. Transformation to photomirex is slow and elimination is mainly via feces and breast milk. Plasma levels in the range 0.1 to 0.6 μg/L are reported (AMAP, 1998).

Mirex has toxic and possible carcinogenic effects (AMAP, 1998).

4.3.6. Chlorobornanes

Toxaphene is an insecticide mixture introduced by Hercules (USA) consisting of several hundred chorinated bornanes (CHBs, the major product), polychlorinated camphenes (PCCs), bornenes, and bornadiens, containing six to ten chlorine atoms (de Geus *et al.*, 1999; Muir and de Boer, 1995). Comparable mixtures were used under the brand names Strobane and Melipax. Most of the CHBs are chiral. Toxaphene is one of the most heavily used pesticides, with a total world production of 1.3 million tonnes up until 1993 (Voldner and Li, 1993). It was primarily used on cotton, cereal grains, fruits, nuts, and vegetables, as well as to control ticks and mites in livestock. Toxaphene and comparable mixtures are now banned in most countries.

CHBs, the major constituent of toxaphene, are semivolatile and enter the Arctic region via long-range atmospheric transport. The compounds are persistent (half-life in soil up to 12 years), lipid soluble, readily absorbed, and are commonly found in human tissue. Absorbed CHBs may be transformed and excreted; however, some congeners remain for prolonged periods. The two most common congeners are an octachlorobornane (Parlar no. 26) and a nonachlorobornane (Parlar no. 50). Values reported in human plasma are in the range 0.1 to 1 μg/L for both congeners (Deutch and Hansen, 2000).

Quantification has been compromised by difficulties in analysis (separation from PCB and organochlorine pesticides) and in the estimation of the amounts of the various chemicals that make up the CHB mixture. The increased number of reference compounds has improved the capability for acceptable quantitation of the most abundant congeners. However, the lack of standards, as well as differences in how data on total CHB amounts (or the sum of toxaphene-like compounds) are presented, has made comparisons of published data on CHBs difficult.

Several adverse effects of toxaphene, including being a possible human carcinogen, are reported (de Geus *et al.*, 1999). However, structure–activity models have shown that the most toxic CHB congeners are not accumulated (Parlar *et al.*, 2001).

4.3.7. Pentachlorophenol

Pentachlorophenol (PeCP) is made by exhaustive chlorination of phenol or by the hydrolysis (or degradation) of HCB. PeCP is insoluble in water but is readily converted to the soluble sodium salt. Depending on the manufacturing process, PeCP may be contaminated with various dioxins and furans. Worldwide production is estimated at less than 30 000 tonnes per year. As a broad-spectrum low-cost pesticide, PeCP and its salts have been used as algicides, fungicides, insecticides, molluscicides, and her-

bicides. Current use is limited to the treatment of lumber, in particular utility poles. Because of its volatility and water solubility, PeCP evaporates or is leached from wood structures to a large extent (ATSDR, 1999a).

Environmental contamination is widespread, PeCP being found in ambient air, surface and ground waters, sediments, soil, and aquatic and terrestrial organisms. PeCP is degraded by light and microorganisms to form numerous transformation products, of which pentachloroanisole and tetrachlorocatechol are the most abundant in the environment. PeCP bioaccumulates in fish but in mammalian systems it is rapidly excreted in the urine, either free or conjugated with glucuronide. A recent study of PeCP in blood shows PeCP concentrations in Arctic samples of 0.6 to 8 μg/L plasma (Sandau *et al.*, 2000a).

No particular difficulties are associated with PeCP analysis.

PeCP is a suspected carcinogen, however contaminants in technical grade PeCP may be the actual culprits.

4.3.8. Endosulfan

Endosulfan is a synthetic, sulfur-containing, organochlorinated hydrocarbon used as an insecticide and acaricide. Technical grade endosulfan is a mixture of two geometric isomers (conformers), alpha and beta, which have slightly different physical and chemical properties, in a proportion of 2:1.

Endosulfan is moderately persistent in the environment. In soil, the half-life ranges from 30 to 200 days, and is affected by pH, the presence of microorganisms, and humidity. In water it is hydrolyzed slowly to form sulfur dioxide and endosulfandiol. In mammals, endosulfan is absorbed rapidly though incompletely by the digestive system. Endosulfan is lipophilic but is rapidly converted to a number of hydrophilic metabolites, including endosulfan sulfate, endosulfandiol, endosulfan ether, and hydroxy endosulfan carboxylic acid, which are more easily excreted. Thus it does not accumulate in the fat, and hence shows little potential for bioaccumulation or biomagnification (ATSDR, 2000a).

As a member of the organochlorine class, endosulfan can be determined by GC with electron capture detection (ECD). For environmental and biological specimens, sample clean up and purification is crucial to the reliability of the analysis (ATSDR, 2000a).

4.4. Heavy metals

4.4.1. Arsenic

Arsenic is the archetypal poison, synonymous with homicidal poisoning. The element As is ubiquitous in the environment, associated with mineral deposits of copper, nickel, iron (as arsenopyrite) as well as As oxides and sulfides. Often found as a natural contaminant of groundwater, it has been responsible for large-scale poisoning of human populations in many countries, notably in Bangladesh (Smith *et al.*, 2000) and Taiwan (Tseng, 1977). The worldwide production of As is estimated at 39 000 tonnes per year (USGS, 2001a). Atmospheric pollution stems mainly from coal burning and the smelting of metals. There is no evidence that Arctic regions are particularly affected by As contamination.

Arsenic forms a variety of inorganic and organic compounds. Among the first class, two oxidation states predominate, trivalent (+3) and pentavalent (+5), readily forming oxides, sulfides and acids. Organic forms include methylarsonic acid (MAA), dimethylarsinic acid (DMA), arsenobetaine and arsenocholine, the last two found in seafood. In mammals, inorganic As is rapidly transformed (metabolized) into MMA and DMA and subsequently rapidly excreted in the urine, thus making urine the medium of choice for evaluating recent As exposure. Care must be taken to speciate in order to distinguish between toxic and non-toxic forms.

To interpret the environmental or health impact of As its determination in environmental and biological samples must take into account the various species present. Total As content can be measured by atomic absorption spectrophotometry (AAS) using either hydride generation or graphite furnace (GF). Chemical pretreatment allows a limited speciation to be made, sufficient to distinguish exposure to toxic forms from ingestion of seafood. Inductively-coupled plasma–mass spectrometry (ICP–MS) coupled with HPLC affords complete speciation of common inorganic and organic compounds (ATSDR, 2000b).

The toxicity of As compounds varies from highly toxic to non-toxic in the range As(III) > As(V) > MAA > DMA > arsenobetaine/choline. Chronic As exposure affects several organs with resulting damage to the peripheral nervous system, skin, liver, and heart. Arsenic is recognized as a human carcinogen (Smith *et al.*, 1992).

4.4.2. Cadmium

Cadmium occurs in nature as oxides, sulfides and salts. Cadmium is released into the environment from both natural and anthropogenic sources, with the former including volcanic activity, and weathering and erosion of rocks. Mining, smelting and refining activities account for the majority of anthropogenic emissions. Incineration of municipal wastes containing nickel–cadmium batteries also contributes significantly. Soil levels are elevated close to sources, and usually decrease rapidly with distance away, although emissions from tall stacks may be transported over long distances (IPCS, 1992). Cadmium entering freshwater from industrial sources is rapidly adsorbed onto particulate matter, which eventually settles out. Cadmium is produced as a by-product in the smelting of zinc ores. Annual worldwide production is estimated at 19 000 tonnes (USGS, 2001b). The principal use of Cd is in the manufacture of nickel–cadmium batteries (75%) (ATSDR, 1999b). Other uses include pigments, coatings and plating, stabilizers for plastic, and nonferrous alloys.

Cadmium accumulates in aquatic organisms such as shellfish and crustaceans (Eisler, 1985), as well as in the liver and kidney of mammals (e.g., moose, reindeer/caribou, deer, and horses) (Crête *et al.*, 1987). Many plants, including tobacco, take up Cd. Uptake is enhanced at low soil pH. Occupational exposure results principally from inhalation of dust during manufacturing operations. Because of the dire health consequences, most countries have implemented strict regulations to control Cd exposure in the workplace (ATSDR, 1999b). Non-occupational exposure occurs through the consumption

of contaminated food (in particular organ meat) and cigarette smoking. Cadmium blood levels in Arctic populations are similar to those in other populations and appear to be affected principally by cigarette smoking. In an Inuit population from Nunavik, levels in smokers were 20-fold higher than in non-smokers, ranging from 4.7 to 6.2 μg/L (Benedetti *et al.*, 1992).

GF–AAS and ICP–MS are two techniques of choice for the determination of Cd in environmental and biological samples. Although the analytical techniques are straightforward, care must be exercised to avoid contamination during both the sampling phase and laboratory analysis (ATSDR, 1999b).

Chronic Cd exposure leads to proteinuria and kidney damage, obstructive lung disease, and osteomalacia, the last exemplified by Itai-Itai disease, as observed in Japanese populations in the 1960s (Fushukima, 1978).

4.4.3. Lead

Lead has been used for several millennia. Current worldwide Pb production is estimated at 3 million tonnes per year (USGS, 1996), with primary Pb (as opposed to recycled Pb) produced by the smelting of Pb sulfide ores. Lead present in the environment is mainly of anthropogenic origin (Nriagu, 1989). Localized anthropogenic sources include Pb smelters, battery recycling plants, and peeling paint from houses and industrial structures. Lead-acid battery manufacturing constitutes the principal contemporary use of Pb. Traditional uses such as paints, pigments, gasoline additives, ammunition, and Pb plumbing have all been severely curtailed due to environmental concerns. Leaded gasoline was a major cause of environmental contamination and human exposure during the twentieth century (US EPA, 1991). With the phasing out of leaded gasoline in North America in the 1980s, average blood Pb levels in the population decreased by up to 80% (Pirkle *et al.*, 1994). Environmental levels have also decreased significantly as evidenced for example by a 7.5-fold reduction in the Pb concentration of Greenland snow (Robinson, 1981).

Human exposure to Pb may occur through inhalation of airborne particles, as well as through the diet. Lead is readily absorbed through the lung. Gastrointestinal absorption of Pb is a complex process influenced by dietary factors, nutritional status, and the chemical form of the element. Once absorbed into the bloodstream, Pb is distributed into soft tissues and the skeleton, where it accumulates due to its chemical similarity to calcium. Lead shot has been implicated as a potentially major source of dietary Pb in Arctic hunter populations, since significant amounts of Pb fragments may remain in game, especially birds (Johansen *et al.*, 2001). Mean blood concentrations in humans in the range 10 to 50 μg/L are reported within the Arctic. Cord blood Pb levels in Nunavik were found to be three times higher than in urban Canadian populations (Dewailly *et al.*, 2001a).

Lead in environmental and biological samples may be measured by several analytical techniques including GF–AAS and ICP–MS. The latter technique allows the measurement of isotopic ratios of Pb, which often yields valuable information as to the source of the metal (Gwiazda and Smith, 2000). Prior to the 1980s, accurate determination of trace levels of Pb was a problem for most laboratories. Since then, improved methodology, as well as the generalized use of external proficiency testing programmes, has resulted in a greatly improved situation (Weber, 1996).

Even at low levels, Pb affects the peripheral and central nervous systems, particularly during their development. Hence the unborn and young children are particularly at risk. Higher exposures result in hematological and gastrointestinal symptoms.

4.4.4. Mercury

Mercury exists in many forms in the environment. It is present in the atmosphere mainly as a metallic vapor; it forms different chemical compounds in water, soil and rock; and it occurs in organic forms, found mainly in living organisms. Mercury has a number of unusual properties. It is the only metal that in elemental form is a liquid at room temperature. Mercury conducts electricity and it expands linearly with increasing temperature. Mercury combines easily with most metals, forming alloys known as amalgams, such as those used in dental fillings. These properties have made Hg a widely used product in household, commercial, medical, and industrial applications. Mercury, in various forms, is also one of the most poisonous natural substances known to humans and most other forms of life, making it an effective pesticide, fungicide and preservative. Due to its high toxicity, Hg in the environment has become an issue of international concern, and this has led many countries to implement controls on Hg emissions including phase-out of many uses.

The main ore is cinnabar, with Spain and Italy producing around 50% of the world's supply of the metal. Worldwide production of Hg is estimated at 1800 tonnes per year (USGS, 2001c). The metal is widely used in laboratory work for making thermometers, barometers, diffusion pumps, and many other instruments. It is used in making mercury-vapor lamps and advertising signs, and in mercury switches and other electronic apparatus. Other uses are in pesticides, mercury cells for chlor-alkali plants, dental preparations, anti-fouling paint, batteries, and catalysts (ATSDR, 1999c).

Mercury in the environment originates from both natural and anthropogenic sources. The former includes degassing of the Earth's crust and geothermal activity. Main sources of anthropogenic Hg include the burning of coal and losses from chlor-alkali plants. As a result of environmental concerns, emissions of Hg are declining in Western countries. However, in developing countries emissions are increasing. The future trend in anthropogenic emissions is therefore difficult to predict.

Metallic Hg is practically insoluble in water; it is however methylated in sediments by microorganisms. The highly toxic methylmercury (MeHg) thus formed is readily taken up by aquatic organisms and biomagnified through the food chain. Methylmercury exposure has been extensively documented in Arctic and subarctic populations since the 1970s (Hansen and Danscher, 1997), notably in Canada (Kosatsky and Dumont, 1991; Wheatley and Paradis, 1998). In some instances, hair was used as a surrogate for blood, and levels were converted using an appropriate conversion factor. Levels

correlate with the consumption of fish or sea mammals. In non-consumers, blood values are generally < 2 μg/L. In people who consume large amounts of fish, however, levels as high as 600 μg/L have been observed, with means of 20 to 40 μg/L. These levels can be compared to the 'no risk' level of 20 μg/L (WHO, 1990).

The physical and chemical characteristics of Hg make it easy to measure and speciate. Analytical problems are related to the very low levels found in some types of environmental sample and to the complexity of some matrices (ATSDR, 1999c).

Methylmercury affects the nervous system and can cause paresthesia, ataxia, and tunnel vision. *In utero* exposure (as seen in Minamata disease) may result in severe neurological damage, including cerebral palsy (Harada, 1995). No confirmed diagnosis of MeHg poisoning has been made in Arctic populations.

4.4.5. Selenium

Selenium (Se) is a metalloid and the element exists under three allotropic forms; red, gray and amorphous. Its four stable valence states are -2, 0, +4 and +6. In the environment, elemental Se is stable in soil and barely soluble in water. Selenites (+4) and selenates (+6) are soluble in water and thus more bioavailable. Selenates are biotransformed into organic compounds such as selenomethionine and selenocysteine, which are subsequently bioaccumulated by aquatic organisms (ATSDR, 1996).

Selenium is a relatively rare element, being sixty-ninth in abundance within the Earth's crust, with an average concentration of 0.05 to 0.09 mg/kg. It is produced as a by-product of the processing of copper ore. Annual worldwide usage is estimated at 1500 tonnes. Much of the Se produced (46%) is used in photocopying for the coating of the transfer cylinders. Other uses include electronics, glassmaking, and pigments. A variety of other uses account for the remaining production. Medically, Se is used as a catalyst in the preparation of pharmaceuticals, as an ingredient in antidandruff shampoos, as a constituent in fungicides, and as a supplement in animal feeds. Selenium may enter the environment as a result of human activity, principally within fly ash resulting from the combustion of coal (ATSDR, 1996).

The determination of trace amounts of total Se in environmental and biological matrices can be accomplished by several techniques including fluorometry (using 2,3-diaminonaphtalene as a fluorophore), neutron activation, GC (formation of volatile piazselenol), AAS (GF or hydride generation) as well as ICP–MS (ATSDR, 1996). It is often useful to determine which species of Se, whether organic or inorganic, is present. Most of the techniques mentioned are, however, not suitable for this since they require prior mineralization of the sample. Coupling HPLC to ICP–MS does allow the identification and quantitation of individual Se species (Michalke *et al.*, 2001).

Selenium is an essential element, present in several protein systems. It appears to offer protection from Hg poisoning as indicated by animal experiments (Cuvin-Aralar and Furness, 1991) and epidemiological studies. However, even a moderate excess of Se can lead to toxicity.

4.4.6. Tributyltin compounds

Tributyltin (TBT) compounds contain three butyl groups covalently bound to tetravalent tin. The main commercial compound is tributyltin oxide, however tributyltin hydroxide, tributyltin chloride, and tributyltin carbonate are also found in the environment. The biocide tributyltin oxide is used extensively as an antifouling agent in numerous formulations of marine paint. It is slowly released from the painted surface as the polymer is hydrolyzed in seawater, thereby entering the marine environment (Champ and Seligman, 1996).

Because of its low water solubility and lipophilic character, TBT is readily adsorbed onto particles and may persist in sediments for several years. It bioaccumulates in organisms, with the highest concentrations found in liver and kidney. Uptake from food is more important than uptake directly from water. However, TBT is rapidly metabolized and excreted from aquatic and terrestrial mammals and has not been shown to biomagnify in higher organisms. TBT has been detected in marine sediments in harbors throughout the world, including the Arctic region (Chau *et al.*, 1997; Ruiz *et al.*, 1996). As a result, most industrialized countries regulate the use of TBT, and its use on vessels shorter than 25 m is banned. As a consequence, environmental levels have decreased steadily since the 1980s. Populations of non-target affected marine organisms such as snails and molluscs have shown recovery since the regulations were put in place (Evans, 1999).

Determination of trace amounts of TBT in water and biota is classically performed by GC after derivatization. Detection limits are in the sub-ppb range (Sadiki and Williams, 1996). A novel technique, stir bar sorptive extraction with thermal desorption-capillary GC–ICP–MS allows the determination of ppq-level (i.e., one part in 10^{15}) traces of organotin compounds in environmental samples (Vercauteren *et al.*, 2001).

TBT is an endocrine disrupter for certain species of snail and other types of mollusc, but has not been shown to similarly affect higher organisms. In humans, acute exposure to organotin compounds (industrial exposure or laboratory accidents) has led to severe central nervous system damage, as well as to skin irritation (Baaijens, 1986). Although no data were found concerning low-level effects of TBT in humans, *in vitro* studies using human cells indicate potential immunological effects (Whalen *et al.*, 1999). Butyltin compounds were recently identified and measured in human blood from Michigan (Kannan *et al.*, 1999) with total concentrations ranging up to 100 μg/L.

4.5. Quality control and quality assurance

Reliable and comparable data are the basis for the AMAP assessment. In order to achieve this, a quality assurance and quality control (QA/QC) programme has been established by the AMAP Human Health Expert Group. This includes guidelines for sampling, transportation and storage, as well as analytical performance criteria including a ring test programme.

Basic prerequisites must be adhered to if quality is to be achieved and maintained. These include competence of personnel, adequacy of infrastructure and equipment,

documentation of all relevant procedures, traceability of measurements, and calibration. Various legislative bodies and international standardization organizations have promulgated guidelines addressing these requirements. ISO guide 17025 'General Requirements for the Competence of Calibration and Testing Laboratories' (ISO, 1999) is generally accepted as an appropriate basis for laboratory quality systems. It is however not sufficient for laboratories to adopt good practices. They must be able to demonstrate conclusively that the data they produce are consistently reliable.

Chemical trace analysis of contaminants in human samples is challenging. Due to risk of accidental exposure to diseases such as HIV, protocols and regulations concerning sample handling need to be carefully followed. Well-designed analytical procedures are required to overcome the difficulties associated with performing complex analyses on human media. These may include low concentrations of the analytes, small sample volume, a high number of contaminants, blank problems for compounds still in use, and interfering compounds. For liposoluble compounds, lipid normalization must also be performed. To ensure valid results, parameters such as identification, detection and quantitation limits, accuracy and precision, as well as the method's robustness must be evaluated. In addition, data treatment, reporting format and data storage must be harmonized.

A key issue is QC, which incorporates a range of activities such as the establishment and implementation of appropriate in-house QA routines, the use of relevant reference materials, and participation in inter-laboratory comparison programmes (also known variously as proficiency testing programmes, external QA schemes, or ring tests). The AMAP Human Health QA/QC system has been established to accomplish the last. At the request of the AMAP Human Health Expert Group, the Centre de Toxicologie of the Institute Nationale de Santé Publique du Québec in Canada has developed QA/QC activities in support of the AMAP Human Health monitoring programme. Main activities to date include running intercomparison programmes on relevant reference samples based on human material. This includes preparation and distribution of test samples, collection and interpretation of data, and the communication of results. In addition to the heavy metals, human samples for the organic contaminants (PCBs, standard pesticides, lipids, new organic xenobiotic compounds, and metabolites) will be provided. All laboratories producing data for AMAP are required to participate in the intercomparison programme and to achieve acceptable results.

4.6. Conclusions and recommendations

Heavy metals and UNEP-listed POPs are of continued concern for human health and should not be neglected. In addition, increased levels of many 'new' POPs and metabolites are a cause of significant concern. However, more data on their presence and possible effects are needed before their environmental impact, including possible implications for human health, can be properly evaluated. These knowledge gaps should be addressed in ongoing and future monitoring work. Where relevant, data reported should be congener-specific and lipid-normalized for the POPs, and speciated for the heavy metals to distinguish toxic and non-toxic forms. Selection criteria for choosing new target compounds must also be developed.

The key component for interpretation of monitoring results is reliable and comparable data. Therefore it is required that all laboratories producing human contaminant data for AMAP participate in the AMAP Human Health intercomparison programme with acceptable results.

Chapter 5

Biological Monitoring: Human Tissue Levels of Environmental Contaminants

Jay Van Oostdam and Neil Tremblay

Summary

Levels of environmental contaminants in blood samples from humans living in the Arctic regions of the eight circumpolar countries confirm that levels of certain persistent organic pollutants (POPs) and mercury (Hg) are generally higher in the Arctic people who consume certain (mainly marine based) traditional/country foods (e.g., the Inuit of Greenland and Arctic Canada). For Greenland Inuit in particular, the levels of polychlorinated biphenyls (PCBs), hexachlorobenzene (HCB), total chlordanes, and Hg found in maternal blood samples are higher than those found in samples from other circumpolar countries, and are likely to reflect the higher consumption of marine mammals by this group.

Other key findings include higher levels of total DDT in a non-indigenous population from Arkhangelsk (Russia) than in any other region, indicating possible continuing use of this pesticide locally or in Russian agricultural regions from which food is transported to the Arkhangelsk region. For β-HCH, the highest levels were also seen in Arctic Russia among non-indigenous groups, but elevated levels were also observed in Iceland and among the 'Others' group (i.e., non-Caucasian, non-Dene/Métis, non-Inuit) in the Canadian Arctic.

Recent data for the Faroe Islands indicate that, due to public health advice for mothers to restrict their consumption of pilot whale, there has been a significant decrease in maternal Hg levels, although very little change in PCB levels. The different response of these two contaminants is probably due to the short half-life of Hg in the body compared to that of PCBs. It is difficult to determine time trends in environmental contaminants of concern in other Arctic human populations since only one or two sequential datasets exist. Most monitoring of human contaminant levels in the Arctic has taken place over only the last five to ten years, and although this has permitted a reasonably good assessment of the spatial variation in contaminant levels in humans, it is too short a period to reliably determine temporal trends. For Hg, the discovery of ancient Greenland mummies, together with some supporting data on biota from their clothing, offers evidence that there has been a significant increase in the concentration of Hg in the Arctic environment over the past 500 years and in people who consume large amounts of marine mammals.

5.1. Introduction

This chapter reports new data obtained since the first AMAP assessment (AMAP, 1998). The data presented for Canada and Greenland do however include findings from the circumpolar maternal blood contaminant study reported in the first AMAP assessment, as this allows a better spatial/regional assessment of contaminant levels in the circumpolar north. For the other circumpolar countries, with the exception of Sweden for which there are no new maternal blood data, only new data have been used. Overall, the combination of the earlier and newer data allows for a greater range of regions/communities to be evaluated than would otherwise have been possible. The locations of the various studies included in the present assessment are presented in Figure 5·1 (see next page).

The results presented in this assessment report focus primarily on maternal blood levels of various POPs (several organochlorine (OC) pesticides and PCBs) and metals (e.g., Hg, cadmium (Cd), and selenium (Se)). A number of these contaminants have been implicated in negative impacts on the developing fetus or young children and are under investigation in various epidemiological studies in the Arctic (see chapters 6 and 9). Data from studies on some adult male populations are provided for comparison. The POPs data are summarized in Tables 5·1 to 5·8 and those for metals in Table 5·12. As there are no new Swedish maternal blood contaminant data, the 1995–96 data presented in the previous AMAP assessment report (AMAP, 1998) are included in Table 5·8. Additional data, on levels of PCBs in breast milk, are presented in Tables 5·9, 5·10, and 5·11.

Blood contaminant levels are discussed within a national and regional context, and then in terms of international comparisons, which includes comparisons between non-indigenous and indigenous populations.

5.1.1. Comparisons of data

Owing to varying national confidentiality requirements for the release or sharing of human data it has not been possible to obtain sufficient raw data to enable statistical comparisons between ethnic peoples or regions. However, comparisons of the population means and ranges for all the circumpolar peoples do permit general patterns of contaminant levels and their spatial relationships to be discerned. The QA/QC activity that has been completed for AMAP Phase II implies an inter-laboratory variability of the order of 20% to 30% for some of the more common analytes of concern (see section 5.5). To ensure that conclusions regarding spatial trends are not simply the result of analytical variability, this assessment is restricted to a consideration of differences of approximately two- to ten-fold between the various comparison groups, which are unlikely to be due to analytical variability.

Data presented in this chapter are on a wet weight basis unless otherwise stated; as these were the values reported by most circumpolar studies. Some data were also made available on a lipid weight basis, and these are tabulated in Annex 5A (Tables 5A·1 to 5A·5) for possible

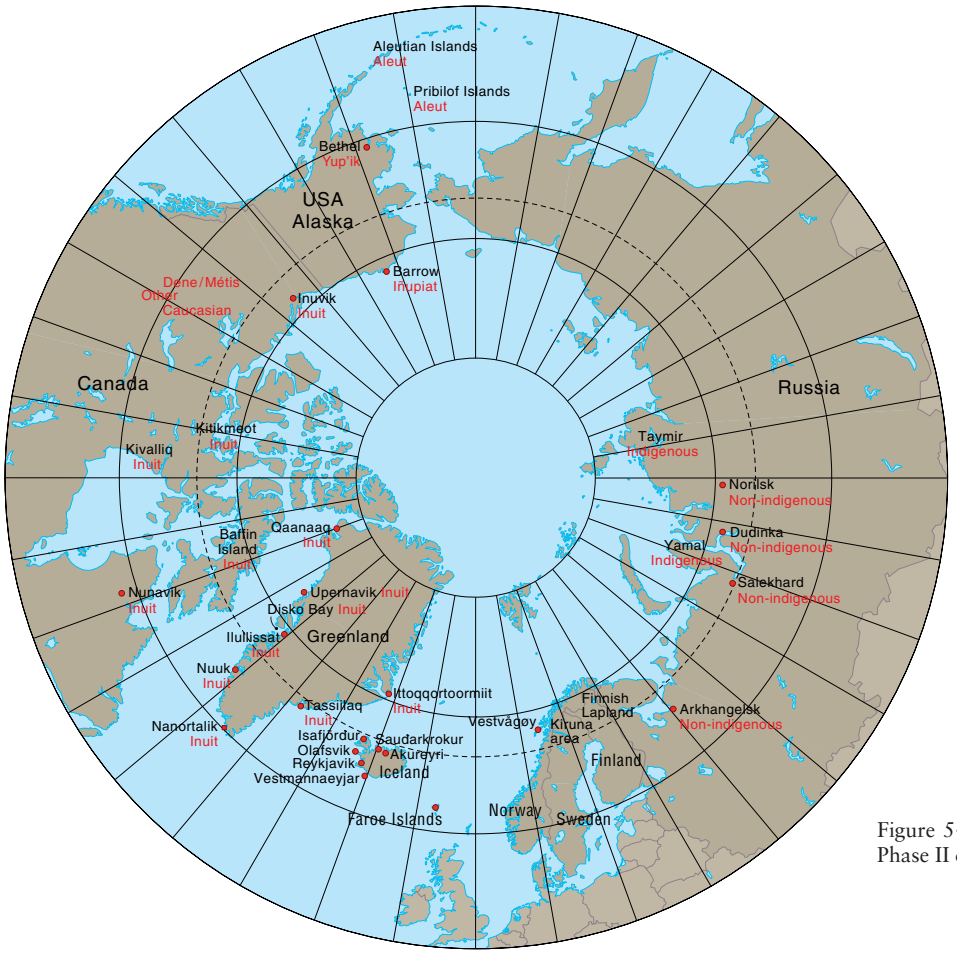

Figure 5·1. Sampling locations in the AMAP Phase II circumpolar blood monitoring study.

future use. Again, unless otherwise stated, comparisons are made using geometric mean values as most contributors were able to supply these values and geometric means are less affected by extreme values than arithmetic means.

Recruitment of subjects for the various circumpolar studies was usually based on the mother's interest in participating, and on residence in the catchment area of a specific birthing center. Any groups that were recruited based on known or probable increased exposure are identified in the text. When comparing the contaminant levels of different population groups, it is useful to have a description of age, parity, breast feeding history, and diet as these are important determinants of contaminant levels. For mothers, age is not a particularly significant factor as most mothers are fairly similar in age (18 to 35 years). Parity and breast feeding history were not available in many circumpolar studies. For men, age is reported, as levels of POPs increase with age and the possible age class is much wider (18 to 90 years). Diet is an important determinant of contaminant levels. Although it was not possible to implement AMAP dietary surveys in parallel with the maternal blood contaminant surveys in all Arctic countries, such surveys have been performed or are underway in several regions. Chapter 7 reviews the most recent dietary information available for the Arctic populations concerned.

Comparisons between the data reported in this chapter and blood guideline values are made in chapter 9. These comparisons permit a useful assessment of the levels found in various circumpolar populations and place these within the context of ongoing human health effects research within the Arctic and worldwide.

5.2. Persistent organic pollutants

5.2.1. National and regional data

Since the first AMAP assessment (AMAP, 1998), new national data on the levels of OC pesticides and PCBs in maternal blood have been provided for all the circumpolar countries except Sweden. Also available are intra-country regional data on specific OC pesticides (e.g., for Canada, Greenland, Alaska (United States), Russia, and Iceland) and data on differences in contaminant levels between ethnic groups (i.e., indigenous vs non-indigenous peoples) in Canada and Russia.

5.2.1.1. Canada

The sampling of maternal and cord blood in Arctic Canada between 1994 and 1999 has allowed a baseline assessment of environmental contaminants in most regions and ethnic groups of the Canadian north (with the exception of the Yukon). Some of the Canadian data were available for the first AMAP assessment; namely data for the Inuit from the Kitikmeot region. A number of additional Inuit groups have now participated in monitoring programmes, as have Dene/Métis and 'Others' (non-indigenous Canadian residents, mainly of African and East Asian ancestry) groups. Since there were no significant differences in contaminant levels in samples collected in 1994 to 1995 and

Table 5·1. Organochlorine contaminants in maternal blood from Canada, by region and ethnic group (geometric mean (range), µg/L plasma).

				Inuit 1994–2000				
	Caucasian[1] 1994–99 (n=134)	Dene/Métis[1] 1994–99 (n=93)	Other[1] 1995 (n=13)	Baffin 1996 (n=30)	Inuvik 1998–1999 (n=31)	Kitikmeot[1] 1994–95 (n=63)	Kivalliq[1] 1996–97 (n=17)	Nunavik[2] 1995–2000 (n=199)
Oxychlordane	0.05 (nd–0.22)	0.04 (nd–0.23	0.04 (nd–0.21)	0.58 (0.09–2.4)	0.15 (0.03–1.1)	0.29 (nd–2.9)	0.36 (nd–6.2)	0.30 (0.01–3.9)
Trans–nonachlor	0.06 (0.02–0.26)	0.06 (nd–0.37)	0.07 (0.02–0.30)	0.64 (0.16–2.5)	0.28 (0.05–1.8)	0.31 (nd–3.0)	0.44 (0.03–3.7)	0.46 (0.01–4.6)
p,p'-DDT	0.05 (nd–0.19)	0.03 (nd–0.13)	0.22 (nd–3.2)	0.14 (0.04–0.47)	0.07 (nd–0.45)	0.08 (nd–0.33)	0.09 (nd–0.35)	0.09 (0.02–1.1)
p,p'-DDE	0.91 (0.22–11.2)	0.69 (0.15–5.3)	4.0 (0.51–34)	2.1 (0.55–6.0)	1.1 (0.40–3.8)	1.3 (0.12–7.8)	1.7 (0.21–7.2)	2.2 (0.14–18)
DDE:DDT ratio	18 (nd–75)	18 (nd–89)	15 (nd–31)	15 (7.1–43)	13 (nd–51)	15 (nd–53)	19 (nd–52)	23 (2.8–209)
HCB	0.12 (0.04–0.61)	0.18 (0.02–1.7)	0.11 (0.02–0.40)	0.53 (0.14–1.5)	0.31 (0.06–1.2)	0.56 (0.05–4.5)	0.46 (0.07–1.8)	0.31 (0.05–2.8)
β-HCH	0.09 (nd–0.55)	0.04 (nd–0.13)	0.48 (0.04–39)	0.11 (nd–0.44)	0.08 (nd–0.25)	0.09 (nd–0.44)	0.09 (nd–0.30)	0.04 (0.02–0.25)
Mirex	0.02 (nd–0.14)	0.02 (nd–0.21)	0.01 (nd–0.07)	0.06 (nd–0.19)	0.03 (nd–0.11)	0.05 (nd–0.38)	0.06 (nd–0.80)	0.07 (0.01–0.60)
Total Toxaphene	0.05[3] (nd–0.50)	0.07[4] (nd–0.81)	na	0.59 (nd–6.4)	0.43 (nd–3.6)	0.68[5]	0.74 (nd–5.2)	na
Parlar 26	0.01[3] (nd–0.04)	0.01[4] (nd–0.06)	na	0.10 (0.02–0.57)	0.05 (nd–0.36)	0.09[5]	0.08 (nd–0.43)	na
Parlar 50	0.01[3] (nd–0.05)	0.01[4] (nd–0.07)	na	0.13 (0.03–0.66)	0.06 (nd–0.43)	0.14[5]	0.10 (nd–0.57)	na
PCBs (>70% detected)								
Aroclor 1260[6]	1.3 (0.24–5.7)	1.3 (0.26–14)	1.1 (0.31–3.7)	8.0 (2.0–27)	2.4 (0.62 7.9)	4.5 (0.20–27)	5.6 (0.41–60)	6.0 (0.10–48)
CB118	0.04 (nd–0.27)	0.04 (nd–0.26)	0.03 (nd–0.09)	0.14 (0.03–0.50)	0.07 (0.02–0.32)	0.09 (nd–0.40)	0.09 (nd–0.66)	0.10 (0.01–0.84)
CB138	0.11 (0.02–0.48)	0.10 (0.02–0.98)	0.10 (0.03–0.29)	0.51 (0.12–1.5)	0.19 (0.05–0.67)	0.30 (0.02–1.6)	0.37 (0.03–3.3)	0.42 (0.01–3.1)
CB153	0.14 (0.03–0.61)	0.16 (0.03–1.8)	0.12 (0.03–0.41)	1.0 (0.12–1.5)	0.26 (0.06–0.88)	0.56 (0.02–3.6)	0.70 0.75 (0.05–8.3)	(0.03–6.1)
CB180	0.09 (nd–0.50)	0.08 (nd–1.2)	0.07 (0.02–0.29)	0.40 (0.07–1.8)	0.08 (0.02–0.30)	0.27 (0.02–1.7)	0.28 (0.03–4.2)	0.32 (0.02–2.3)
ΣPCB_{14}[7]	0.52 (0.11–2.2)	0.52 (0.12–5.5)	0.43 (0.13–1.4)	2.7 (0.70–9.4)	0.82 (0.23–2.7)	1.6 (0.12–9.4)	1.9 (0.17–22)	2.3 (0.17–16)

nd: not detected; na: not available.

[1]Walker *et al.* (2001); [2]Muckle, pers. comm. (2000), Muckle *et al.* (2001b); [3]n=25; [4]n=42; [5]composite value based on four composite sub-samples (n=12, 12, 12 and 14) (Inuit); [6]Aroclor 1260 quantified as 5.2 (CB138 + CB153), Weber, pers. comm. (2002); [7]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

1998 to 1999 in the Canadian Arctic for Caucasians, Dene/Métis, or Others, the data for these time periods were combined.

Table 5·1 presents regional data on mean levels of various OC pesticides and PCBs in maternal plasma from Canada (Muckle, pers. comm., 2000; Muckle *et al.*, 2001b; Walker *et al.*, 2001).

Table 5·1 indicates that the Inuit in the Arctic regions of the Northwest Territories (NWT) and Nunavut (Walker *et al.*, 2001) and Nunavik in northern Quebec (Muckle, pers. comm., 2000; Muckle *et al.*, 2001b) have levels of oxychlordane and *trans*-nonachlor that are 4 to 15 times higher than those in the other population groups within the NWT/Nunavut region, i.e., Caucasians, Dene/Métis, or Others. When Inuit groups from Nunavik and the four subregions of the NWT/Nunavut region (Baffin, Inuvik, Kitikmeot, and Kivalliq) are examined, the Baffin Inuit are seen to have the highest levels of *trans*-nonachlor (0.64 µg/L) and oxychlordane (0.58 µg/L), while the Kivalliq Inuit have the highest levels of total toxaphene (0.74 µg/L). Among Inuit, levels of mirex and *p,p'*-DDE are highest in Nunavik Inuit. Higher levels of many POPs in Inuit populations from the eastern Arctic regions (i.e., Nunavik, Baffin, and Kivalliq) are due to the greater consumption of marine mammals by these groups relative to other regions.

In contrast, the patterns shown by β-HCH and DDE are quite different. Levels of β-HCH are 5 to 12 times higher in the Others group than among Inuit, Caucasians, or Dene/Métis (0.48 vs 0.04 to 0.11 µg/L). The levels of DDE in the Others group are also roughly two to six times higher than levels observed in Inuit, Caucasians, or Dene/Métis. The Others group comprises people of African, Caribbean and East Asian ancestry, and their exposure to these contaminants may have taken place in these areas of the world or via the consumption of food imported from regions where these compounds are still widely used. For example, Sharma and Bhatnagar (1996) report markedly higher levels of these compounds in the plasma of mothers from India.

The Inuit have higher levels of PCBs estimated as Aroclor 1260 (2.4 to 8.0 µg/L) than Caucasians, Dene/

Table 5·2. Organochlorine contaminants in blood of pregnant women and women of child-bearing age from Greenland, by region (geometric mean (range), μg/L plasma).

	Disko Bay[1,2,3] 1997–98 (n=95)	Ilullissat[1,2,3] 1999–2000 (n=29)	Nuuk[3,4] 1999 (n=32)	Ittoqqortoormiit[1,2,3] 1999–2000 (n=8)	Tassiilaq[1,2,5] 1997 (n=10)
Oxychlordane	0.54 (0.02–3.9)	0.26 (0.01–1.1)	0.17 (0.02–0.75)	1.5 (0.41–4.8)	1.2 (0.28–4.1)
Trans-nonachlor	1.1 (0.03–8.4)	0.49 (0.01–2.3)	0.40 (0.04–2.1)	1.3 (0.61–4.5)	2.2 (0.63–5.5)
p,p'-DDT	0.11 (0.01–13)	0.04 (0.01–0.37)	0.05 (0.02–0.34)	0.26 (0.14–1.3)	0.31 (0.16–0.73)
p,p'-DDE	3.6 (0.56–17)	1.7 (0.39–6.0)	2.0 (0.63–7.8)	5.2 (2.7–18)	6.9 (2.6–24)
DDE:DDT ratio	33 (0.06–300)	48 (13–432)	40 (9.3–136)	20 (14–38)	22 (10–59)
HCB	0.80 (0.14–4.0)	0.39 (0.10–1.6)	0.38 (0.14–1.2)	0.78 (0.37–2.0)	1.0 (0.30–2.7)
β-HCH	0.15 (0.03–0.50)	0.07 (0.01–0.18)	0.11 (0.05–0.26)	0.24 (0.12–0.61)	0.20 (0.04–0.48)
Mirex	0.08 (0.01–1.9)	0.04 (0.01–0.19)	0.03 (0.01–0.15)	0.18 (0.05–0.88)	0.25 (0.06–0.85)
Sum of Toxaphene[6]	0.81 (nd–4.7)	0.24 (0.05–1.1)	0.27 (0.05–1.4)	0.61 (0.37–1.2)	1.2 (0.48–2.4)
Parlar 26	0.26 (0.01–2.1)	0.08 (0.01–0.40)	0.09 (0.01–0.57)	0.24 (0.12–0.47)	0.56 (0.23–1.1)
Parlar 50	0.33 (0.01–2.6)	0.11 (0.01–0.63)	0.14 (0.01–0.83)	0.31 (0.16–0.72)	0.67 (0.25–1.3)
PCBs (>70% detected)					
Aroclor 1260[7]	15 (3–60)	6.4 (2.0–22)	7.9 (2.6–28)	36 (14–125)	33 (12–82)
CB118	0.32 (0.05–1.3)	0.13 (0.03–0.47)	0.15 (0.05–0.83)	0.53 (0.25–1.6)	0.57 (0.18–1.6)
CB138	1.1 (0.22–4.5)	0.47 (0.14–1.8)	0.59 (0.20–2.2)	2.3 (1.1–7.7)	2.4 (0.84–5.9)
CB153	1.8 (0.36–7.0)	0.76 (0.23–2.6)	0.92 (0.30–3.2)	4.7 (1.6–16)	3.9 (1.5–9.9)
CB180	0.72 (0.16–2.9)	0.32 (0.10–1.0)	0.39 (0.14–1.2)	2.4 (0.66–10.1)	2.2 (0.58–5.5)
ΣPCB_{14}[8]	5.5 (1.1–21)	2.5 (0.72–8.1)	3.1 (0.97–10.2)	14.5 (6.1–49)	12.4 (4.9–30)

[1]Deutch, pers. comm. (2001); [2]Deutch and Hansen (2000); [3]pregnant women; [4]Bjerregaard, pers. comm. (2001); [5]women of child-bearing age; [6]parlars 26 + 50; [7]Aroclor 1260 quantified as 5.2 (CB138+CB153); Weber, pers. comm. (2002); [8]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

Métis or Others (1.3, 1.3 and 1.1 μg/L, respectively). When the Inuit data for the NWT/Nunavut (Walker *et al.*, 2001) and Nunavik (Muckle, pers. comm., 2000; Muckle *et al.*, 2001b) areas are separated regionally, it is evident that the Baffin Inuit have the highest levels of PCBs as Aroclor 1260, although levels in Nunavik, Kivaliq and Kitikmeot Inuit are only slightly lower.

When PCBs are examined on a congener-specific basis, CB138 and CB153 are present at the highest levels exhibiting a pattern corresponding to that for PCBs as Aroclor 1260.

Most of the dietary assessments undertaken in connection with the maternal and cord blood sampling programme in the Canadian Arctic were relatively basic, but a consistent pattern relating increased consumption of marine mammal tissues among Inuit populations to increased body burdens of PCBs and a number of pesticides (chlordane derivatives, toxaphene, and mirex) was noted. A more detailed assessment of more specific components of the traditional diet is underway and the results should be available shortly.

5.2.1.2. **Greenland**

Contaminant levels in women of child-bearing age are currently available for the Disko Bay, Ilullissat, Nuuk, Ittoqqortoormiit and Tassiilaq regions of Greenland (Table 5·2) (Deutch, in prep; Deutch and Hansen, 2000).

Contaminant concentrations in the blood plasma of women from Ittoqqortoormiit and Tassiilaq were two to three times higher than in women from Disko Bay, i.e., oxychlordane: 1.5 and 1.2 vs 0.54 μg/L; *p,p'*-DDE: 5.2 and 6.9 vs 3.6 μg/L. The OC levels in women from Ilullissat and Nuuk are even lower, often only 50% of those found in the Disko Bay women (Table 5·2). The concentrations of toxaphene measured as Parlars 26 and 50 are at least two-fold higher in women from the east coast community of Tassiilaq compared to the other populations sampled.

Blood levels of CB118, CB138, CB153 and CB180 were also consistently higher in the Tassiilaq and Ittoqqortoormiit women compared to pregnant women from Disko Bay (Table 5·2). Levels of PCBs estimated as Aroclor 1260 followed the same pattern, and were about

Table 5·3. Organochlorine contaminants in blood of men from Greenland, by District, 1997 (geometric mean (range), μg/L plasma).

	Ittoqqortoormiit (n=15)	Nanortalik (n=5)	Nuuk (n=15)	Ilullissat (n=16)	Upernavik (n=11)
Mean age	38 (19–60)	36.6 (23–52)	28.5 (19–36)	42 (23–59)	31.6 (25–38)
Oxychlordane[1]	3.9 (0.49–15)	2.4 (0.93–5.1)	0.75 (0.13–3.0)	2.0 (0.25–7.2)	1.0 (0.35–6.6)
Trans-nonachlor[1]	3.0 (0.32–50)	4.5 (1.8–8.0)	1.5 (0.23–7.0)	3.9 (0.46–14)	1.8 (0.73–7.5)
p,p'-DDT[1]	0.17 (0.04–0.98)	0.79 (0.29–2.2)	0.11 (0.03–0.37)	0.14 (0.03–0.76)	0.10 (0.04–0.24)
p,p'-DDE[1]	11 (1.6–32)	15 (7.1–27)	5.2 (1.3–16)	8.0 (1.9–25)	4.7 (2.2–17)
DDE:DDT ratio	63 (29–220)	19 (12–32)	48 (23–122)	58 (15–357)	46 (23–101)
HCB[2]	1.5 (0.40–3.9)	1.2 (0.4–2.6)	1.1 (0.22–5.1)	2.4 (0.38–8.4)	0.90 (0.25–2.7)
β-HCH[2]	0.56[3] (0.17–1.8)	0.20 (0.08–3.0)	0.18 (0.06–0.66)	0.31 (0.07–0.85)	0.18 (0.10–0.42)
Mirex[2]	0.52 (0.02–2.2)	0.61 (0.29–1.4)	0.16 (0.06–0.51)	0.26[1] (0.07–0.64)	0.16 (0.05–1.0)
Sum of Toxaphene[2,4]	0.71 (0.18–2.1)	1.6 (0.50–3.7)	0.78 (0.07–5.2)	1.9 (0.19–7.0)	0.79 (0.29–3.1)
Parlar 26[1]	0.34 (0.09–1.0)	0.67 (0.21–1.6)	0.38 (0.03–2.1)	0.74 (0.09–3.2)	0.37 (0.14–1.4)
Parlar 50[1]	0.37 (0.09–1.1)	0.89 (0.28–2.1)	0.45 (0.04–3.1)	0.93 (0.10–3.8)	0.41 (0.15–1.7)
PCBs					
Aroclor 1260[1,5]	107 (18–331)	63 (29–113)	21 (7–71)	39 (8–87)	18 (10–81)
CB118[1]	1.0 (0.18–4.3)	0.48 (0.17–1.0)	0.29 (0.06–1.6)	0.57 (0.08–2.0)	0.31 (0.13–0.86)
CB138[1]	6.0 (1.0–19)	4.3 (1.8–8.4)	1.6 (0.50–5.5)	2.6 (0.56–6.5)	1.3 (0.72–5.0)
CB153[1]	14 (2.4–44)	7.7 (3.8–13)	2.6 (0.81–8.2)	4.4 (0.94–10)	2.2 (1.3–11)
CB180[1]	9.6 (1.4–31)	3.5 (1.6–6.7)	1.2 (0.35–4.0)	2.0 (0.47–4.6)	1.1 (0.51–4.4)
ΣPCB_{14}[2,6]	41 (6.6–127)	21 (9.6–40)	7.6 (2.4–27)	14 (2.8–29)	6.6 (3.9–27)

[1]Deutch, pers. comm. (2001); [2]Deutch and Hansen (2000); [3]n=14; [4]parlars 26 and 50; [5]Aroclor 1260 quantified as 5.2 (CB138 + CB153); Weber, pers. comm. (2002); [6]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

twice as high in women from the Tassiilaq and Ittoqqortoormiit regions as in Disko Bay women; even lower levels were seen in women from Ilullissat and Nuuk. There are some age differences in these populations, with slightly older average ages in Tassiilaq, but when these data are sorted by age group the same regional patterns emerge (Deutch, in prep).

Table 5·3 outlines mean blood plasma levels of OC pesticides and four PCB congeners in men from five districts of Greenland (Deutch, in prep; Deutch and Hansen, 2000). The regional pattern of OCs in men is very similar to that for women. Levels of oxychlordane were highest in men from Ittoqqortoormiit (3.9 μg/L). Levels of oxychlordane in men from Nanortalik (2.4 μg/L) and Ilullissat (2.0 μg/L) were also relatively high – more than twice those found in men from Nuuk and Upernavik. The levels of DDT (0.79 μg/L) and DDE (15 μg/L) in men from Nanortalik were roughly 5 to 8 times and 1.5 to 3 times higher, respectively, than those from any other region. Nanortalik men also had the highest mean level of mirex. The highest mean level of HCB was found in men from Ilullissat (2.4 μg/L), and that of β-HCH in men from Ittoqqortoormiit (0.56 μg/L). Ittoqqortoormiit men also showed the highest concentrations of the four PCB congeners listed in Table 5·3. Men from Nuuk and Uppernavik had lower levels of many of these contaminants but are on average five to thirteen years younger than men from the other three communities.

It is clear from these data that there are strong regional differences in the levels of POPs in blood plasma throughout Greenland. These differences are related mainly to different intakes of traditional/country foods (e.g., marine mammals such as seals), which have very high POP levels along the east coast of Greenland, which includes the Tassiilaq and Ittoqqortoormiit regions (Deutch and Hansen, 2000).

Strong correlations were found between POP concentrations in the blood plasma of mothers and newborns. The association between reported monthly food intake and POP concentrations was relatively weak, but the POP levels were strongly correlated with plasma and erythrocyte n-3/n-6 fatty acid ratios as biomarkers of

Table 5·4. Organochlorine pesticides and total PCBs in serum[1] samples from Aleutian and Pribilof villages in Alaska (median or arithmetic mean (range), μg/L serum). Source: Middaugh, pers. comm. (2001).

	Akutan (n=11)		Atka (n=30)		Nikolski (n=10)		St. George (n=19)		St. Paul (n=96)		Total (n=166)	
	median	am	median	am	median	am	median	am	median	am	median	am
Oxychlordane	0.65	0.84	0.63	1.3	0.41	0.39	0.51	0.59	0.28	0.49	0.37 (nd–4.2)	0.66
Trans-nonachlor	0.69	1.3	1.8	3.2	0.82	0.80	0.96	1.3	0.67	1.3	0.82[2] (nd–12.4)	1.6
p,p'-DDT	nd	0.05	nd	0.15	nd	0.07	nd	0.01	nd	0.02	nd (nd–0.58)	0.05
p,p'-DDE	9.7	12.3	9.8	16.9	11.3	10.4	7.8	11.7	6.5	14.0	7.5 (nd–158)	13.9
DDE:DDT ratio	na		na		na		na		na		na	
HCB	na		na		na		na		na		na	
β-HCH	0.26	0.35	0.30	0.53	0.25	0.24	0.23	0.39	0.15	0.30	0.19 (nd–2.6)	0.35
Mirex	nd	0.04	0.18	0.22	nd	0.07	0.10	0.12	nd	0.06	nd (nd–0.80)	0.10[3]
Total Toxaphene	na		na		na		na		na		na	
Heptachlor Epoxide	0.12	0.15	0.06	0.19	nd	0.06	nd	0.08	nd	0.10	nd (nd–1.6)	0.11
Dieldrin	nd	0.04	nd	0.10	nd	0.01	nd	0.02	nd	0.04	nd (nd–0.53)	0.05
ΣPCB_{36}[4]	5.5 (2.8–18)	8.4	8.0 (nd–54)	15	5.7 (0.9–13)	6.0	6.6 (nd–30)	7.1	3.4 (nd–42)	5.7	4.8 (nd–54)	7.7

am: arithmetic mean; nd: not detected; na: not available.

[1]The serum samples were from a group of 166 individuals consisting of 83 females and 83 males, with an age range of 18–91 years. A further age–sex breakdown by village and by contaminant was not available; [2]n=160; [3]n=162; [4]CB8, CB20, CB44, CB49, CB52, CB66, CB74, CB87, CB99, CB101, CB105, CB110, CB118, CB128, CB138 + CB158, CB146, CB149, CB151, CB153, CB156, CB157, CB167, CB170, CB172, CB177, CB178, CB180, CB183, CB187, CB189, CB194, CB195, CB196 + CB203, CB201, CB206, and CB209.

marine food intake (Deutch and Hansen, 2000). Marine mammal meat and organs are consumed by the Greenland Inuit to such an extent that it results in a relatively high exposure to environmental contaminants such as POPs. In the northern and eastern regions, consumption of seal meat is higher than for any other food item, while fish consumption predominates on the south and east coasts (AMAP, 1998).

There was also a strong positive correlation between smoking and POP plasma levels, after correction for age, alcohol intake, marine food, plasma lipids, and n-3/n-6 fatty acid ratios (Deutch and Hansen, 2000). This implies that the most important determinants of high plasma POP levels in Greenlanders are age, high plasma n-3 fatty acid levels (which indicate the consumption of marine foods), residence in the east coast region, and heavy smoking (Deutch and Hansen, 2000).

5.2.1.3. **Alaska**

Table 5·4 shows the mean and median concentrations of OC pesticides in serum samples from 166 individuals (83 men and 83 women) from five Aleutian and Pribilof villages in Alaska (Middaugh *et al.*, 2001). The mean and median levels of all pesticides measured in samples from St. Paul Island and St. George Island are generally similar to or lower than the levels found in Atka, Akutan, and Nikolski. Mean and median levels in samples from all five villages were strongly associated with age; the highest levels were found in individuals over 50 years old (Middaugh *et al.*, 2001).

Included in the 115 samples from the Pribilof Island villages of St. Paul and St. George were 29 women of child-bearing age. Mean pesticide levels among these women were lower than those in the eleven such women from the Aleutian Island villages of Atka, Akutan, and Nikolski. The age range for the women of child-bearing age was 15 to 45 years and there were no known pregnant women in the sample (Middaugh *et al.*, 2001).

Recently data have become available for contaminants in maternal blood from Yup'ik mothers from the Yukon–Kuskokwim river delta or from villages on the Bering Sea (these mothers all delivered in Bethel) and Iñupiat mothers living in the villages on the northern Arctic coast (these mothers all delivered in Barrow) (Berner, pers. comm., 2001).

Data received to date for these mothers are presented in Table 5·5. Care must be taken in comparing the contaminant levels in women of child-bearing age from the Aleutian/Pribilof Islands with those of mothers from Yup'ik or Iñupiat mothers since the Aleutian/Pribilof women were specifically selected for high traditional food consumption and therefore possible higher contaminant exposure. This may explain the higher levels of DDE in the Aleutian/Pribilof women compared to the Iñupiat and Yup'ik mothers (4.1 vs 0.65 and 1.3 μg/L, respectively). It is also interesting to note that the ratio of DDE to DDT is very different for the Bethel and Barrow mothers (16 and 8.6) compared to the women of child-bearing age from the Aleutian and Pribilof Islands (a ratio of 203, based on population means). This indi-

Table 5·5. Organochlorine contaminants in maternal blood and blood of women of child-bearing age from Alaska (geometric mean, median, or arithmetic mean, (range), g/L serum).

	Yupik (Bethel)[1] 2000 (n=23) gm	Inupiat (Barrow)[1] 2000 (n=22) gm	Aleutian–Pribilof women of child-bearing age[2] 1999 (n=40)[3] median	am
Oxychlordane	na	na	0.18	0.26
Trans-nonachlor	na	na	0.3	0.62
Total DDT	0.08[4] (0.04–1.4)	0.08[4] (0.05–0.19)	nd	0.03
p,p'-DDE	1.3 (0.17–6.1)	0.65 (0.11–1.5)	4.1	6.1
DDE:total DDT ratio [5]	16	8.6	203[6]	
HCB	na	na	na	
β-HCH	na	na	nd	0.12
Mirex	na	na	nd	0.02
Total Toxaphene	na	na	na	
Parlar 26	na	na	na	
Parlar 50	na	na	na	
PCBs				
Aroclor 1260[7]	na	na	na	
CB118	0.07 (0.01–0.15)	0.03 (0.01–0.15)	na	
CB138	na	na	na	
CB153	0.33 (0.06–1.7)	0.09 (0.01–0.58)	na	
CB180	0.12 (0.03–0.92)	0.04 (0.01–0.21)	na	
ΣPCB_{36}[8]	na	na	2.0 (nd–15)	2.9

gm: geometric mean; am: arithmetic mean; na: not available; nd not determined.

[1]Berner, pers. comm. (2001); [2]Middaugh, pers. comm. (2001); [3]n=40: 29 from St. Paul and St. George, and 11 from Atka, Akutan, and Nikolski; [4]values are for total DDT; [5]the DDT value in this ratio is for total DDT. The *o,p'*-DDT values were very low relative to *p,p'*-DDT values; thus, total DDT values are approximately equal to *p,p'*-DDT values; [6]this DDE:total DDT ratio is based on population means; [7]Aroclor 1260 quantified as 5.2 (CB138 + CB153); Weber, pers. comm. (2002); [8]CB18, CB20, CB44, CB49, CB52, CB66, CB74, CB87, CB99, CB101, CB105, CB110, CB118, CB128, CB138 + CB158, CB146, CB149, CB151, CB153, CB156, CB157, CB167, CB170, CB172, CB177, CB178, CB180, CB183, CB187, CB189, CB194, CB195, CB196 + CB203, CB201, CB206, and CB209.

cates that there is likely to be a different source of exposure for these population groups, as is also reflected in the higher levels of the parent compound (DDT) in the Bethel and Barrow mothers.

Dietary differences might explain the marked difference in DDT/DDE exposure between the Aleutian/Pribilof and Bethel/Barrow cohorts. Although there is no dietary information available for any of the Aleutian/Pribilof cohort, they reside in an isolated region with a high dependence on subsistence foods. Although speculative, it is clear that DDE levels increase with age, and there were a fair number of older people in the sample. Older people eat a lot of fish and seals, all of which feed in the North Pacific Ocean, in the currents that sweep up the Asian coast, so it could well represent biomagnification combined with decades of DDT use in Asia. Women from the Yukon–Kuskokwim river delta eat considerably more salmon and pike, and seals, while the Arctic coast women eat more bowhead whale (*Balaena mysticetus*) and terrestrial animals (Berner, pers. comm., 2001).

Limited PCB data are available for Alaska. Of the three congeners for which data are available, CB153 occurred at the highest concentrations, with the mothers from Bethel having higher concentrations than those from Barrow (0.33 vs 0.09 μg/L). Similar patterns were seen for CB118 and CB180. Data have recently become available for the sum of 36 PCB congeners in the blood of Aleutian/Pribilof women of child-bearing age (2.9 μg/L, arithmetic mean) but these data are not directly comparable with any other data collected in AMAP programme.

In conclusion, the recent findings for OC pesticide levels in blood confirm earlier reports from the Alaska Department of Health and Social Services. For women of child-bearing age in particular, the low levels of OC pesticides strongly support current recommendations by

Table 5·6. Organochlorine contaminants in maternal blood from Russia, by region and indigenous status (geometric mean (range), μg/L plasma).

	Non-indigenous regions			Indigenous regions		Non-indigenous
	Norilsk[1] 1995–96 (n=49)	Salekhard[2] 1996–98 (n=31)	Dudinka[1] 1995–96 (n=27)	Taymir[1] 1995–96 (n=18)	Yamal[2] 1996–98 (n=12)	Arkhangelsk[3] 1999 (n=30)
Oxychlordane	na	na	na	na	na	0.18[4] (nd–0.67)
Trans-nonachlor	0.10 (0.05–0.25)	0.12 (0.07–0.24)	0.15 (0.07–0.34)	0.09 (0.04–0.15)	0.10 (0.04–0.23)	0.12[4] (nd–0.66)
p,p'-DDT	0.21 (0.08–0.57)	0.16 (0.03–0.75)	0.14 (0.05–0.33)	0.07 (0.04–0.13)	0.05 (0.03–0.08)	0.83[5] (0.28–5.1)
p,p'-DDE	1.8 (0.62–4.0)	1.5 (0.35–4.4)	1.3 (0.45–3.6)	1.1 (0.39–2.0)	0.72 (0.32–1.4)	4.5[6] (1.7–13.1)
DDE:DDT ratio	8.0 (5.1–14)	8.8 (5.4–14)	9.3 (5.9–13)	15 (7.8–21)	14 (6.4–21)	5.5 (na)
HCB	0.21 (0.05–0.52)	0.26 (0.15–0.59)	0.30 (0.06–0.09)	0.20 (0.02–0.71)	0.18 (0.05–0.42)	0.47[4] (0.18–1.4)
β-HCH	1.1 (0.40–3.7)	0.45 (0.09–3.4)	0.31 (0.04–1.6)	0.35 (0.02–0.76)	0.45 (0.18–0.94)	3.1[4] (1.3–11.6)
Mirex	0.01 (nd–0.04)	0.01 (nd–0.03)	0.01 (nd–0.02)	0.01 (nd–0.02)	0.01 (nd–0.02)	0.20[4] (0.14–0.51)
Toxaphene	na	na	na	na	na	na
Parlar 26	na	na	na	na	na	0.05 (nd–0.10)
Parlar 50	na	na	na	na	na	0.06 (0.02–0.70)
PCBs		(n=5)				
Aroclor 1260[7]	3.8[8] (1.2–9.1)	4.3[8] (2.3–9.2)	3.3[8] (2.0–5.5)	1.5[8] (0.5–4.2)	3.0[8] (1.7–4.6)	4.2[7,9] (1.2–16.9)
CB118	na	0.33 (0.24–0.45)	na	na	na	0.29[9] (0.10–1.0)
CB138	na	0.43 (0.20–0.89)	na	na	na	0.42[9] (0.12–1.5)
CB153	na	0.45 (0.30–0.57)	na	na	na	0.39[9] (0.11–1.7)
CB180	na	0.20 (0.06–0.47)	na	na	na	0.13[9] (0.04–1.0)
ΣPCB_{14}[10]	na	2.1 (1.0–3.2)	na	na	na	1.7[9, 11] (0.6–6.8)

na: not available.

[1]Klopov *et al.* (1998); [2]Klopov (2000), Klopov and Shepovalnikov (2000), Klopov and Tchachchine (2001); [3]Odland, pers. comm. (2000);[4]n=24; [5]n=16; [6]n=26; [7]Aroclor 1260 quantified as 5.2 (CB138 + CB153), Weber, pers. comm. (2002); [8]calculated using method of Sergei Vlasov, Vlasov, pers. comm. (2001); [9]n=27; [10]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187; [11]does not include CB28.

Alaskan public health officials for continued unrestricted consumption of traditional foods (Middaugh *et al.*, 2001).

5.2.1.4. **Russia**

Generally, the major source of exposure to environmental contaminants in Russia is via food consumption. For example, freshwater fish consumption is a key source of contaminant exposure in Salekhard and Norilsk (AMAP, 1998).

From Table 5·6, it is evident that the mean maternal blood plasma levels for all the OC pesticides are higher in the non-indigenous population from the Arkhangelsk region (Odland, pers. comm., 2000) than in any other areas of Russia for which new data are available (Klopov, 2000). In particular, the levels of *p,p'*-DDT (0.83 μg/L) and *p,p'*-DDE (4.5 μg/L) are much higher in the Arkhangelsk region than in the other Russian regions studied. Arkhangelsk women also had the highest blood levels of β-HCH (3.1 μg/L) and HCB (0.47 μg/L).

When earlier data (AMAP, 1998) from the industrial area of Nikel on the Kola Peninsula are included in the analysis, it is evident that this region also has high levels of OC pesticides with concentrations only slightly lower than those in Arkhangelsk; for example, *trans*-nonachlor (0.09 μg/L), DDT (0.34 μg/L), DDE, (3.0 μg/L), β-HCH (1.7 μg/L), and HCB (0.47 μg/L).

The levels of *trans*-nonachlor are similar within the non-indigenous and indigenous populations of Arctic Russia. DDT levels show a different pattern with concentrations two to four times higher in non-indigenous populations, Norilsk having the highest levels. DDE levels are also slightly to moderately elevated in non-indigenous populations. These DDE and DDT levels result in lower DDE: DDT ratios in non-indigenous regions of Siberia, suggesting a current exposure to DDT due to its use within the local environment or within commercial food production.

Table 5·7. Organochlorine contaminants in blood from Iceland, 1999 (geometric mean (range), μg/L plasma). Source: Olafsdottir, pers. comm. (2001).

	Pregnant mothers (n=33)					
	Males (n=27)	Reykjavik (n=8)	Vestmannaeyjar (n=8)	Olafsvik (n=8)	Sauðarkrokur (n=9)	Total (n=33)
Oxychlordane	0.05 (0.01–0.12)	0.03 (nd–0.07)	0.05 (0.03–0.17)	0.02 (nd–0.06)	0.05 (0.03–0.12)	0.04 (nd–0.17)
Trans-nonachlor	0.13 (0.04–0.49)	0.11 (0.06–0.17)	0.13 (0.07–0.37)	0.10 (0.05–0.15)	0.14 (0.08–0.31)	0.12 (0.05–0.37)
p,p'-DDT[1]	0.07 (<0.03–0.41)[1]	0.04 (0.02–0.09)	0.02 (nd–0.13)	0.03 (nd–0.22)	0.07 (nd–0.22)	0.04 (nd–0.22)
p,p'-DDE	1.2 0.30–4.6)	0.76 (0.41–1.7)	0.76 (0.30–1.8)	0.64 (0.26–1.4)	0.99 (0.40–2.4)	0.78 (0.26–2.4)
DDE:DDT ratio	18 (6.5–98)	16 (7.6–33)	15 (7.5–23)	12 (6.5–23)	14 (9.4–30)	14.5 (6.5–33)
HCB	0.39 (0.18–0.93)	0.38 (0.18–0.54)	0.38 (0.25–0.76)	0.35 (0.21–0.68)	0.44 (0.31–0.71)	0.39 (0.18–0.76)
β-HCH	0.21 (0.07–0.73)	0.18 (0.08–0.37)	0.16 (0.09–0.35)	0.19 (0.09–0.56)	0.21 (0.11–0.49)	0.19 (0.08–0.56)
Mirex	na	na	na	na	na	na
Total Toxaphene	na	na	na	na	na	na
Parlar 26[2]	(nd–0.14)[2]	(nd–0.03)	(nd–0.05)	nd	(nd–0.09)	(nd–0.09)
Parlar 50	0.05 (nd–0.23)	0.06 (0.04–0.09)	0.05 (0.03–0.08)	0.04 (0.03–0.06)	0.07 (nd–0.20)	0.05 (nd–0.20)
PCBs						
Aroclor 1260[3]	6.2 (3.0–6.2)	4.4 (2.9–7.4)	4.4 (2.1–9.6)	3.4 (1.7–6.8)	4.2 (2.4–8.2)	4.1 (1.7–9.6)
CB118	0.14 (0.04–0.52)	0.10 (0.06–0.19)	0.11 (0.03–0.30)	0.12 (0.07–0.22)	0.12 (0.06–0.24)	0.11 (0.03–0.30)
CB138	0.49 (0.21–1.3)	0.35 (0.21–0.56)	0.33 (0.17–0.71)	0.26 (0.13–0.50)	0.32 (0.18–0.61)	0.31 (0.13–0.71)
CB153	0.75 (0.36–1.7)	0.50 (0.32–0.86)	0.52 (0.23–1.1)	0.39 (0.19–0.83)	0.49 (0.28 0.96)	0.47 (0.19–1.1)
CB180	0.48 (0.28–0.91)	0.26 (0.13–0.51)	0.32 (0.15–0.77)	0.23 (0.11–0.55)	0.30 (0.16–0.57)	0.28 (0.11–0.77)
ΣPCB_{14}[4]	2.6 (1.4–5.5)	1.7 (1.2–3.0)	1.8 (0.89–3.9)	1.5 (0.76–2.7)	1.7 (0.98–3.2)	1.7 (0.76–3.9)

nd: not detected; na: not available.

[1]Detection limit for the male *p,p'*-DDT data is 0.02–0.03 mg/L. The detection limit for other *p,p'*-DDT values is 0.02 mg/L; [2]detection limit for the male parlar 26 data is 0.02–0.06 mg/L. The detection limit for other parlar 26 values is 0.02 mg/L; [3]Aroclor 1260 quantified as 5.2 (CB138 + CB153), Weber, pers. comm. (2002); [4]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

For indigenous peoples of Russia living in the Taymir and Yamal regions of Siberia, traditional activities include reindeer herding, fishing, and hunting. Siberia's non-indigenous population depends to a much greater extent on the commercial Russian food supply. The non-indigenous populations in Arkhangelsk have consistently higher levels of DDE and β-HCH in maternal blood plasma than the indigenous peoples of the Taymir and Yamal regions (Klopov, 2000) (Table 5·6). This is probably due to the use of these pesticides in commercial Russian food production or within the local environment.

New data on PCB levels in maternal blood are available for Arkhangelsk and Salekhard. Blood levels of CB118, CB138, CB153, and CB180 in Arkhangelsk and Salekhard were very similar to those previously observed in Nikel (AMAP, 1998).

5.2.1.5. **Iceland**

Iceland has a socially and culturally homogenous population, and human levels of environmental contaminants are generally similar to or slightly higher than those reported in other Northern Hemisphere countries. The main source of exposure is via the diet, mainly fish consumption (AMAP, 1998). The mean maternal blood plasma levels of OC pesticides in four regions of Iceland (Olafsdottir, pers. comm., 2001) were similar, although slightly higher in Sauðarkrokur than in Reykjavik, Vestmannaeyjar, and Olafsvik (Table 5·7). The β-HCH levels were relatively high in all four regions (0.16 to 0.21 μg/L), and were similar to the higher Icelandic levels of β-HCH cited in the 1994–1997 AMAP maternal blood study (Van Oostdam *et al.*, in prep). These levels are also much higher than the mean maternal plasma β-HCHlevel of 0.05 μg/L found in Norwegian women (Odland, pers. comm., 2000) (see section 5.2.2.1.). Finally, on a country-wide basis, the levels of *trans*-nonachlor, oxychlordane, DDE, DDT, β-HCH and HCB are similar to those reported in the first AMAP assessment (AMAP, 1998).

The mean maternal plasma levels of PCBs in the four areas studied are similar, and are also similar to those observed in Scandinavian countries (see section 5.2.1.6.). In addition, the aggregate levels of PCBs for all four regions combined are slightly lower than those reported previously (AMAP, 1998) (Table 5·7).

Table 5·8. Organochlorine contaminants in maternal blood from Norway, Finland, Sweden, and the Faroe Islands (geometric mean (range), μg/L plasma).

	Norway[1] (Vestvågøy in Lofoten) 1999 (n=50)	Finland[2] (Lapland Region) 1996–98 (n=13)	Sweden[2] (Kiruna Region) 1995–96 (n=40)	Faroe Islands[3] 2000–2001 (n=148)
Oxychlordane	0.04[4] (0.02–0.11)	0.03 (0.01–0.04)	0.02 (0.01–0.05)	0.12 (0.03–1.4)
Trans-nonachlor	0.11[4] (0.04–0.32)	0.05 (0.03–0.08)	0.04 (0.01–0.10)	0.38 (0.02–4.2)
p,p'-DDT	na	0.02 (0.02–0.04)	0.02 (0.02–0.12)	0.26 (0.10–1.5)
p,p'-DDE	0.95[5] (0.20–5.08)	0.58 (0.19–0.79)	0.84 (0.33–5.5)	3.6 (0.35–39.4)
DDE:DDT ratio	na	26 (13–48)	35 (9–367)	14 (na)
HCB	na	0.19 (0.12–0.31)	0.16 (0.07–0.32)	0.28 (0.05–1.9)
β-HCH	0.05[5] (0.02–0.36)	0.07 (0.02–0.09)	0.09 (0.02–0.28)	0.11 (0.05–0.60)
Mirex	na	0.01 (0.01–0.01)	0.01 (0.01–0.22)	na
Total Toxaphene	na	na	na	0.39
Parlar 26	0.03[6] (nd–0.18)	na	na	0.13 (0.03–1.5)
Parlar 50	0.05[6] (nd–0.62)	na	na	0.16 (0.03–1.6)
PCBs				
Aroclor 1260[7]	6.6[6] (2.2–16.7)	3.8 (1.9–5.3)	6.1 (2.7–15)	14.9 (1.1–129)
CB118	0.11[8] (0.01–0.67)	0.07 (0.04–0.11)	0.11 (0.06–0.40)	0.31 (0.03–2.9)
CB138	0.79[6] (0.24–2.3)	0.30 (0.15–0.40)	0.48 (0.22–1.1)	1.3 (0.11–10.3)
CB153	0.47[6] (0.17–1.23)	0.43 (0.21–0.61)	0.70 (0.31–2.0)	1.6 (0.10–14.5)
CB180	0.40[9] (0.13–0.84)	0.24 (0.15–0.33)	0.34 (0.15–0.91)	1.0 (0.06–7.4)
ΣPCB_{14}[10]	2.3[6,8] (0.8–6.2)	1.5 (0.80–2.0)	2.3 (1.1–5.6)	6.3 (nd–14.5)

na: not available; nd: not detected.

[1]Odland, pers. comm. (2000); [2]Van Oostdam *et al.* (in prep); [3]Weihe, pers. comm. (2001); [4]n=25; [5]n=45; [6]n=47; [7]Aroclor 1260 quantified as 5.2 (CB138 + CB153), Weber, pers. comm. (2002); [8]does not include CB28, CB52, or CB156; [9]n=46; [10]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

5.2.1.6. Norway, Finland, and Sweden

The maternal blood data available for Norway, Finland, and Sweden are more limited than for the other circumpolar countries discussed in the preceding sections. Both Norway and Finland have provided new data, while for Sweden no new maternal blood data are available (although new data on PCBs in breast milk were provided). Consequently, data reported for the Kiruna (Giron) area of Sweden in the previous AMAP assessment (Van Oostdam *et al.*, in prep) are used for comparison (Table 5·8).

Northern (mainland) Norway, which consists of three counties – Nordland, Troms, and Finnmark – has only one significant source of industrial pollution: an iron-producing plant in Kirkenes which closed down in 1996. Exposure to POPs and Hg in the coastal regions is primarily via consumption of marine foods, mainly fish, and to a much lesser extent, marine mammals. This constitutes an important difference in dietary pattern compared to the indigenous populations of Canada and Greenland (AMAP, 1998). The levels of most POPs in human tissues have remained unchanged or have only slightly decreased over the years, and are lower in Norway than in Russia (AMAP, 1998).

A comparison of the new Norwegian data from the Vestvågøy area in Lofoten (Odland, pers. comm., 2000) with the combined earlier data from the Hammerfest and Kirkenes regions of Norway (AMAP, 1998) shows that maternal blood levels of various OC contaminants are still low in Norway but slightly higher in Vestvågøy. Levels of *trans*-nonachlor and DDE are about 2 and 1.6 times higher, respectively, in Vestvågøy relative to those in the Hammerfest/Kirkenes regions (0.11 vs 0.05 μg/L, and 0.95 vs 0.60 μg/L). Regarding PCBs, levels of CB118, CB138, CB153, CB180, and the sum of 14 PCB congeners, are consistently higher in Vestvågøy than in Hammerfest/Kirkenes (0.11, 0.79, 0.47, and 0.40 μg/L vs 0.08, 0.27, 0.41, and 0.20 μg/L, respectively for the individual CB congeners).

The new Norwegian data from Vestvågøy (Odland, pers. comm., 2000) can be compared with those for Finnish Lapland in the most northern and northeastern part of Finland (Soininen, pers. comm., 2001), and with the 1995 Swedish data from the Kiruna (Giron) area, in the northernmost part of Sweden (AMAP, 1998). Table 5·8 shows that maternal blood levels of oxychlordane, *trans*-nonachlor, DDE, and β-HCH are similar in Finland, Norway and Sweden, and that the absolute values are low.

Mean blood levels of CB118, CB138, CB153, and CB180 are lower in Finland than in Norway and Sweden; Swedish levels of all four congeners are approximately 50% higher than those observed in Finland. The Swedish levels are also higher than the earlier Norwegian data from the initial maternal blood study (AMAP, 1998), but lower for CB138 and CB180 when compared to the new Norwegian data. This is probably due to regional differences, as the earlier Norwegian data were from the Hammerfest/Kirkenes regions, while the more recent data were collected from the Vestvågøy area.

5.2.1.7. Faroe Islands

Pilot whale blubber is thought to be the main source of exposure to OC contaminants in the Faroe Islands. Dietary surveys in the 1980s indicated that the local population consumed on average 7 grams of pilot whale blubber per day, which resulted in high levels of PCBs in human adipose tissue, breast milk and cord blood. In 1998 pregnant women and women who intended to become pregnant were advised to stop eating pilot whale blubber and meat. A dietary survey and a blood contaminant sampling programme were undertaken in 2000–2001 to assess the success of this advice (Weihe, pers. comm., 2001). These surveys indicated that pilot whale blubber and meat consumption had decreased by a factor of ten. However, they also indicated that PCB levels in Faroese mothers were still two to three times higher than the corresponding levels in other Scandinavian countries (Table 5·8), and had not decreased markedly since the 1980s (Weihe, pers. comm., 2001). This lack of decrease in maternal PCB levels is probably due to the long half-lives of PCBs in the body or to other unknown sources of PCB in the diet. PCB exposures continue to be considered a potential health problem in the Faroese community (see chapter 9 for comparisons with blood guidelines and health effect levels). Quite different findings were obtained for Hg as a result of this dietary intervention; as discussed in section 5.3.1.6.

5.2.2. International comparisons

In the present AMAP assessment, sufficient data are available to allow comparisons between countries and regions, and between different ethnic groups (i.e., indigenous and non-indigenous peoples). Comparisons are also made among non-indigenous populations (consumers of commercial foods) from different countries; among indigenous populations (consumers of traditional foods) from different countries; and between indigenous and nonindigenous populations.

5.2.2.1. Non-indigenous populations

The non-indigenous populations of Norway (Odland, pers. comm., 2000), Iceland (Olafsdottir, pers. comm., 2000), Finland (Soininen, pers. comm., 2001), and Canada (Walker *et al.*, 2001) have low levels of OC contaminants such as oxychlordane (Figure 5·2) (0.04 to 0.05 µg/L) when compared to the non-indigenous population of the Arkhangelsk region of Russia (0.18 µg/L)

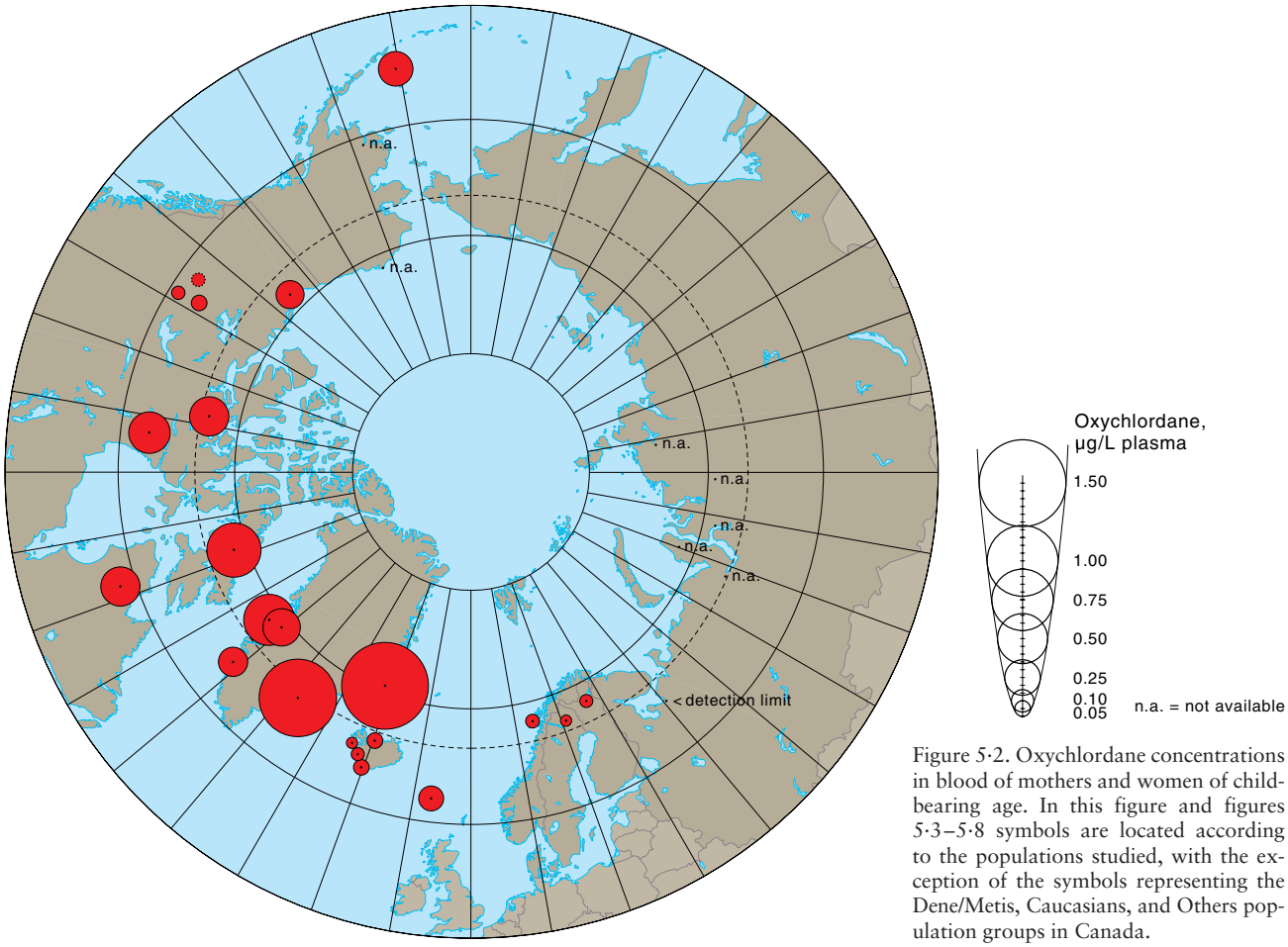

Figure 5·2. Oxychlordane concentrations in blood of mothers and women of childbearing age. In this figure and figures 5·3–5·8 symbols are located according to the populations studied, with the exception of the symbols representing the Dene/Metis, Caucasians, and Others population groups in Canada.

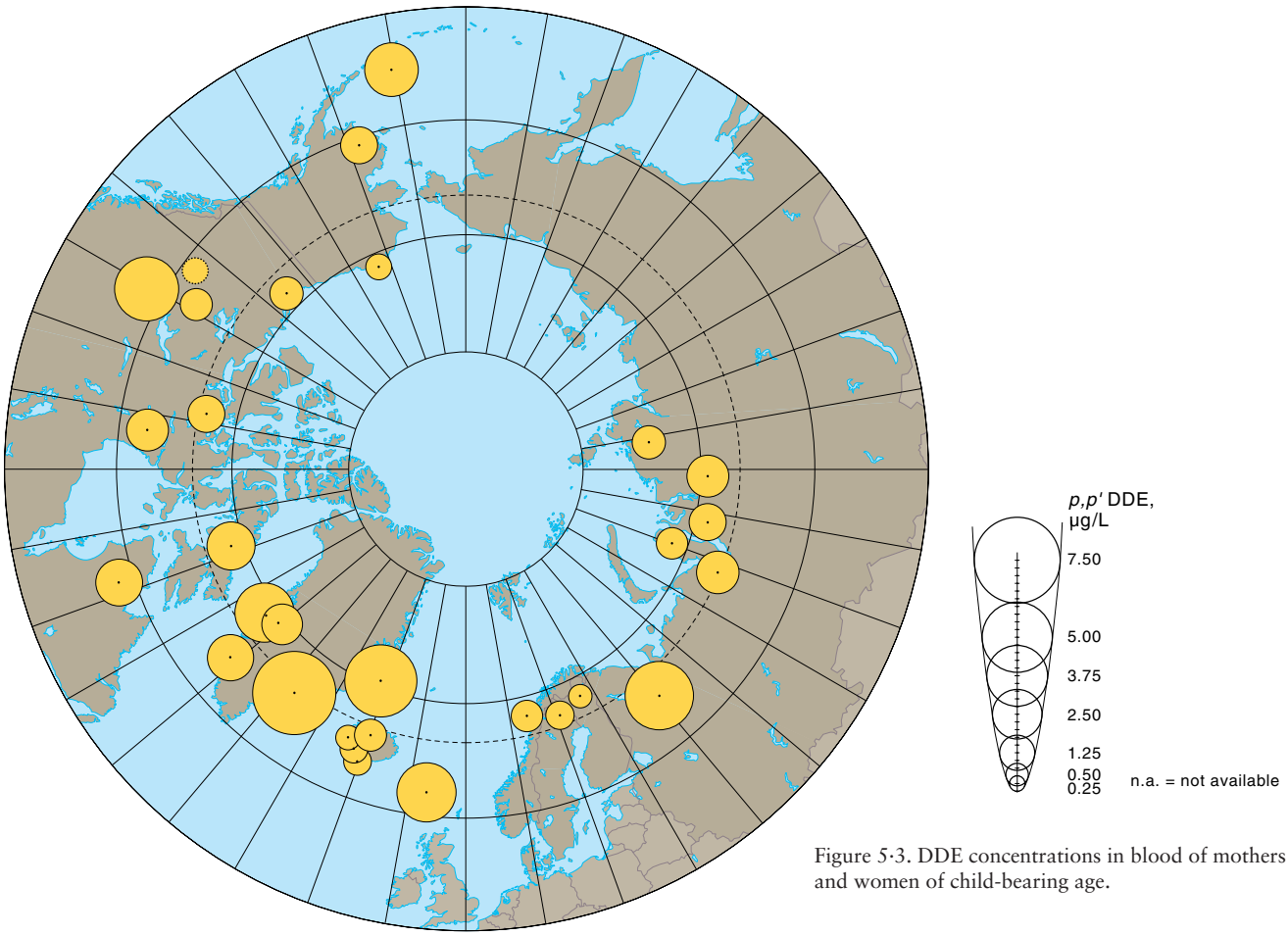

Figure 5·3. DDE concentrations in blood of mothers and women of child-bearing age.

(Odland, pers. comm., 2000). This may indicate that chlordane is being used in the Arkhangelsk region or in commercial Russian food production.

A similar pattern is observed for DDE (Figure 5·3), where lower levels are seen in Finland (0.47 µg/L), Norway (0.95 µg/L), Iceland (0.78 µg/L), and Canadian Caucasians (0.9 µg/L); and higher levels in non-indigenous peoples in Arctic Russia (1.3 to 1.8 µg/L) (Klopov, 2000) and in Arkhangelsk (4.5 µg/L) (Odland, pers. comm., 2000). Levels of β-HCH (Figure 5·4) also follow a similar pattern. These differences also indicate the probable use of these pesticides within commercial Russian food production or for controlling insects in the local environment.

DDE and β-HCH levels are also higher in maternal samples from the Others group in Canada (4.0 and 0.48 µg/L, respectively) than in those from Norway, Iceland, or Caucasians in Canada (Figures 5·3 and 5·4). As noted in section 5.2.1.1., if the mothers included in the Others group are of African or East Asian ancestry, regions where these pesticides are still being used, their higher exposure to these contaminants may have occurred there or through foods imported from these regions. However, whether these individuals were exposed to DDT and β-HCH in Africa or East Asia was unspecified and remains unclear.

The levels of OC contaminants in the Norwegian, Icelandic, and (1995) Swedish samples are very similar and virtually indistinguishable from values found at lower latitudes (AMAP, 1998). This is probably because, with the exception of the Saami people in northern Norway and Sweden, these three countries all have Caucasian (i.e., non-indigenous) populations, whose main source of exposure to environmental contaminants is via the consumption of foods that are common to these and other western countries (in contrast to the traditional foods consumed by some indigenous peoples).

It is useful to compare the Norwegian data with the Icelandic data, since both countries (like Sweden) have mainly Caucasian populations and some similarity in diet. The maternal blood plasma levels of OC contaminants in Norway are similar to those in Iceland, except for the level of β-HCH, which is three to four times higher in Iceland (0.16 to 0.21 vs 0.05 µg/L for Norway) (Figure 5·4). The higher β-HCH levels in the Icelandic mothers are consistent with results of earlier studies in circumpolar countries (AMAP, 1998). However, increased levels of β-HCH have not been found in the Icelandic marine environment. The use of γ-HCH has been banned since 1994 and the use of technical HCH has never been registered in Iceland (Olafsdottir, pers. comm., 2001).

The levels of PCBs (estimated as Aroclor 1260) in maternal samples for indigenous and non-indigenous women are presented in Figure 5·5. Among the non-indigenous populations, Caucasians of Arctic Canada have the lowest PCB levels, estimated as Aroclor 1260, the sum of PCB congeners, or as individual congeners (Tables 5·1 to 5·8). Intermediate levels of PCBs are found in mothers from Iceland and Finland, and higher levels in mothers from Norway, Sweden and Russia.

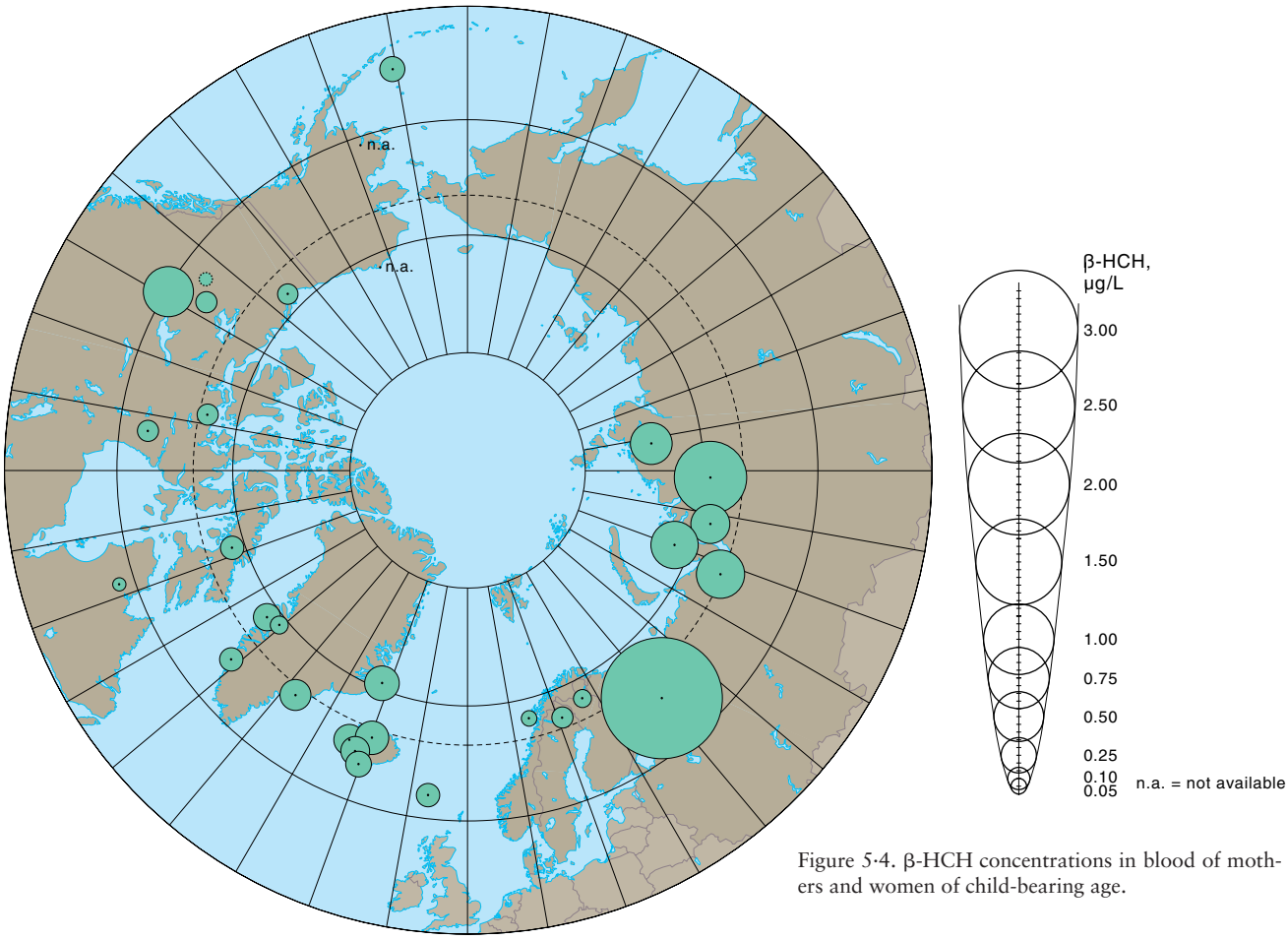

Figure 5·4. β-HCH concentrations in blood of mothers and women of child-bearing age.

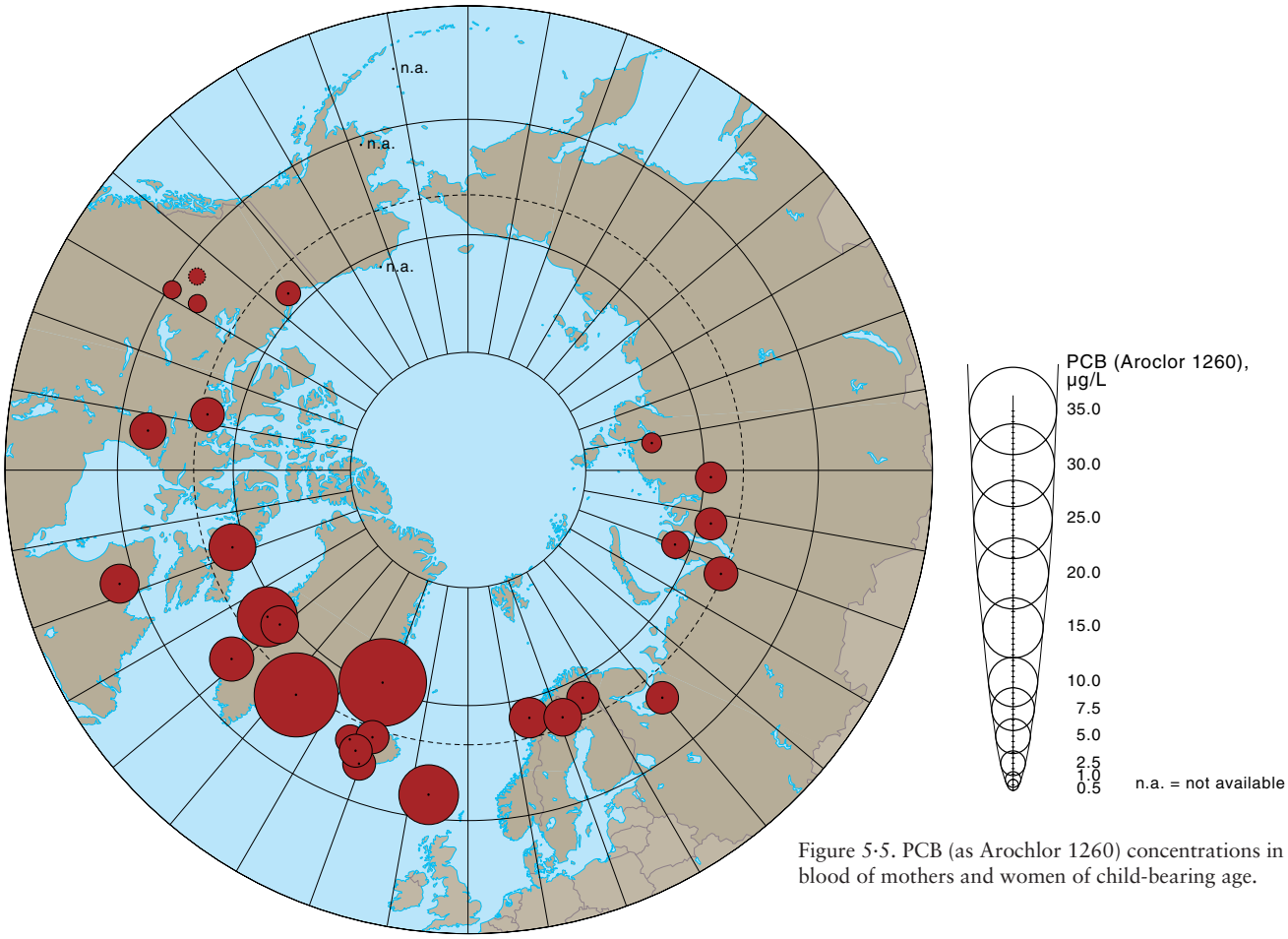

Figure 5·5. PCB (as Arochlor 1260) concentrations in blood of mothers and women of child-bearing age.

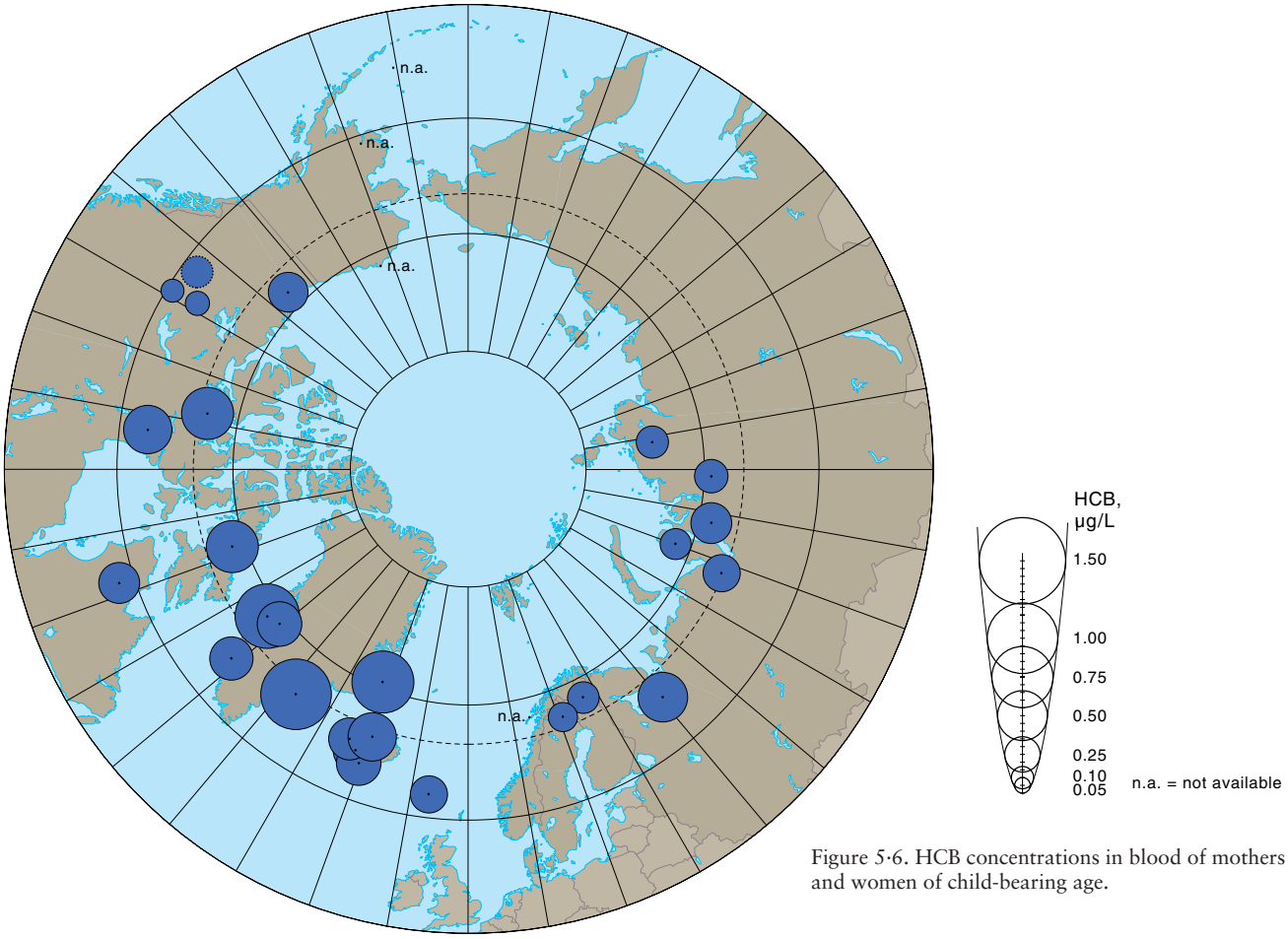

Figure 5·6. HCB concentrations in blood of mothers and women of child-bearing age.

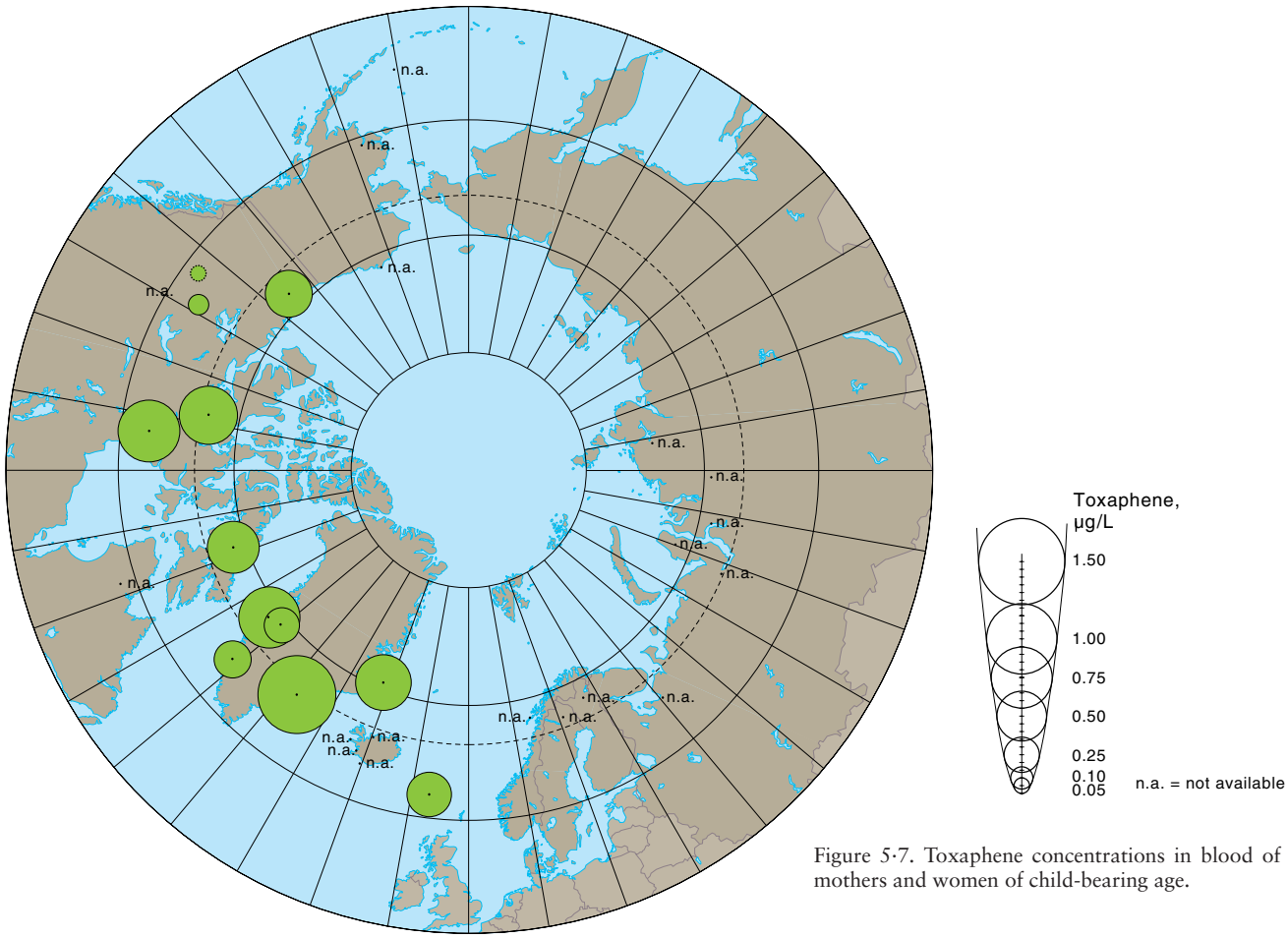

Figure 5·7. Toxaphene concentrations in blood of mothers and women of child-bearing age.

Table 5·9. Organochlorine contaminants in breast milk from Canada, and selected PCB congeners in breast milk from Sweden (geometric mean (range), μg/kg lipid).

	Nunavik, Canada[1] 1996–2000 (n=116) mean age: 24.6 ± 5.7[3]	Kiruna, Sweden[2] 1995 (n=11) mean age: 28 ± 5
Oxychlordane	81 (11–642)	na
Trans-nonachlor	113 (15–547)	na
p,p'-DDT	30 (1.0–161)	na
p,p'-DDE	420 (86–2295)	na
DDE:DDT ratio	na	na
HCB	50 (7.6–226)	na
β-HCH	11 (1.3–60)	na
Mirex	5.8 (0.4–35)	na
Toxaphene	na	na
Parlar 26	na	na
Parlar 50	na	na
PCBs		
Aroclor 1260[4]	na	na
CB118	19 (3.7–108)	13[5] (3.3–28)
CB138	78 (14–409)	81[5] (37–124)
CB153	132 (22–728)	98[5] (44–140)
CB180	48 (11–214)	44[5] (19–70)
ΣPCB_{14}[6]	386 (76–1916)	309[5]

na: not available.

[1]Muckle, pers. comm. (2000), Muckle *et al.* (2001b); [2]Lejon (1996); [3](n=175); [4]Aroclor 1260 quantified as 5.2 (CB138 + CB153), Weber, pers. comm. (2002); [5]arithmetic mean; [6]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

Similar general patterns are found in the data for HCB (Figure 5·6) and toxaphene (Figure 5·7).

5.2.2.2. Indigenous populations

In comparing the Inuit populations of Greenland and Canada it is clear that much higher levels of total PCBs (estimated as Aroclor 1260, Figure 5·5) are found in mothers from Greenland (6.4 to 36 μg/L) (Deutch, in prep; Deutch and Hansen, 2000), than in Canadian Inuit mothers (2.4 to 8.0 μg/L) (Muckle, pers. comm., 2000; Muckle *et al.* 2001b; Walker *et al.*, 2001). A similar pattern is found for DDT. This difference is probably due to the higher consumption of marine mammals by Greenland Inuit. The Dene/Métis of Canada, and the indigenous peoples of Russia (Klopov, 2000), have much lower levels of many contaminants than the Inuit populations, as observed in the maternal data from these countries. The differences in contaminant levels are probably explained by diet; i.e., the Dene/Métis of Canada consume large amounts of fish and terrestrial mammals that have markedly lower levels of POPs than the marine mammals consumed by the Inuit.

5.2.2.3. Comparisons of indigenous and non-indigenous peoples or regions

As stated in the previous sections, Inuit mothers of the circumpolar north, particularly in Greenland, have higher levels of many contaminants (e.g., oxychlordane, Figure 5·2; HCB; and PCBs, Figure 5·5) than other northern indigenous populations (e.g., Dene/Métis in Canada; and indigenous people in the Taymir and Yamal regions of Arctic Russia). They also have higher levels of these contaminants than non-indigenous peoples from Canada, Norway, and Iceland (AMAP, 1998). Levels in the Dene/Métis of Canada and the indigenous peoples of Russia are either similar to or lower than those in many of the non-indigenous populations. The Dene/Métis of Canada depend on terrestrial mammals such as caribou or moose and on freshwater fish, which have relatively low levels of POPs. Many of the indigenous peoples of Arctic Russia surveyed to date also consume mainly fish and terrestrial mammals.

Few data on contaminant levels in men were available for the circumpolar north. Samples were, however, available for men from Greenland and Iceland, and these show a very similar pattern to that found in mothers. Three to twenty times higher levels of PCBs, DDE and chlordane derivatives were observed in Greenlandic Inuit men compared to Icelandic men (Tables 5·3 and 5·7).

5.2.2.4. Comparison of breast milk levels of contaminants

Data from Sweden on the mean levels of PCBs in breast milk (on a lipid weight basis) (Lejon, 1996) can be compared to levels in Inuit from Nunavik (Muckle *et al.*, 2001b), to highlight both geographic and ethnic differences. Table 5·9 shows that the breast milk levels of four PCB congeners, as well as of the sum of 14 congeners, in Nunavik Inuit women were consistently higher than those in women from the Kiruna (Giron) area of Sweden (386 vs 309 μg/kg lipid, respectively, for ΣPCB_{14}). The Kiruna area is one of the two main industrial areas in the Swedish Arctic. However, the main source of exposure to environmental contaminants there and in other parts of Sweden is through the consumption of commercial foods (e.g., marine fish, and terrestrial mammals such as sheep, cattle, and pigs; AMAP, 1998), similar to the situation in other western countries. The higher levels of PCBs in Inuit breast milk are due to the consumption of traditional/country foods which have higher levels of POPs such as PCBs.

In Sweden, nine of the 11 women sampled were breast feeding their first baby. The PCB levels in the breast milk of the remaining two women, who had breast fed four and three children, respectively, were approximately 40% lower than in the breast milk of the other nine (Lejon, 1996). This emphasizes the importance of birth order in PCB exposure through breast milk.

Some data have recently become available for a limited number of contaminants in breast milk of women

Table 5·10. Organochlorine contaminants in breast milk from indigenous and non-indigenous regions of Siberian Russia (geometric mean (range), μg/kg lipid).

	Non-indigenous regions			Indigenous regions	
	Norilsk[1] 1995–96 (n=49)	Salekhard[2] 1996–98 (n=31)	Dudinka[1] 1995–96 (n=27)	Taymir[1] 1995–96 (n=18)	Yamal[2] 1996–98 (n=12)
Oxychlordane	na	na	na	na	na
Trans-nonachlor	17 (8–31)	19 (8–36)	16 (7–36)	14 (5–45)	18 (7–44)
p,p'-DDT	49 (19–212)	56 (17–198)	49 (16–188)	24 (8–57)	28 (8–67)
p,p'-DDE	399 (191–1292)	425 (105–1502)	435 (166–1283)	314 (176–747)	375 (143–1262)
DDE:DDT ratio	8.8 (5.1–14)	8.7 (4.8–14)	9.3 (5.9–13)	16 (9.6–21)	14 (6.4–21)
HCB	123 (29–387)	70 (25–195)	73 (19–188)	111 (65–210)	78 (22–166)
β-HCH	142 (49–582)	59 (10–447)	40 (8–203)	46 (3–124)	59 (21–171)
Mirex	1.2 (0.4–5.1)	1.9 (0.4–3.7)	1.6 (0.4–2.9)	0.8 (0.1–2.2)	1.6 (0.4–3.1)
Total Toxaphene	na	na	na	na	na
Parlar 26	na	na	na	na	na
Parlar 50	na	na	na	na	na

na: not available.

[1]Klopov *et al*. (1998); [2]Klopov (2000), Klopov and Shepovalnikov (2000), Klopov and Tchachchine (2001).

Table 5·11. Organochlorine contaminants in breast milk from four regions of northern Russia (arithmetic mean (range), μg/kg lipid). Source: Polder *et al*. (2002a).

	Kargopol		Severodvinsk		Arkhangelsk		Naryan–Mar	
	Primipara (n=10)	Multipara (n=9)	Primipara (n=37)	Multipara (n=13)	Primipara (n=40)	Multipara (n=11)	Primipara (n=11)	Multipara (n=9)
Mean age (SD)	21.6 (1.7)	25.3 (3.5)	22.6 (4.3)	28.9 (4.8)	22.0 (2.8)	28.4 (5)	25.1 (6.1)	25.9 (4.4)
Oxychlordane	6 (4–11)	8 (4–19)	9 (4–13)	10 (3–17)	9 (<1–19)	12 (4–22)	13 (5–28)	15 (4–28)
Trans-nonachlor	14 (5–23)	17 (10–37)	20 (7–49)	22 (7–45)	22 (<1–60)	32 (13–52)	21 (12–39)	21 (3–47)
p,p'-DDT	108 (51–174)	115 (50–262)	147 (28–415)	79 (33–176)	194 (3–691)	136 (44–281)	171 (58–389)	118 (25–293)
p,p'-DDE	869 (352–1454)	944 (186–2587)	979 (416–2395)	724 (120–1296)	1192 (352–3824)	947 (594–1664)	923 (150–2143)	632 (70–1729)
DDE:DDT ratio	6.25 (2.5->10)	5.88 (3.33->10)	6.25 (2.5->10)	7.69 (3.33->10)	6.25 (2.5->10)	7.14 (5.0->10)	5.0 (2.5->10)	4.54 (2.0->10)
HCB	79 (47–127)	77 (40–192)	87 (41–240)	80 (31–157)	77 (20–188)	82 (43–119)	129 (49–472)	120 (46–248)
β-HCH	304 (114–932)	187 (104–429)	376 (171–736)	292 (123–519)	401 (14–1202)	317 (105–586)	183 (57–524)	120 (49–253)
Mirex	na	na	na	na	na	na	na	na
Total Toxaphene	na	na	na	na	na	na	na	na
Parlar 26[1]	2.3		2.9		4.3		3.4	
Parlar 50[1]	3.7		4.8		4.8		5.8	
PCBs								
Aroclor 1260[2]	na	na	na	na	na	na	na	na
CB118	29 (11–52)	34 (17–64)	46 (16–96)	45 (15–115)	41 (18–110)	42 (22–63)	36 (17–96)	35 (12–76)
CB138	45 (14–66)	52 (26–124)	69 (25–158)	59 (22–96)	67 (21–192)	79 (36–109)	73 (35–189)	69 (25–122)
CB153	52 (19–86)	60 (36–163)	72 (29–210)	73 (30–121)	73 (28–213)	105 (43–143)	98 (41–321)	99 (36–222)
CB180	24 (9–48)	31 (20–88)	31 (10–100)	34 (14–57)	36 (13–85)	48 (23–80)	52 (26–150)	70 (20–143)
ΣPCB_{14}[3]	na	na	na	na	na	na	na	na

na: not available.

[1]Concentrations in pooled milk samples; [2]Aroclor 1260 quantified as 5.2 (CB138 + CB153), Weber, pers. comm. (2002); [3]CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

Table 5·12. Metal concentrations in maternal blood from circumpolar countries (geometric mean (range), μg/L whole blood).

Country/Ethnic Group/Region	n	Mercury (total)	Mercury (organic)	Selenium	Lead	Cadmium
Canada						
Caucasian[1] (1994–99)	134	0.9 (nd–4.2)	0.69 (nd–3.6)	123 (80–184)	21 (2.1–58)	0.43 (nd–8.5)
Métis/Dene[1] (1994–99)	92	1.4 (nd–6.0)	0.80 (nd–4.0)	117 (67–160)	31 (5.0–112)	0.65 (nd–5.9)
Other[1] (1995)	13	1.3 (0.20–3.4)	1.2 (nd–3.0)	128 (97–156)	22 (5.0–44)	0.36 (nd–3.2)
Inuit						
Baffin[1] (1996)	31	6.7 (nd–34)	6.0 (nd–29)	118 (99–152)	42 (5.0–120)	1.7 (0.03–6.2)
Inuvik[1] (1998–99)	31	2.1 (0.60–24)	1.8 (nd–21)	118 (88–151)	19 (2.1–102)	1.0 (nd–7.1)
Kitikmeot[1] (1994–95)	63	3.4 (nd–13)	2.9 (nd–11)	122 (86–171)	36 (6.2–178)	1.9 (0.01–7.8)
Kivalliq[1] (1996–97)	17	3.7 (0.60–12)	2.7 (0.40–9.7)	106 (77–156)	29 (12–64)	1.4 (0.11–7.7)
Nunavik[2] (1995–2000)	162	9.8 (1.6–44)	na	318 (150–1232)	50 (5.2–259)	na
Greenland						
Disko Bay[3] (1997)	94	na	na	140[4]	na	na
Thule[3] (1997)	4	50[4]	na	409[4]	na	na
Ilullissat[3] (1999–2000)	29	12.4	na	158	50	1.2
Nuuk[5] (1999)	34	3.6	na	142 (n=38)	37	0.68
Ittoqqortoormiit[3] (1999–2000)	8	10.5	na	133	31	0.96
Alaska						
Bethel[6] (2000)	23	5.5 (1.6–14.3)	na	na	33[4] (nd–91)	0.3[4] (nd–1.6)
Barrow[6] (2000)	23	1.3[4] (nd–4.5)	na	na	11 (7.0–27)	0.2[4] (nd–0.9)
Siberian Russia						
Non-indigenous						
Norilsk[7] (1995–96)[7]	49	1.4 (1–5)	na	90 (62–134)	32 (12–44)	0.29 (0.1–1.5)
Salekhard[7] (1996–98)	31	1.5 (1–5)	na	91 (64–130)	24 (12–40)	0.40 (0.1–1.4)
Dudinka[7] (1995–96)	27	1.6 (1–5)	na	85 (56–122)	21 (14–42)	0.38 (0.1–1.4)
Indigenous						
Taymir[7] (1995–96)	18	2.7 (2–8)	na	89 (58–126)	29 (12–48)	0.33 (0.1–1.0)
Yamal[7] (1996–98)	12	2.9 (2–7)	na	80 (60–122)	24 (12–40)	0.20 (0.1–0.8)
Finland[8] (1996–98)	130	1.4 (0.2–6.0)	na	74 (51–122) (n=148)	11 (5–58)	0.13 (0.1–2.2)
Faroe Islands[9] (2000–2001)	124	1.2 (nd–7.5)	na	105 (54–169)	21 (13–100)	0.21 (0.2–2.9)

nd: not detected; na: not available.

[1]Walker *et al.* (2001); [2]Muckle *et al.* (2001b); [3]Deutch, pers. comm. (2001); [4]arithmetic mean; [5]Bjerregaard, pers. comm. (2001); [6]Berner, pers. comm. (2001); [7]Klopov (2000), Klopov and Tchachchine (2001); [8]Soininen, pers. comm. (2001), Soininen *et al.* (2000); [9]Weihe, pers. comm. (2001).

from Arctic Russia (Table 5·10). The breast milk samples from non-indigenous regions do not show the same pattern as that seen in the maternal blood samples, i.e., higher levels of β-HCH and DDE in the non-indigenous mothers. Only non-indigenous mothers from Norilsk had higher levels of β-HCH in their breast milk compared to indigenous mothers (142 vs 46 or 59 μg/kg lipid). The Inuit mothers from Nunavik (Canada) had markedly higher levels of mirex and *trans*-nonachlor compared to those in the Russian Arctic. Breast milk from both indigenous and non-indigenous mothers in Russia had four to ten times higher levels of β-HCH than found in Nunavik Inuit (40 to 142 vs 11 μg/kg lipid, respectively). This indicates the use of β-HCH in commercial Russian food production or in the local environment, as was concluded in the evaluation of the Russian maternal blood data. Additional data have been supplied for northern Russia by Polder *et al.* (2002a), see Table 5·11.

5.3. Metals

New data are currently available on maternal blood levels of a number of priority metals, i.e., mercury (Hg), lead (Pb), cadmium (Cd), and selenium (Se). These data are available for six countries within the circumpolar area – Canada, Finland, Greenland, the Faroe Islands, Arctic Russia, and United States (Alaska).

5.3.1. National and regional data

5.3.1.1. Canada

Mercury has long been a contaminant of concern in traditional foods in the Arctic. In Canada, in NWT/Nunavut and Nunavik, significantly higher levels of total Hg were found in maternal blood from Inuit compared to Caucasian, Dene/Métis or Others (2.1 to 9.8 vs 0.9 to 1.4 μg/L) (Muckle, pers. comm., 2000; Muckle *et al.*, 2001b; Walker *et al.*, 2001) (Table 5·12). Markedly higher levels of Hg (2 to 5 times) were seen in Inuit from the Baffin region of Nunavut (6.7 μg/L) and Nunavik (9.8 μg/L). The Canadian dataset contains both total and organic Hg levels. On the basis of the mean values presented in Table 5·12, 57 to 92% of Hg in blood occurs as organic Hg, but there does not appear to be a relationship with ethnic origin or Hg concentration. Se levels in maternal serum were very similar among Caucasian, Dene/Métis, Others, and Inuit (Baffin, Inuvik, Kitikmeot, Kivalliq) peoples from the NWT/Nunavut. Only among the Nunavik Inuit, who also had the highest levels of Hg, were Se levels elevated (318 μg/L). High concentrations of Se are generally found in the traditional foods of the Inuit in Greenland and Canada, particularly in foods derived from marine mammals (e.g., muktuk). Se is a component of glutathione peroxidases and may act as an antagonist to methylmercury (MeHg), thereby offering some protection against po-

tential adverse health effects from MeHg exposure (AMAP, 1998).

Lead levels are moderately elevated among some of the Inuit and the Dene/Métis (50 to 31 μg/L), while levels are lower among Caucasians, Others and some Inuit (19 to 22 μg/L). Pb isotope signatures indicate that these elevations in blood Pb levels are probably due to the presence of Pb shot in consumed game (Dewailly *et al.*, 2000b).

The highest Cd levels were observed in Inuit mothers (1.0 to 1.9 μg/L), while lower levels were seen in Caucasian, Dene/Métis and Others mothers (0.36 to 0.65 μg/L). This difference is probably due to the high rate of smoking among Inuit mothers and the high Cd content of Canadian tobacco. Benedetti *et al.* (1994) found that non-smoking Canadian Inuit had markedly lower levels of blood Cd (0.27 μg/L) compared to Inuit who smoked (5.3 μg/L).

5.3.1.2. **Greenland**

Mercury levels are extremely variable among Greenland Inuit peoples (Table 5·12), ranging from a maximum of 50.4 μg/L among a small sample of Inuit mothers from the Thule region (Deutch, in prep) to a more moderate 3.6 μg/L in mothers from Nuuk. Intermediate but still somewhat high levels of Hg are seen in the women from Ilullissat and Ittoqqortoormiit (Table 5·12). Along with these higher levels of Hg, many of these populations have moderately to highly elevated levels of Se (133 to 409 μg/L). As noted in section 5.3.1.1., high Se concentrations are generally found in the traditional diet of the Inuit in Greenland and Canada, particularly in foods derived from marine mammals (e.g., muktuk).

Lead levels among Greenland Inuit mothers are similar (31 to 50 μg/L) to the moderately increased levels among some of the Canadian Inuit and Dene/Métis. Analyses of seabirds in Greenland have shown that Pb shot in game is a significant contributor to human Pb exposure (Johansen *et al.*, 2001).

Cadmium levels are higher in the Greenland Inuit than in the Canadian Arctic Caucasians and Others groups, but lower than levels seen in Canadian Inuit. The increased Cd levels among Greenland Inuit are also likely to be due to increased rates of smoking relative to other population groups, such as Danes living in Greenland. However, based on blood samples from non-smokers, diet is also a significant source of Cd (Hansen, 1990).

5.3.1.3. **Alaska**

Mercury levels in the Iñupiat mothers from the Barrow region are on average 75% lower than concentrations in Yup'ik mothers from the Bethel region (1.3 vs 5.5 μg/L) (Table 5·12). Concentrations in the Yup'ik mothers are of a similar magnitude to those in Canadian Inuit (5.5 vs 2.1 to 9.8 μg/L). Both the Iñupiat and the Yup'ik peoples are considered Inuit, but the differences in their blood contaminant levels indicate significant dietary differences. The Yup'ik mothers consume significant amounts of freshwater fish and some marine mammals that may have elevated levels of Hg; while the Iñupiat mothers consume terrestrial mammals and bowhead whales (*Balaena mysticetus*) that have lower levels of Hg. Without dietary surveys, numeric dietary comparisons cannot be made. To date there are no data available on Se levels in Alaskan mothers, but the maternal blood levels of Pb and Cd are low and similar to those in many of the non-indigenous population groups.

5.3.1.4. **Russia**

Levels of metals in maternal tissues are a concern in parts of the Russian Arctic, in particular due to the presence of large non-ferrous metal smelters in Norilsk and Nikel. The data in Table 5·12 indicate that non-indigenous Russians from Norilsk, Salekhard, and Dudinka have lower levels of Hg than the indigenous peoples of Taymir and Yamal, but very similar levels to those in the non-indigenous (Caucasian and Others) Arctic Canadians. Indigenous Russians from Taymir and the Yamal regions have intermediate levels of Hg (2.7 and 2.9 μg/L) which are similar to those in Canadian Inuit from Inuvik (2.1 μg/L) but markedly lower than levels in Inuit from Greenland or the Baffin and Nunavik regions of Canada (Table 5·12). This may indicate exposure to Hg through consumption of local fish. Se levels among all Russian ethnic groups (80 to 91 μg/L) are approximately 30% lower than those in Caucasians or Dene/Métis in Arctic Canada, and up to 80% lower than levels among Canadian and Greenland Inuit who have high levels of both Se and Hg.

Lead and Cd levels are similar among indigenous and non-indigenous women of Arctic Russia (21 to 32 μg/L and 0.20 to 0.40 μg/L, respectively) and the mean values are similar to or lower than those in Arctic Canada or Greenland. The data presented here do not indicate that these women are exposed to higher levels of Pb or Cd, supporting the view that the effects of point sources such as the smelters in Norilsk remain local.

5.3.1.5. **Finland**

Exposure to metals is a major concern in the northern parts of Finnish Lapland. There is no major domestic source of pollution in this area, but metals originating from the smelters on the Kola Peninsula (Russia) are a significant concern. Also, Hg is known to accumulate in freshwater fish, which is one of the most important components of the diet in Lapland (AMAP, 1998). The mean blood level of Hg in pregnant women from the most northern and northeastern parts of Finnish Lapland (Soininen *et al.*, 2000) is much lower than the levels found in Canadian Inuit and Greenlandic Inuit women (1.4 μg/L vs 2.1 to 9.8 and 3.6 to 50 μg/L, respectively) (Table 5·12). The Finnish value is similar to corresponding values found in previous studies in Arkhangelsk (Russia), and in Sweden (Soininen *et al.*, 2000). Se levels in the Finnish mothers are the lowest of those observed in the Arctic populations studied (74 vs 117 to 318 μg/L in Canada, and 133 to 409 μg/L in Greenland).

Lead levels in the Finnish mothers tend to be lower than those in the other Arctic populations reported here. Cd levels are also lower than in the other Arctic pop-

ulations sampled. The data presented here do not indicate that the smelters on the Kola Peninsula contribute to increased levels of Pb or Cd in mothers from northern Finland.

5.3.1.6. Faroe Islands

The consumption of pilot whale meat is thought to be the main source of Hg in the Faroe Islands population, and dietary surveys in the 1980s indicated that the local population consumed on average 12 grams of whale meat per day. As stated in section 5.2.1.7., in 1998 pregnant women and women who intended to become pregnant were advised to stop eating pilot whale blubber and meat. A dietary survey and blood contaminant sampling programme were undertaken in 2000–2001 to assess the effect of this advice (Weihe, pers. comm., 2001). These surveys indicated that pilot whale blubber and meat consumption had decreased by a factor of ten in the target groups. Hg levels in maternal blood had also decreased markedly since the 1980s (12.1 vs 1.3 μg/L), and there appears to have been a very positive response to the dietary advice (Grandjean *et al.*, 1992; Weihe, pers. comm., 2001), which is very specific and aimed particularly at pregnant women and women intending to become pregnant. Hg levels are now quite low in the Faroese population and similar to levels found in Finland, in indigenous peoples from Barrow (Alaska), and in non-indigenous populations in Russia and Canada (Table 5·12). Additional monitoring is needed to validate these very marked trends.

5.3.2. International comparisons

5.3.2.1. Comparisons of indigenous and non-indigenous peoples

The highest maternal blood Hg levels occur in the Inuit of Canada and Greenland and in the Yup'ik Inuit from the Bethel region of Alaska (5.5 to 50 μg/L) (Figure 5·8). These high blood levels in the Inuit are associated with consumption of muscle and fatty skin (muktuk) from marine mammals, both of which have high levels of Hg and Se. Intermediate levels of Hg (1.3 to 2.9 μg/L) occur in the Dene/Métis and in some Inuit populations from Canada, and in the indigenous peoples of the Taymir and Yamal regions of Arctic Russia. Lower levels of Hg were observed in all non-indigenous populations from Canada, Finland, and Russia. The lowest levels of Se occur in mothers from Finland and northern Russia, and only some of the Inuit populations with elevated Hg levels also have markedly higher levels of Se (318 and 409 μg/L in Nunavik and Thule, respectively).

Lead levels are moderately increased (30 to 50 μg/L) among some Inuit mothers from Canada and Greenland compared to other Arctic regions. This increase is probably related to the use of Pb shot in the hunting of traditional foods. Cd is also elevated in the Dene/Métis and Inuit mothers from Arctic Canada and in Inuit mothers from Greenland. This increase in Cd is thought to be related to increased cigarette smoking among indigenous peoples (Benedetti *et al.*, 1994) and also, in some areas, to the consumption of marine mammals.

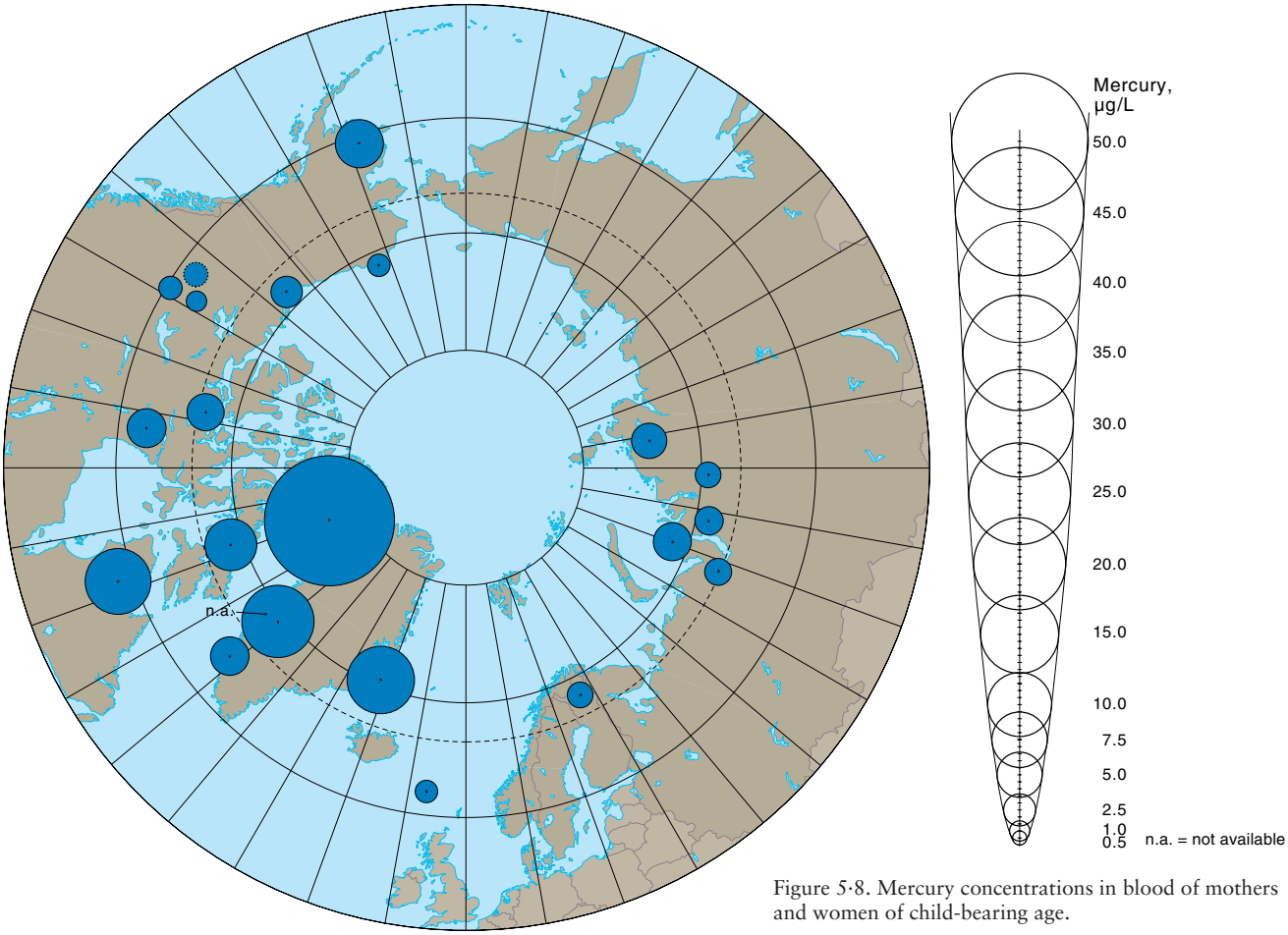

Figure 5·8. Mercury concentrations in blood of mothers and women of child-bearing age.

Lead and Cd levels are not markedly elevated among non-indigenous mothers from northern Russia and Finland. This indicates that these mothers are not being exposed to significant amounts of these metals from local point sources such as the smelters on the Kola Peninsula and in Norilsk.

5.4. Temporal trends

Sampling human blood for contaminant analyses is relatively new in the Arctic. Data for AMAP human health assessments were obtained from blood or breast milk samples collected during the period 1994 to 1999. This is a very short period on which to base estimates of temporal trends in contaminant levels in human tissues. There are often only one or two sampling points from specific countries, ethnic groups, or regions, for example, for Sweden maternal blood data were available for the first AMAP assessment report (AMAP, 1998), but not since then. In other cases (e.g., Alaska, Russia, and Norway), data were obtained during the late-1990s from regions for which they had not previously been reported. For some other countries (e.g., Canada) limited data from the initial circumpolar maternal blood contaminants studies were combined with newer data to produce more robust datasets, after confirming that there were no major temporal differences in contaminant levels between the two datasets. Overall, the data presented in the present assessment report provide a more reliable basis for assessing spatial variation in human contaminant levels in the circumpolar Arctic, but are insufficient for temporal trend analyses.

There are some data for Greenland, from preserved mummies and their clothing, that provide an indication of possible trends in Hg levels over the past 500 years. Figure 5·9 shows concentrations of Hg in hair of Inuit and animals from Greenland for samples representing the fifteenth, sixteenth, and twentieth centuries (Hansen, pers. comm., 2001; Hansen *et al.*, 1989). It is evident that Hg levels are three- to seven-fold higher in the twentieth century Inuit hair samples than in the fifteenth- and sixteenth-century samples. The concentrations of Hg in

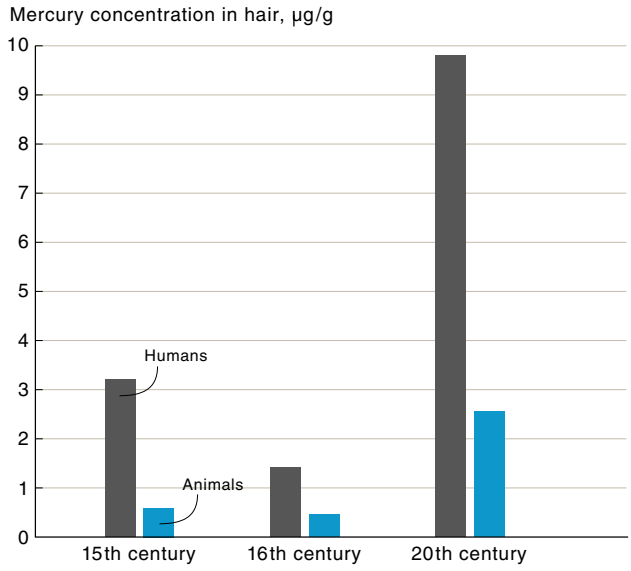

Figure 5·9. Changes in mercury concentration in human and animal hair from Greenland.

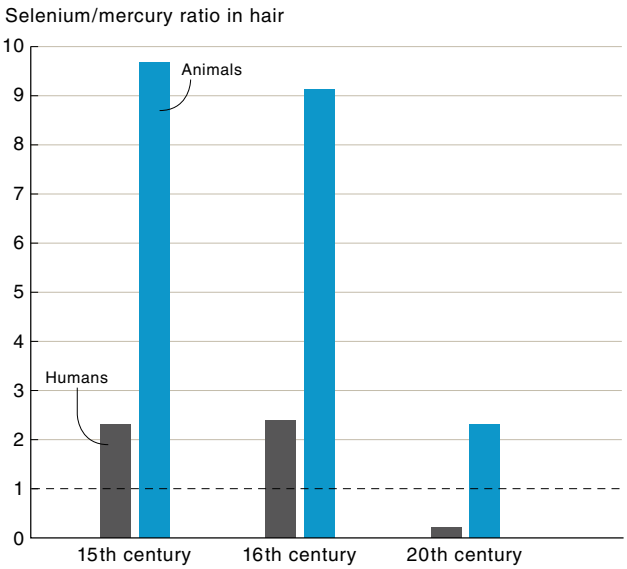

Figure 5·10. Changes in selenium/mercury ratios in human and animal hair from Greenland.

animal hair (seal and reindeer) from Greenland are also four- to six-fold higher in the twentieth century samples (Figure 5·9). These markedly higher concentrations in the Greenland Inuit and their traditional foods may indicate substantially higher exposure to Hg in the twentieth century.

This study also determined Se levels in these samples, and Figure 5·10 presents the associated Se:Hg ratios (Hansen, pers. comm., 2001; Hansen *et al.*, 1989). The Se:Hg ratio has decreased ten-fold in humans and four-fold in animals over the 500-year period. Most of this change is due to the increasing Hg concentrations in the hair of animals and humans as well as to the decreasing concentration of Se in twentieth century human hair (Hansen, pers. comm., 2001; Hansen *et al.*, 1989). With lower levels of Se in relation to Hg, the mitigating effect that Se is thought to have on Hg toxicity may be reduced, and Hg may be having impacts on human health and biota that were not previously occurring. A number of studies are underway in the Arctic which address the possible impacts of Hg and other contaminants on human health (see chapter 9).

5.5. Quality assurance/quality control

The AMAP circumpolar blood monitoring programme was initiated under AMAP Phase I. This took the form of a single circumpolar maternal blood contaminant study in which a single laboratory conducted all the analyses. This programme has been expanded and further developed under AMAP Phase II. In its present form sample analyses are performed by several laboratories in different countries (Table 5·13).

In order to ensure the comparability of the data from the different laboratories, a QA/QC activity was established specifically to support the AMAP Human Health Monitoring Programme. The various laboratories may use similar, but slightly different methods to measure the contaminant concentrations, and the QA/QC programme provides information about the level of comparability of the results. The QA/QC activity addresses both sampling and analytical issues. AMAP human

Table 5·13. Laboratories participating in AMAP Human Tissue Analyses.

Laboratory	Origin of samples
Blood	
L'Institute Nationale de Santé Publique du Québec, Sainte-Foy, QC, Canada	Greenland, Canada, Finland, Sweden
Dept. Pharmacology and Toxicology, Univ. Iceland, Reykjavik, Iceland	Iceland
National Center for Environmental Health of the Centers for Disease Control for Disease Control and Prevention in Atlanta, Georgia, USA	Alaskan mainland and Aleutian and Pribilof Islands
Norwegian Institute of Air Research (NILU), Polar Environmental Centre, Tromsø, Norway	Norway, Archangelsk
Regional Centre Monitoring of the Arctic (RCMA), St. Petersburg, Russia	Siberian Russia
Institute and Out-Patient Clinic for Occupational, Social and Environmental Medicine, Univ. Erlangen, Nuremberg, Germany	Faroe Islands
Breast milk	
L'Institute Nationale de Santé Publique du Québec, Sainte-Foy, QC, Canada	Canada
Regional Centre Monitoring of the Arctic (RCMA), St. Petersburg, Russia	Siberian Russia
Laboratory for Environmental Toxicology at the Norwegian School of Veterinary Science, Oslo, Norway	Kargopol, Severodvinsk, Archangelsk, Naryan Mar
Dept. Environmental Chemistry, Umea Univ., Umea, Sweden	Sweden

health laboratories are currently participating in a series of ring-tests, currently coordinated by the Institute Nationale de Santé Publique du Québec. These ring-tests are also open to other (non-AMAP) laboratories. Two such ring-tests, for PCBs and organic pesticides (i.e., DDTs and mirex), were completed prior to the preparation of this assessment. Metals have not been included in the AMAP ring-tests to date. Results indicate that most of the laboratories involved in the AMAP Human Health Monitoring Programme produce results for PCBs that are within 30% of expected values; and within 20% for DDTs. Results for mirex are, however, less comparable.

5.6. Conclusions

It is apparent that the levels of certain POPs and Hg are generally higher in the maternal blood samples of Arctic peoples who consume traditional foods (e.g., the Inuit of Greenland and Arctic Canada). For the Greenland Inuit, in particular, blood levels of several environmental contaminants (e.g., PCBs, HCB, total chlordanes, and Hg) are higher than those in maternal blood samples from Canada and other circumpolar countries, and this probably reflects a higher consumption of marine mammals. Levels of total DDT are higher in the non-indigenous population from Arkhangelsk (Russia) than in any other region, indicating possible continuing use of DDTs in Russian agriculture or local pesticide use. For β-HCH, the highest levels were also found in Arctic Russia among the non-indigenous population groups, but elevated levels were also seen in Iceland and among the Others group in the Canadian Arctic.

Recent data for the Faroe Island population indicate that, due to public health advice to restrict pilot whale consumption, particularly in the case of pregnant women and nursing mothers, there has been a significant decrease in maternal blood Hg levels, but very little change in PCB levels. The different response of these two contaminants is probably due to the short half-life of Hg in the body compared to that of PCBs. For other Arctic populations, for which there are generally only one or two sequential datasets covering mainly the 1990s, it is very difficult to determine any time trends for the contaminants of concern. Most human health related monitoring in the Arctic has taken place only over the last five to ten years, and although this has provided a much better basis for assessment of the spatial variation in contaminant levels, this period is too short to reliably identify any temporal trends. For Hg, the discovery of ancient Greenland mummies, together with supporting data on biota from their clothing, offers evidence that there has been a significant increase in the concentration of Hg in the Greenland Arctic environment and in peoples who consume large amounts of marine mammals (Hansen *et al.*, 1989; Hansen, pers. comm., 2001).

Chapter 6

Toxicological Properties of Persistent Organic Pollutants and Related Health Effects of Concern for the Arctic Populations

Eva Cecilie Bonefeld-Jørgensen and Pierre Ayotte

Summary

Human exposure to environmental contaminants is ubiquitous and not only limited to individuals living close to the sources of contaminants. Everyone carries a burden of persistent organic pollutants (POPs) in their body. The burden of POPs in Arctic peoples has been monitored for some years, however, it is only recently that a programme for measuring the potential biological effects of these contaminants has been established: the AMAP Human Health Effects Monitoring Programme. Body burden data alone are not enough to allow the health risks associated with exposure to environmental contaminants in Arctic peoples to be assessed. Furthermore, laboratory studies on the effects of single chemicals or chemical mixtures in laboratory animals and cell cultures cannot fully elucidate the human health risks. Integration of epidemiological and biomarker studies on humans from exposed populations in the Arctic is needed in order to obtain information about the real health risks resulting from exposure to the accumulated mixtures of contaminants in the Arctic.

The broad category of human health effects that are suspected to result from exposure to environmental contaminants include cancer, birth defects, effects on the reproductive and the neuro-endocrine-immune systems, altered metabolism, and specific organ dysfunction. This chapter gives an introduction to these various health effects and presents possible biomarkers that may be useful to include in epidemiological studies. It also discusses the connection between traditional toxicological studies and new methods designed to study the potential of chemicals to interfere with the normal homeostasis by exerting endocrine-disrupting effects.

6.1. Overview

The AMAP Phase I assessment report (AMAP, 1998) included an overview of the classical toxicology of contaminants. In 1997, the Alta Declaration extended AMAP's mandate to cover assessment of the combined effects of environmental stressors. This chapter presents a comprehensive and detailed description of the rationale for conducting effects studies. There is some overlap with that part of chapter 9 dealing with epidemiological studies, but this is necessary to discuss the evaluation of effects parameters. Several studies considered below were conducted outside the Arctic as only a few investigations have been carried out in this region to date.

Over the past decade most efforts have been focused on the characterization of exposure of Arctic peoples to contaminants. Epidemiological studies have been conducted in which clinical endpoints, such as psychometrics, neurophysiological parameters, infection incidence, bone density, and sexual maturation among others, were the main focus. However, in order to detect the early biological changes preceding disease, knowledge about the mechanism of action of toxicants is required. Thus, biomarkers of effect need to be validated and used. Effect biomarkers are early biological responses of the organism to an external toxic stress. Since the overall weight of evidence at the epidemiological level for adverse endocrine-related human health effects is not strong, further studies including validated biomarkers in epidemiological studies may help in identifying the possible relevant associations between exposure to contaminants and detrimental health effects in Arctic populations.

The Canadian Arctic Contaminants Assessment Report (Jensen *et al.*, 1997) identified areas with information gaps toward which Arctic contaminant research programmes should be oriented; effect biomarkers were, however, not considered. They were, however, adopted for use in the AMAP Phase II Human Health Effects Monitoring Programme (see section 6.2).

In this chapter, the main focus is on effect biomarkers of early biological responses to evaluate neurobehavioral, immunological, and reproductive organ status of newborns in the Arctic. It therefore, concentrates on biological effects related to reproductive and developmental effects, the neurological and immune system function, and oxidative stress. Discussions are mainly restricted to cover effects due to POPs, including methylmercury (MeHg). Other contaminants, such as cadmium (Cd) and lead (Pb), are now considered of lower priority. Their major sources, relevant to human health in the Arctic, are smoking (for Cd) and lead shot (for Pb) and information on their toxicity and on biomarkers of effects is already available, validated and widely used (e.g., urinary β2-microglobulin level, blood δ-aminolevulinic dehydratase activity). Furthermore, benchmark doses as well as biological guidelines for Cd and Pb have been adopted by international health organizations. In contrast, health risk assessments related to the presence of MeHg and POPs in the Arctic food chain carry much more uncertainty.

6.1.1. The emergence of endocrine disruption

Human exposure to environmental contaminants is ubiquitous. Exposure is not restricted to individuals who live next to industries or waste disposal sites, or those who reside in inner cities or third-world countries

where, e.g., insecticides are widely used. Everyone carries a burden of POPs and heavy metals in their body. Persistent organochlorine (OC) compounds, such as dioxins/furans, polychlorinated biphenyls (PCBs) and certain pesticides, e.g., toxaphene and DDT/DDE, accumulate in body fat; Hg accumulates in organs, Pb in bones, etc. Environmental contamination is a global issue and POPs are transported to the Arctic by atmospheric and oceanic currents. Because of the lipophilic and persistent nature of POPs, bioaccumulation and biomagnification occur in the Arctic marine food web and in some freshwater predatory fish and piscivorous birds. Although far distant from the major pollution sources, some populations living in regions north of the Arctic Circle display a greater body burden of POPs than people living in industrialized regions, largely due to their reliance on a traditional diet that includes species high up in the marine food chain (Asplund *et al.*, 1994; Dewailly *et al.*, 1992, 1994b, 1999; Jensen and Clausen, 1979). Use of several OCs, such as DDTs and PCBs, was restricted or banned in most countries in the 1970s. Even though their concentrations in the environment have been slowly declining over the past 30 years, these compounds are still the most abundant persistent OCs found in wildlife and in human tissue and milk samples in the Arctic region (Safe, 2000).

While concentrations of several OCs are decreasing, the continual introduction of 'new compounds', such as brominated flame retardants, into the environment has generated new concerns (Rahman *et al.*, 2001). In addition, attention has recently shifted from chronic diseases and reproductive endpoints to effects that are induced following exposure during the sensitive period of *in utero* development. Of particular concern are effects on development resulting from prenatal exposure to endocrine-disrupting compounds.

To date, no clear-cut evidence for adverse endocrine-related human health effects has been obtained at the individual or population level. However, data from studies on wildlife species, studies on laboratory animals, and biomarker studies *in vitro* have strengthened the need for further research to address the uncertainty and alleviate concerns. Taking a precautionary approach, the weight of evidence would suggest that exposure levels seen in the Arctic have some potential for adverse effects on human health.

Studies on wildlife populations have documented adverse effects that correlate with exposure to one or more putative endocrine-modulating chemicals (Safe, 2000). Adverse developmental and reproductive effects have been primarily linked to POPs and alkylphenols derived from alkylphenol ethoxylate surfactants used in industrial detergents. In many instances, it has been difficult to assign causality because of the complexity of environmental contaminant mixtures and the level of exposure during critical developmental windows. However, lower concentrations of POPs in the Great Lakes region were correlated with dramatic improvements in reproductive success and significant increases in an array of predatory birds in the Great Lakes basin (Tremblay and Gilman, 1995).

The range of toxicological effects that estrogenic chemicals can produce is illustrated by work on the synthetic estrogen diethylstilbestrol (DES). DES was used pharmaceutically from the late 1940s to the early 1970s to prevent miscarriages and pregnancy complications in women. However, it was removed from the market in the 1970s when studies found DES exposure to correlate with increases in abortions, neonatal death and premature birth, and an increase in the incidence of vaginal adenocarcinoma in young women who were exposed *in utero* (Herbst *et al.*, 1971). A study of men exposed *in utero* showed 31.5% had abnormalities of the reproductive tract compared with 7.8% of controls (Gill *et al.*, 1979). The abnormalities included cryptorchidism and hypospadias, and reduced sperm concentration and quality, although reduced fertility was not observed in these men (Wilcox *et al.*, 1995). Exposure of mice *in utero* induced very similar effects to those seen in humans (McLachlan, 1981). Not all the effects of DES are ascribed to its binding to the estrogen receptor and recent studies have shown that several endocrine-disrupting compounds induce their effects via different receptors and signaling pathways (Andersen *et al.*, 2002; Bonefeld-Jørgensen *et al.*, 2001a).

The convergence of several lines of inquiry was crucial for the rapid growth of interest in the issue of endocrine disruption in the 1990s. A number of worrying trends related to human male reproductive health had been reported globally, including decline in semen quality parameters and increases in the incidence of testicular cancer, hypospadias and cryptorchidism. At the same time, adverse trends in the reproductive health of wildlife in some regions outside the Arctic had also been noted and correlated with exposure to environmental contaminants, and in some cases specific chemicals were implicated. Evidence was also emerging from a variety of experimental studies that many widely used chemicals, distributed extensively in the environment, had the ability to bind and activate estrogen receptors. Although their affinity for the receptor was weak compared with either the natural ligand or DES, their activity was regarded as sufficient to support a working hypothesis that environmental chemicals might be damaging the reproductive health of human and wildlife populations by interfering with sex hormone activities. Behind this concern was the suspicion that chemicals acting through hormone receptors might mimic the natural hormones and have profound effects at very low concentrations. The conjunction of threat both to human and wildlife populations led to responses from international organizations (including AMAP), governments, and the chemical industry. The following general needs were identified.

- Further research to confirm the existence of effects from environmental exposure on reproductive health of humans and wildlife.
- In cases where an adverse effect was confirmed, establishment of the causative link to exposure to an environmental chemical.
- Development of reliable methods, and possibly new methods, for detecting chemicals with potential to cause adverse effects (monitoring).
- Ranking of known and suspected endocrine-disrupting compounds for possible regulatory action (prioritization).
- Possible action to limit release of certain chemicals to the environment.

In order to establish consensus on the scope of this issue, to facilitate the identification of active chemicals, and to underpin future regulatory control it is essential to agree on a precise definition of an endocrine-disrupting compound. In 1998, the International Programme on Chemical Safety and the U.S. EPA's Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC) proposed the following working definition:

An endocrine disrupter is an exogenous chemical substance or mixture that alters the structure or function(s) of the endocrine system and causes adverse effects at the level of the organism, its progeny, populations, or subpopulations of organisms, based on scientific principles, data, weight-of-evidence, and the precautionary principle.

Thus, the term 'endocrine disrupters' covers all kinds of exogenous interfering chemicals; including synthetic chemicals and synthetic and naturally occurring hormones. Exposure can occur via dairy products and food intake, drinking water, and pharmaceuticals, etc. The ability of a chemical to affect humans or wildlife depends on factors such as structure and concentration, bioavailability, degradation/metabolism, and uptake, etc. The observed potency of a chemical is, therefore, very dependent on concentration and the system applied for testing. This can result in several classifications for any one single chemical, for example as carcinogenic, teratogenic, toxic, and endocrine disrupter, depending on which characteristic of the chemical is studied.

Many of the compounds suspected of endocrine-disrupting activity are known to be toxic (in some cases acutely toxic) at higher concentrations. They were therefore banned or controlled in some countries, either on this basis or because of their persistence and capacity to bioaccumulate in biota. Chronic low dose exposure and the subsequent bioaccumulation of lipophilic POPs with long biological half-lives is of special concern. These POPs may over time bioaccumulate to a critical level capable of eliciting an effect. Moreover the 'life-long' duration of exposure, together with increasing environmental levels, may maximize the likelihood of induction of effects. Such factors must be taken into account in sub-chronic, chronic and/or multi-generation tests. Because of the complexity of the endocrine system, and the complex nature of human epidemiological studies, animal studies and *in vitro* screening methods are widely used for toxicity evaluation and risk assessment.

The U.S. EDSTAC has recently developed a strategy for testing chemicals for endocrine modulating activity including an initial sorting of chemicals (based on existing data), priority setting (based on knowledge of exposure), and tier 1 screening and tier 2 testing, comprising:

Tier 1 screening

In vitro assays
- Estrogen receptor binding and reporter gene assays.
- Androgen receptor binding and reporter gene assays.
- Steroidogenesis assay with minced testis.

In vivo assays
- Rodent 3-day uterotrophic assay: increase in uterine weight in ovariectomized rat.
- Rodent 20-day pubertal female with thyroid: age of rats at time of vaginal opening.
- Rodent 5-7 day Hershberger assay: change in weight of prostate and seminal vesicles in castrated rats.
- Frog metamorphosis assay: rate of tail resorption in *Xenopus laevis*.
- Fish gonadal recrudescence assay: effects on light and temperature sensitive sexual maturation.

Tier 2 testing
(Intended to determine and characterize the effects of the chemical on the endocrine system.)
- Two-generation mammalian reproductive toxicity study or a less comprehensive test.
- Avian reproduction test.
- Fish life-cycle test.
- Mysid (shrimp) life-cycle test.
- Amphibian development and reproduction test.

6.1.2. Single compound and chemical mixture exposures

There are a number of factors that complicate the toxicological evaluation of mixtures. First, it is important to remember that no test can evaluate all possible endpoints. However, existing methods in general include numerous endpoints that are sensitive to both strong and weak xenoestrogens such as the reproductive and developmental effects in humans and rodents of DES (Gill *et al.*, 1979; Herbst *et al.*, 1971; McLachlan, 1981; Wilcox *et al.*, 1995) and DDT or chlordecone (Daston *et al.*, 1997). These endpoints, obtained by multi-generation studies in rodents, are sufficient to indicate a hazard. Subsequent decisions to further characterize the cellular and molecular steps in the hazard evaluation require mechanistic research for risk assessment, taking into account the possibility that the observed adverse effects may not be the most sensitive manifestation of toxicity. Second, two or more compounds may have additive effects as a result of acting via the same mechanism in concert. They may also elicit antagonistic (less then additive) or synergistic (greater than additive) effects. Some studies have suggested synergistic responses of steroidal estrogens *in vitro* (yeast) and *in vivo* (turtle) (Arnold *et al.*, 1997a,b). However, estrogenic tests with mixtures of dieldrin and toxaphene in human breast cancer MCF-7 cells, yeast-based human estrogen receptor assays, and mouse uterus tests showed no apparent synergism (Ramamoorthy *et al.*, 1997).

There are several other complications that must be taken into account when generalizing about what is known concerning the toxicity of single compounds and/or mixtures. A compound may have multiple sites of action and its toxicity may be mediated by different mechanisms. Many substances are biotransformed to metabolites (e.g., hydroxylated PCB metabolites) that may have a different biological activity than that of the parent compound. In addition, a single environmental contaminant may induce different effects depending on the organism's age and reproductive state at the time of exposure. Lead is an example of a contaminant having little effect on neurobehavioral function in adults but irreversible effects on intelligence quotient (IQ) and behavior when exposure occurs *in utero* during the development of the nervous system (Carpenter *et al.*, 1998).

It is known that developmental toxicity is dependent on highly susceptible periods of organogenesis, as demonstrated by prenatal exposure to, e.g., DES and thalidomide, and postnatal exposure to Pb, pesticides and radiation (Selevan *et al.*, 2000).

Toxicity scales have been developed for compounds that share a common mechanism of action. This concept was applied to mixtures of dioxin-like compounds that bind the aryl hydrocarbon receptor (AhR). The AhR is an intracellular ligand-dependent transcription factor expressed in most tissues of mammals. Dioxins and furans (polychlorinated dibenzo-*p*-dioxins, PCDDs; polychlorinated dibenzofurans, PCDFs) as well as non- or mono-*ortho* chloro-substituted PCBs are ligands to the AhR (Birnbaum, 1995; Brouwer *et al.*, 1999; Carpenter *et al.*, 1998). The activated ligand-receptor complex triggers the expression of enzymes including P4501A1, P4501A2, P4501B1, glutathione S-transferase, glucuronyl transferase, δ-α aminolevulinate synthethase, epidermal transglutaminase, NAD(P)H:quinone oxidoreductase and aldehyde-3-dehydrogenase, which are involved in metabolism and detoxification of many POPs (Hahn, 1998; Safe and Krishnan, 1995).

A common practice in risk assessment is to calculate the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) toxic equivalents (TEQs) for mixtures comprising dioxin-like compounds. TEQs are calculated by multiplying the concentration of each dioxin-like compound by its Toxic Equivalency Factor (TEF), which corresponds to the relative potency of the specific compound in generating an AhR-mediated effect, in relation to that of TCDD, the most potent dioxin-like compound. Consequently, the classical TEQ/TEF risk assessment only accounts for potential dioxin-like properties of a mixture and not other relevant toxicological endpoints such as effects mediated via other receptors and biochemical pathways (e.g., interference with the sex hormones and thyroid hormone systems). For example, *ortho*-substituted PCBs are either weak ligands or do not bind at all to the AhR, therefore either very low or no TEF values are given for these compounds. Recently, however, it was reported that the three most highly bioaccumulated di-*ortho* substituted PCBs (CB138, CB153, and CB180) elicit the potential, *in vitro*, to interfere with cell proliferation as well as the function of the androgen and estrogen receptors (Figures 6·1 and 6·2) (Bonefeld-Jørgensen *et al.*, 2001a). These results emphasize that a full assessment of the toxicological potential of a chemical mixture is much more complex than can be deduced by the use of TEQ values alone.

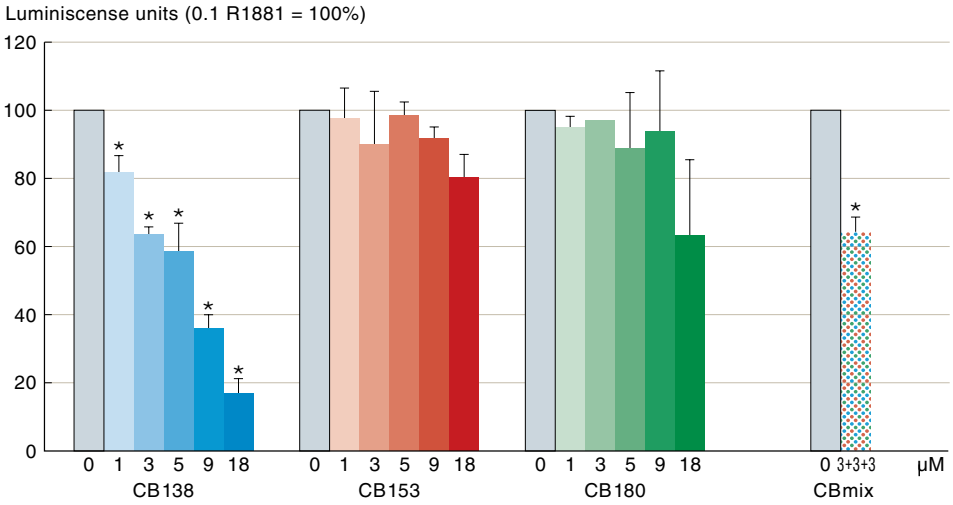

Figure 6·1. Effects of PCB congeners on androgen receptor (AR) trans-activity in Chinese hamster ovary cells (CHO cells). The response of PCBs and the AR agonist methyltrienolone (R1881, positive control) were obtained by transiently co-transfection with the pMMTV-LUC reporter plasmid and the pSVAR0 expression plasmid encoding the human AR. Asterisks indicates statistically significant ($P \leq 0.05$) decrease relative to cells treated with 0.1 nM R1881 (which is set to 100%). Source: Bonefeld-Jørgensen *et al.* (2001a).

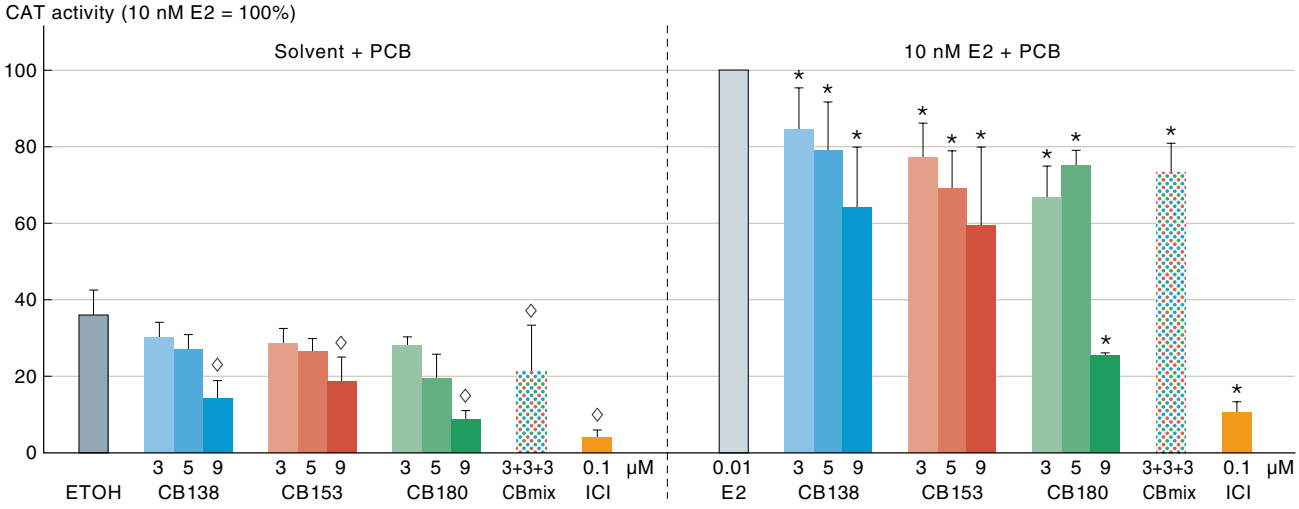

Figure 6·2. Effects of PCB congeners on estrogen receptor trans-activity in human breast cancer MCF-7 cells. The response of the PCBs and the ER agonist 17β-estradiol (E2, positive control) on transactivation of the reporter plasmid pERE-tk-cat in MCF-7 cells. Diamonds indicate a statistically significant ($P \leq 0.05$) difference from the solvent (ETOH) and asteriks from the 10 nM E2 treated cells, respectively. Source: Bonefeld-Jørgensen *et al.* (2001a).

Table 6·1. The AMAP Human Health Effect Monitoring Programme.

Bio-Physical Indicators	Epidemiological Effect Markers	Molecular/Genetic Effect Markers
Health Statistics		
	E Morbidity/Mortality data R Cancer incidence	
Genetic susceptibility studies		
Gene polymorfisms	R Gene polymorfisms	R Genotypes Gene expression (mRNA)
Fertility studies		
Time to pregnancy	R Time or number of menstrual cycles it takes a couple to conceive from discontinuation of contraception	R Receptor/hormone toxicology (estrogenic- and androgenic-like activities are performed in steroid hormone cleared serum samples). R Estrogenic- and androgenic-like activities. Dioxin-like activities in blood serum. *In vitro* hormone receptor bindings.
Semen quality and quantity	R Sperm count/volume Sperm quality/mobility	
Sex hormones (in blood from women and from their male partners providing semen samples)	R Sex hormones	R FSH, Inhibin-B, LH, testosterone, estradiol, sex hormone binding globulin, osteocalcin, pyridolins
Pregnancy outcome		
General indices	E Abortion (spontaneous) Gestational age Birth weight/length Sex (single/multiple) Placenta weight	R Estrogenic-, androgenic- and dioxin-like activities R Cytochrome P450 modulations, DNA adducts
Developmental anomalies	R Maldescent testis Hypospadias Epispadias Ano-genital distance and other indices	
Developmental effects	R Breast milk (POPs, fatty acids)	
Immunological effects		
	R Hospitalization	
	R Vaccination response	R Antibody (HIB)
		R Vitamin A and cytokines, complement system R Dioxin-like activities
Neurological effects		
	R Milestones + age R Pre-school tests: neurophysiological tests neuropsychological tests audiogram and visual tests	R Thyroid hormone R Estrogenic- and dioxin-like activities GSHRd, GSHPx, Ubiquinol 10/Ubiquinone 10, Ox-LDL, F2-isoprostanes

E: Essential; R: Recommended.

The AMAP Human Health Effect Monitoring Programme is designed to examine the effects on reproduction and development of dietary exposure to POPs and heavy metals within the Arctic. One requirement is that a suite of studies are carried out in parallel, including dietary questionnaires and indicators, and contaminant measurements carried out by laboratories with documented QA/QC.

6.2. The AMAP Human Health Effects Monitoring Programme

The broad categories of human health effects that may be linked to exposure to environmental contaminants include: cancer, birth defects, decreased fertility, altered sex hormone balance, immune system defects, neurological effects such as reduced IQ and behavioral abnormalities, altered metabolism, and specific organ dysfunctions (Carpenter *et al.*, 1998). At AMAP Human Health Expert Group meetings held in Ottawa, Canada, September 1999; Rovaniemi, Finland, January 2000; and Tórshavn, Faroe Islands, October 2000, a Human Health Effects Monitoring Programme was recommended to the eight Arctic nations.

The AMAP Human Health Effects Monitoring Programme, as shown in Table 6·1, includes several molecular biomarker endpoints for use in Arctic environmental health studies. Substances commonly found in the environment may have the potential to affect several organ

systems. The diseases listed are identified on the basis of studies of both humans and animals, and in most cases these investigations were focused on a single contaminant. Several of these diseases, when found in a given individual, are difficult to ascribe to a particular exposure (Sharpe, 1993; Sharpe and Skakkebaek, 1993). This is generally the case for cancer, reproductive effects (such as infertility, early birth, etc.), many of the endocrine modulators and nervous system actions. Others are clearly attributable to particular exposures, such as kidney disease following Cd exposure or the loss of particular neurons following MeHg exposure (Carpenter *et al.*, 1998).

The main objective of the AMAP Human Health Effects Monitoring Programme is to characterize the impact of dietary exposure to POPs by monitoring biophysical indicators, and epidemiological and molecular/genetic effect markers (see Table 6·1). These effects studies are directed towards examining the hypothesis of xenobiotic interference with homeostasis of hormone functions, with a special focus on circumpolar populations. A number of persistent OCs exhibit estrogenic (and anti-estrogenic), androgenic (and anti-androgenic) and dioxin-like activities. Some bind to the estrogen receptor (e.g., DDT, toxaphene, CB138, CB153, CB180) (Bolger *et al.*, 1998; Bonefeld-Jørgensen *et al.*, 1997, 2001a), and some bind to the androgen receptor (e.g., DDE, vinclozolin) (Bonefeld-Jørgensen *et al.*, 2001a; Crisp *et al.*, 1998; Kelce *et al.*, 1997; Kelce and Wilson, 1997) or bind to both receptors (e.g., metabolites of methoxychlor, CB138). Dioxins have been characterized as anti-estrogenic due to their AhR-mediated interference with estrogen receptor activities (Kharat and Saatcioglu, 1996; Safe and Krishnan, 1995). Because of the wide variety of endocrine-disrupting effects possibly induced by mixtures of persistent OCs, there is a need to develop markers that integrate the effects of several chemicals on specific hormonal pathways and to combine them with epidemiological studies that are also part of the AMAP Human Health Effects Monitoring Programme.

Sonnenschein and colleagues have devised a method for estimating human exposure to a complex mixture of xenohormones (environmental compounds with hormone-like activities) (Sonnenschein *et al.*, 1995). First, endogenous steroids are separated from persistent OCs in human serum samples by high-performance liquid chromatography (HPLC) and the resulting fractions are tested for estrogenic activity using a proliferation assay with MCF-7 cells. Other investigators have further developed and applied the HPLC fractionation of human serum for separating endogenous hormones from xenohormones to obtain integrative measurements of estrogenic, androgenic, and dioxin-like effects of compounds using reporter-gene cell assays. Recent data, using Inuit serum samples from Greenland, have indicated that the concerted action of accumulated persistent OCs in the human samples exerts an inhibitory effect on the estrogen receptor function in human cells, whereas an increase in AhR activity was observed (Bonefeld-Jørgensen, in prep.).

The morbidity/mortality data and pregnancy outcomes are considered essential effect markers, whereas the other biomarkers listed in Table 6·1 are recommended measurements for inclusion within AMAP monitoring implementation plans. The biophysical indicators and epidemiological and molecular/genetic effect markers included in Table 6·1 are, as far as possible, linked to the different studies. In addition, dietary questionnaires, relevant markers of a seafood based diet (e.g., n-3 fatty acid content in plasma phospholipids), and biomarkers of exposure to POPs should also be included in the studies. Laboratories performing POPs, heavy metal, and lipid analyses must have documented quality assurance / quality control (QA/QC).

Sections 6.3 to 6.8 describe the background and rationale for conducting the health effects studies in the Arctic that are listed in the Human Health Effects Monitoring Programme (Table 6·1). Some studies have already been initiated in some parts of the Arctic, while others are still at the planning phase.

6.3. Genetic considerations

Central to many of the influences on the biological system are effects that occur at the gene level. Genes regulate almost everything, including many aspects of hormonal production and the reproductive system, brain development and function, immune system balances, and organ physiology. A genetic disruption can, therefore, affect different organ systems, as a result of the extensive interactions between these systems; i.e., effects on one organ system may influence the function of other organs. During normal development, genes are activated and deactivated at different stages, often under the control of growth factors and hormones. Environmental factors interfere with these biologically balanced processes and may result in genetic dysfunction. Mutations in genes, inherited or induced by environmental factors, may thus result in reproductive effects, birth defects, and cancer.

Gene polymorphism is known to exist between different ethnic groups, which can result in differences in tolerance, e.g., to food components such as lactose (Harvey *et al.*, 1998; Nei and Saitou, 1986). In addition, gene polymorphism in metabolizing enzymes is suspected to influence susceptibility to environmental carcinogens, affecting the risk of cancer (Autrup, 2000; Coughlin and Piper, 1999; Morabia *et al.*, 2000). Genetic polymorphism and breast cancer risk has been extensively analyzed, and significant differences in genotype frequencies between cases and controls have been found, including the aromatase cytochrome P450 (CYP19) gene which catalyses the conversion of androgens to estrogens (Dunning *et al.*, 1999). Recently, a study suggested an association between PCB concentrations and CYP1A1 gene polymorphism in women breast cancer patients compared to control groups (Moysich *et al.*, 1999).

Serum concentrations of *p,p'*-DDT, *p,p'*-DDE and CB138, CB153, and CB180 were found to be significantly associated to K-ras mutations in exocrine pancreatic cancer (Porta *et al.*, 1999). These results suggest new roles for OCs in the development of several cancers in human beings.

Mitochondrial DNA (mtDNA), which is inherited maternally via the oocyte, has been mapped completely (Thrasher, 2000). The variation of mtDNA can be used

to determine the ancestry of a population. For example, using restriction fragment length polymorphism and DNA sequence technology, the present Inuit from Greenland were shown to be descended essentially from Alaskan Neo-Eskimos; European mtDNA types were not found in the Inuit samples in this study (Saillard *et al.*, 2000). Because of inadequate DNA repair mechanisms, relatively high rates of mutation are accumulated in the mtDNA. Mitochondrial DNA mutations are responsible for several mitochondrial syndromes. A recent study presented a theory of possible linkages between mitochondrial defects and a possible global developmental delay in some children with maternal exposure to environmental OCs. The author suggests that investigators conduct further research into the cause of maternal mtDNA mutations following exposure to mutagenic xenobiotic compounds (Thrasher, 2000).

6.4. Breast cancer

The incidence of breast cancer has increased steadily over the past few decades in women from a number of countries including Finland, Denmark, the United States, and the UK (Hakulinen *et al.*, 1986; Quinn and Allen, 1995). The upward trend is estimated at about 1% per year since 1940. In the Arctic, the prevalence of breast cancer in Greenland Inuit is much lower than in the general population of the Western Hemisphere; however, during the 1990s an increasing incidence was also observed in this population (Nielsen, 2000). The established risk factors, such as genetic inheritance and factors resulting in an increased total lifetime exposure to biologically active estrogens, can explain only about a third of the cases (Davis and Bradlow, 1995). Estrogens have a prominent role in the pathogenesis of breast cancer (Lippman and Dickson, 1989), and it has been hypothesized that xenoestrogens may contribute to the total estrogenic burden.

Several studies on DDE, PCB and hexachlorobenzene (HCB) concentrations in breast cancer patients versus controls have been carried out in Europe, Asia, and North and South America. Overall these studies do not support a major role for exposure to persistent OCs as a risk factor (Laden and Hunter, 1998; Safe, 1997). However, the results are inconclusive, particularly for high-level exposure. Six studies reported elevated levels of DDT or DDE among women with breast cancer. Seven studies found no differences in DDT or DDE level between cases and controls, and one study reported higher DDE levels in serum samples among women with breast cancer (Romieu *et al.*, 2000). The limitation of these studies has been discussed with regard to information on duration of lactation, other potential sources of estrogens, and replacement estrogen therapy. The lack of controlling for other sources of estrogens or potentially confounding factors may have masked a real association between OC exposure and breast cancer (Romieu *et al.*, 2000). In Denmark, Høyer *et al.* (1998) reported a significant dose-related association between accumulation of the pesticide dieldrin and the risk of breast cancer. As previously mentioned, a case-control study in western New York State found an increased risk of breast cancer to be associated with the polymorphism of CYP1A1 among women with PCB levels higher than the control group (Moysich *et al.*, 1999). Thus, the importance of environmental xenohormones in the etiology of breast cancer remains controversial.

Accumulation in the fatty breast tissue and the potential of many persistent OCs to exert estrogenic/androgenic- or anti-estrogenic/anti-androgenic-like effects are hypothesized to promote the cancer process through the modulation of the estrogen receptor regulated responses (Wolff and Toniolo, 1995). Therefore, to reject or verify the hypothesis future studies must include – in addition to the epidemiological investigation and burden of POPs – information on genetic polymorphisms and biomarkers related to the total impact of components with estrogenic (or anti-estrogenic), androgenic (or anti-androgenic), and dioxin-like activities. Currently, a pilot study including these endpoints is being carried out in Greenland (Bonefeld-Jørgensen, pers. comm., 2002).

PCBs and dioxin are well known for their ability to induce certain iso-enzymes of P450 in mammalian liver via the AhR. Some of these enzymes; P4501A1, P4501A2, and P4501B1, are involved in estradiol metabolism and might disrupt hormone levels (Spink *et al.*, 1992a,b, 1994, 1998). *In vitro*, several persistent OCs have been shown to increase the 16α-OHE1:2-OHE1 estradiol metabolite ratio; 16α-OHE1 is regarded as highly estrogenic while 2-OHE1 is a weak anti-estrogen (Bradlow *et al.*, 1995). Some studies have reported higher levels of the 16α-OHE1 metabolite in urine of breast cancer patients (Bradlow *et al.*, 1995; Safe, 2000), whereas other studies did not observe this association (McDougal and Safe, 1998; Ursin *et al.*, 1997). Thus, inconclusive results exist and await further research.

In animal studies the anti-estrogenic capacity of TCDD was suggested to be responsible for a decrease in the incidence of mammary tumors observed in female rats (Kociba *et al.*, 1978). *In vitro* bioassays have suggested that hydroxy metabolites of several PCB congeners also possess anti-estrogenic properties (Moore *et al.*, 1997).

6.5. The reproductive system and fertility studies

The development and maintenance of reproductive tissues is to a large extent controlled by steroidal hormones. Studies *in vitro* or in whole animal model systems have demonstrated that some environmental chemicals either mimic and/or antagonize natural hormone activities. Studies dating back to the late 1960s identified 1-[2-chlorophenyl]-1-[4-chlorophenyl]-2,2,2-trichloroethane (*o,p'*-DDT), a minor constituent of technical DDT, as a weak estrogenic compound capable of causing an augmentation of rat uterine weight in the classic immature female rat model (Bitman and Cecil, 1970). This compound and a few others that share estrogenic properties have been implicated in abnormal sexual development in reptiles (Gaido *et al.*, 1992; Guillette *et al.*, 1994, 1995), birds (Fahrig, 1993; Fry, 1995; Fry and Toone, 1981) as well as feminized responses in male fish (Jobling *et al.*, 1995).

Male reproductive disorders may be mediated by the estrogen receptor; however, they are also consistent with inhibition of androgen receptor-mediated events. Kelce

et al. (1995) identified the major and persistent DDT metabolite, 1,1-*bis*[4-chlorophenyl]-2,2-dichloroethylene (*p,p'*-DDE), as a potent anti-androgenic agent in male rats. In addition to inhibiting androgen binding to the androgen receptor, this compound, when administered to pregnant dams, also induced characteristic anti-androgenic effects in male pups (reduced anogenital distance; presence of thoracic nipples). Treatment with *p,p'*-DDE at weaning delayed the onset of puberty, while treatment of adult rats resulted in reduced seminal vesicle and ventral prostate weights.

TCDD is yet another OC which has been shown to alter sexual development in male rats (Mably *et al.*, 1992). Decreases in epididymis and cauda epididymis weights, decreases in daily sperm production and cauda epididymal sperm number were observed at day 120 and at most earlier times, when a dose as low as 64 ng/kg was administered to dams on day 15 of gestation.

During the differentiation of reproductive organs, hormones, growth factors, and other endogenous mediators regulate gene expression and direct differentiation. The marked difference between exposure to chemicals including endocrine-disrupting compounds during critical periods in development versus during adulthood is the irreversibility of an effect during development. Evidence indicates that changes in concentrations of androgen and estrogen result in permanent changes in cell function. For example, the higher level of testosterone in male mouse fetuses relative to female fetuses results in the differentiation to prostate tissue as opposed to vaginal tissue. In addition, a small increase in total circulating estradiol (50 pg/mL) permanently altered prostate size in mice (Bigsby *et al.*, 1999). Thus it is plausible that disruption of the action of estrogen or androgen during critical periods can lead to permanent alterations in the development of reproductive organs and other tissues with receptors for these hormones.

Animal experiments indicate reproductive toxicity following low-level exposure to persistent OCs. In laboratory animals it has been shown that prenatal exposure to PCBs, PCDD or the DDT-metabolite *p,p'*-DDE is associated with reduced male fertility (Kelce *et al.*, 1995; Peterson *et al.*, 1993; Sager *et al.*, 1987).

In wildlife studies on Baltic grey (*Halichoerus grypus*) and ringed seals (*Phoca hispida*) and on Wadden Sea harbor seals (*Phoca vitulina*) there is strong evidence that PCBs in the food chain had impaired reproductive function resulting in population declines (SCTEE, 1999). Most recently, high levels of POPs have been found in Arctic polar bears (*Ursus maritimus*) in Svalbard (Skaare *et al.*, 2000), and a possible association between the reported incidence of pseudohermaphroditism in polar bears and environmental chemicals has been discussed (Wiig *et al.*, 1998).

More information about effects of POPs on Arctic animals can be found in the AMAP 2002 assessment on POPs in the Arctic (AMAP, 2003c).

6.5.1. Time to pregnancy

Time to pregnancy is a measure of the joint reproductive performance of the parents. Temporal changes in human fertility in relation to body levels of OCs have not been extensively investigated. A time-to-pregnancy study did not reveal delayed conception among consumers of fish from Lake Ontario (Buck *et al.*, 1997), but the duration of exposure was rather short and not quantified by measurements. Results of a Scandinavian time-to-pregnancy study indicate delayed conception related to persistent OC body burdens in smokers but not in non-smokers (Axmon *et al.*, 2000).

6.5.2. Semen quality and quantity

A study of sperm counts conducted worldwide suggested that an annual fall of 0.8% had occurred between 1938 and 1990 (Carlsen *et al.*, 1992). Since then, falling sperm count and quality have been reported in a number of countries (Auger *et al.*, 1995; de Mouzon *et al.*, 1996; Irvine *et al.*, 1996; Van Waeleghem *et al.*, 1996) and a study of testicular morphology in Finland (Pajarinen *et al.*, 1997) suggested a reduction in spermatogenesis between 1981 and 1991. In contrast, no evidence for a decline in sperm counts or quality has been found in a number of locations studied within the United States (Fisch *et al.*, 1996), although considerable geographical variation in sperm counts was observed.

Sperm production is controlled by the sex hormones (Sharpe, 1993; Sharpe and Skakkebaek, 1993), and may therefore be influenced by sex-hormone-mimicking compounds. Certain chemicals lower sperm count in animals and in exposed workers. Dioxins and the pesticide endosulfan are known to lower testosterone levels and produce testicular atrophy in male rats, and dioxin, kepone, 2,4-dichlorophenoxyacetic acid (2,4-D), and dibromochloropropane have been suggested to reduce sperm count in men (Paigen, 1999). A number of other possible factors may affect sperm production, including changes in lifestyle. Intake of selenium (Se) is reported to be falling in the UK and Europe (Rayman, 1997) and dietary deficiency of Se has been suggested as a causative agent of lowered sperm production since selenoenzymes play a role in the maintenance of normal sperm motility, testicular morphology and testosterone metabolism. There is general consensus that, in some countries at least, semen quality and counts have declined. However, taking into consideration the influence of bias in recruitment of study subjects and uncertainty in methodologies (Bromwich *et al.*, 1994; Lerchl and Nieschlag, 1996) it is not known to what extent semen quality reflects incidence of infertility or sub-fertility of males as such.

The only known study on semen quality in the Arctic took place in Iceland. A study of 73 men including 27 men with normal semen, who came to the fertility center because of their wives' fertility problems (52% were of proven fertility), 20 men with idiopathic sterility, and 26 men with poor semen quality, showed no correlation between fertility and persistent OC levels. There was a direct relationship between OC levels in plasma and in semen; with concentrations approximately 20 to 50 times lower in semen. Prevalence of obesity (body mass index (BMI) > 30 kg/m^2) was more than three times higher in the group of men with semen problems, and sperm density correlated to BMI (P = 0.003), raising the possibility that increased prevalence of obesity may partly be involved in the decline in male fertility (Magnúsdottir *et al.*, 2002).

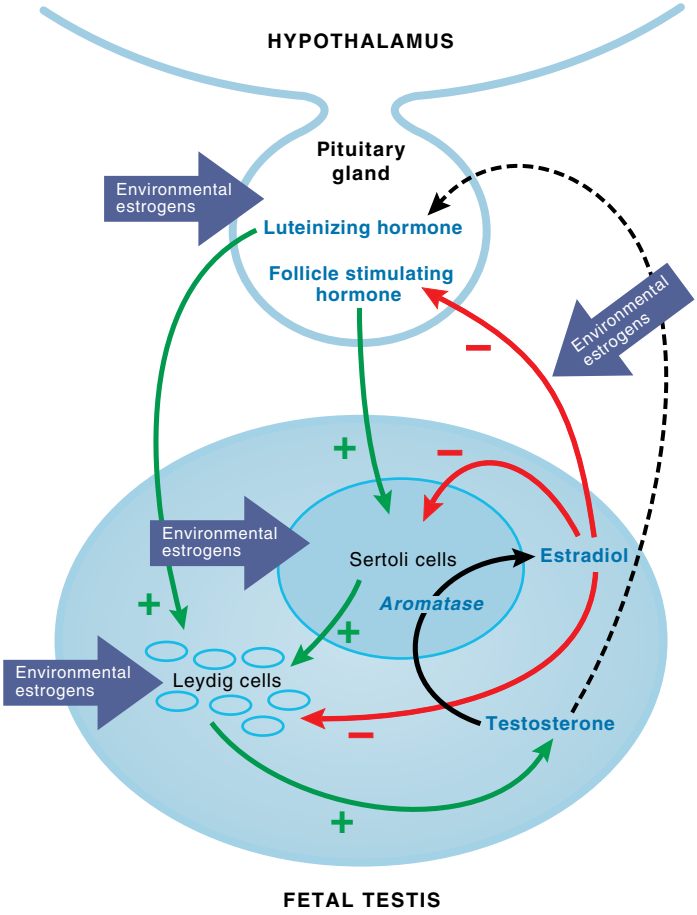

Figure 6·3. Means by which environmental estrogens are thought to disrupt the major hormonal mechanisms involved in growth and function of fetal/neonatal testis. Green (+) and red (–)arrows represent positive and negative feedback mechanisms, respectively. For explanation see the text to the right.

6.5.3. Male reproduction, testicular and prostate cancer

The incidence of testicular cancer has increased quite dramatically in many countries having cancer registries, including Scandinavian countries, the countries around the Baltic Sea, Germany, the UK, the United States, and New Zealand (Adami *et al.*, 1994; Brown *et al.*, 1986; Hakulinen *et al.*, 1986; HMSO, 1992; Wilkinson *et al.*, 1992). Interestingly, the increasing incidence of testicular cancer in Denmark is several times higher than in Finland and further study of this geographical gradient may give important clues on etiology. Prostate cancer incidence has also increased in many countries (Boyle *et al.*, 1995; Merrill and Brawley, 1997). The incidence of congenital malformations such as cryptorchidism (maldescent testis) and hypospadias (malformation of the penis) are thought to be increasing in the Western countries (Berkowitz *et al.*, 1993; Kallen *et al.*, 1986). Testicular cancer has been related to cryptorchidism (Giwercman *et al.*, 1993, 1987) and the testicular maldescent has also been linked to hypospadias (Kallen *et al.*, 1986; Moller *et al.*, 1996; Prener *et al.*, 1996). Moreover it is widely accepted that men with testicular cancer have a higher incidence of impaired spermatogenesis in both cancerous as well as contra lateral testis (Petersen *et al.*, 1998). The increases in the incidence of testicular cancer, hypospadias, cryptorchidism, and reduced sperm count are believed to be associated with *in utero* exposure, i.e., fetal development, and may therefore have common etiology (Sharpe, 1993; Sharpe and Skakkebaek, 1993).

A variety of epidemiological data suggest that the hormonal environment of the fetus may be involved in the development of testicular cancer and congenital malformations. The main evidence, which suggests that prenatal exposure to estrogens has an influence on the development of the male reproductive tract, originates from the treatment of pregnant women with DES. Alteration in estrogen exposure may be influenced by endogenous sources such as a change in diet (low-fiber, high fat, and increase in dairy products) and increase in body fat. Intake and increase of synthetic estrogens such as DES and ethinyl estradiol may occur through the use of oral contraceptive pills, components of which are recycled into drinking water, and also by intake of non-persistent phytoestrogens from plants. Finally, persistent OCs such as PCBs and dioxins are suspected to play a role because of their potential to interfere with hormone homeostasis. In animal studies, TCDD caused changes in both male and female gonadal development and male reproduction (Peterson *et al.*, 1993).

Figure 6·3 summarizes the major hormones which are involved in growth and function of the fetal testis and illustrates how exogenous environmental estrogens may disrupt the normal hormone homeostasis. The basis for susceptibility to adverse effects of estrogen on development of the male reproductive tract centers on the normal hormonal control of the fetal testis.

Sertoli cells play an essential role in spermatogenesis. The production of estrogen and Müllerian inhibiting substance by the Sertoli cells are thought to co-ordinate the processes relating to testicular development and masculinization. Sertoli cells are also thought to regulate the differentiation and multiplication of the early germ cells and fetal Leydig cells and their production of testosterone, which is converted to the more potent androgen 5α-dihydrotestosterone. The follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary gland control Sertoli cell multiplication and maintain testosterone production by fetal Leydig cells, respectively. A negative feedback system operates in which steroid hormones produced by the testis, testosterone and estrogen, act to regulate FSH and LH and is the basis for the so-called estrogen hypothesis (George and Wilson, 1994; Sharpe, 1993, 1994; Sharpe and Skakkebaek, 1993). Estrogen seems to be necessary in male development and function. In addition, immature Sertoli cells, Leydig cells, and germ cells possess the enzyme aromatase, which is responsible for the synthesis of estradiol from testosterone. Estrogens, including environmental estrogens, have the potential to act via various points within this feedback loop to alter hormone level and testicular function.

Sertoli cells produce inhibin-B in a feedback loop, which regulates FSH secretion. Neonatal secretion of inhibin-B can be used as a measure of Sertoli cell number and a sensitive marker for Sertoli cell toxicants. In *in vitro* responses of immature rat Sertoli cells, estrogens, bisphenol-A and the pesticide lindane were shown to increase the production of inhibin-B, whereas mercury(II) and platinum(II) markedly decreased inhibin-B levels (Monsees *et al.*, 2000).

The extreme sensitivity of the fetus to its hormonal environment is illustrated by studies in mice demonstrating that intrauterine fetal position can influence male sexual behavior and androgen responsiveness (Nonneman *et al.*, 1992). It has been known for some years that DDT has both estrogenic (*o,p'*-DDT) and anti-androgenic (*p,p'*-DDE) isomers (Kelce *et al.*, 1995). However, the range of synthetic chemicals with potential estrogenic activities includes other OC pesticides (Andersen *et al.*; 2002, Kelce *et al.*, 1995; Soto *et al.*, 1994), PCBs (Connor *et al.*, 1997), alkylphenolic compounds (Routledge *et al.*, 1998), phthalate esters (Harris *et al.*, 1997) and bisphenol-A (Ben-Jonathan and Steinmetz, 1998; Gould *et al.*, 1998). All chemicals identified as having estrogenic activity are approximately 10^3- to 10^6-fold less potent than estradiol and recent data suggest that they have similar binding affinity for the ER-α and ER-β estrogen receptors (ER) (Kuiper *et al.*, 1998). Moreover, new data suggest that a number of phthalates and alkylphenol chemicals, which act as weak ER agonists *in vitro*, also elicit weak androgen receptor antagonism *in vitro* (Sohoni and Sumpter, 1998). This complicates the prediction of *in vivo* activity of the chemicals. There is some *in vivo* evidence that high exposure of rats to dibutyl-phthalate during gestation and lactation causes abnormalities of the male reproductive tract (Mylchreest *et al.*, 1999). Processes regulated by testosterone were also affected by dibutyl-phthalate exposure resulting in reduction of anogenital distance, hypospadias testicular maldescent, atrophy and underdevelopment of seminal vesicles and prostate. Almost no effect was observed on the female offspring. These observations are similar to effects of prenatal exposure to the anti-androgen flutamide and the anti-androgenic fungicide vinclozolin (Gray *et al.*, 1994; Kelce *et al.*, 1994; Mylchreest *et al.*, 1999). Also, the herbicide Linuron (3-[3,4-dichlorophenyl]-1-methoxy-1-methylurea) was shown to impair testosterone-mediated reproductive development in rats (McIntyre *et al.*, 2000).

The strongest evidence, which implicates exposure to synthetic chemicals as a factor in reproductive tract abnormalities, comes from wildlife. The best-known endocrine-disrupting compound causing serious reproductive abnormalities is tributyltin (TBT). TBT acts as an anti-estrogen since it inhibits aromatase causing an increase in androgens and masculinization of female marine gastropods (Yamabe *et al.*, 2000). In human prostate cancer cells TBT and triphenyltin (TPT) are shown *in vitro* to stimulate cell proliferation and androgen receptor transcription such as prostate specific antigen (Yamabe *et al.*, 2000). Moreover, a number of polycyclic aromatic hydrocarbons (PAHs) were shown, *in vitro*, to possess anti-androgenic activities (Vinggaard *et al.*, 2000).

In summary, more studies are required to support the involvement of environmental chemicals as a risk factor in the proposed decline in male fertility.

6.5.4. Effect on hormone receptor numbers

The responsiveness of a tissue to a hormone depends on the density of receptors within its component cells. The number of receptors is determined by their rate of synthesis and catabolism, which is in turn controlled by complex feedback mechanisms involving hormone action. Some chemicals are shown to interfere with this regulation. For example, TCDD can act to decrease or increase the expression of the ER (Romkes *et al.*, 1987), and compounds which bind to the ER (e.g., ICI 182,780, toxaphene, CB138 and several pesticides) influence receptor functions as well as the cellular level of ER mRNA (Andersen *et al.*, 2002; Bonefeld-Jørgensen *et al.*, 2001a; Jensen *et al.*, 1999).

6.5.5. Effects on synthesis, storage, release, transport, and clearance of hormones

Hormones, including sex steroids, thyroid hormones and glucocorticoids, are transported bound to carrier proteins and their effects are to some extent influenced by the level of these proteins in the blood. Sex hormone-binding globulin (SHBG) is a plasma glycoprotein that binds certain estrogens and androgens with high affinity. Hormones bound to SHBG are not bioavailable for transport into effector cells. In mammals, estrogen increases the concentration of SHBG in plasma, whereas it is decreased by androgens. Plant estrogens (phytoestrogens) also stimulate SHBG synthesis (Murkies *et al.*, 1998). A positive correlation was recently reported between *p,p'*-DDE concentrations in plasma lipids and plasma concentrations of SHBG in young men exposed to DDT during anti-malarial campaigns in Chiapas, Mexico. *p,p'*-DDE levels were also negatively correlated with bioavailable testosterone concentration, semen volume and total sperm count (Ayotte *et al.*, 2001).

Xenobiotic ligands such as hydroxy-PCBs, phthalate esters and chlorinated pesticides in general either do not bind to SHBG or show low affinity compared to 17β-estradiol (Jury *et al.*, 2000). Although these compounds bind to SHBG with much lower affinity than endogenous sex steroids, these interactions may be physiologically relevant in situations where SHBG levels are high and endogenous hormones are low, such as prepubescent children and women taking contraceptives. Moreover, the lack of binding of xenobiotic ligands to SHBG might cause biologically relevant concentrations in spite of their relatively low concentration compared to endogenous hormones.

6.5.6. Hormone profiles

To obtain a steroid profile of androgens for both precursors and metabolites of dihydrotestosterone (DHT) a series of steroids, including DHT, could be measured: dehydroepiandrosterone (DHEA), androst-5-ene-3β, 17β-diol, androstenedione, testosterone, estrone, estradiol, DHEA sulfate, androstane-3α, 17β-diol glucuronide, and androsterone glucuronide. Information on these steroid levels enables a better understanding of any alteration in steroidogenic enzymes in classical steroidogenic tissues, such as adrenal glands and the testis, and for steroidogenic transforming enzymes localized in peripheral tissues such as the prostate and skin.

In the Arctic, no full studies have yet been conducted on hormone profiles and contaminant exposure. Dewailly and colleagues recently carried out a pilot study in Greenland (n=48 males) and the following male hormones were measured: DHEA, δ5-diol, δ4, testosterone,

DHT, E1 and E2. These hormone levels will be correlated with persistent OC levels after adjustment for age, BMI and smoking (Dewailly, pers. comm., 2001).

6.6. Osteoporosis

Persistent OCs have recently been associated with an increased risk of osteoporosis in humans (Beard *et al.*, 2000). The relationship between DDE and bone mineral density was recently examined in 68 sedentary women who reported adequate dietary intake of calcium. Reduced bone mineral density was significantly correlated with age ($r = -0.36$, $P = 0.004$), as well as with increases in the log of DDE levels in serum ($r = -0.27$, $P = 0.03$). These results suggest that past community exposures to DDT may be associated with reduced bone mineral density in women. As a potent androgen receptor antagonist, DDE may reduce the inhibitory effect on cytokines and result in the inappropriate turnover of osteoclasts or inadequate production of osteoblasts within bone marrow, thus leading to reduced bone density (Beard *et al.*, 2000). Bone metabolism markers that could be used are: serum markers of bone formation (osteocalcin), and calcium resorption (urinary pyridinolines). A study of factors associated with osteoporosis in Greenland women is underway and results will be available in the near future (Dewailly, pers. comm., 2001).

6.7. Pregnancy outcome

6.7.1. Developmental anomalies

Developmental anomalies related to OC burden are discussed in section 6.1.1. There are relatively few reports of possible effects of OCs in humans on abortion, gestational age, and birth weight and length, and in general this issue remains to be elucidated.

6.7.2. Placental biomarkers of *in utero* development

Cytochrome P450 1A1 (CYP1A1) is a phase I biotransformation enzyme expressed in extra-hepatic tissues in humans, and its regulation is mediated by the AhR (Safe and Krishnan, 1995).

Hydroxylation of toxicants by P450s leads to the formation of reactive intermediates that may damage DNA. PCBs were shown to form such reactive intermediates *in vitro* and to form DNA adducts following their bio-activation in hepatic microsomal systems containing high levels of P450s (McLean *et al.*, 1996; Oakley *et al.*, 1996).

CYP1A1 induction and DNA adducts were investigated as possible markers of early biological effects related to OC exposure in Inuit women from Nunavik. CYP1A1-dependent ethoxyresorufin-*O*-deethylase activity (EROD) and DNA adducts were measured in placenta samples obtained from 22 Inuit women from Nunavik. These biomarkers were also measured in 30 women from a Quebec urban center (Sept-Îles) as a reference group. Prenatal OC exposure was determined by measuring these compounds in umbilical cord plasma. Placental EROD activity and the amount of DNA adducts thought to be induced by OC exposure were significantly higher in the Nunavik group than in the reference group. For both biomarkers, smoking was found to be an important confounding factor, but OC exposure was significantly associated with EROD activity and DNA-adduct levels after stratifying for self-declared smoking status. It was concluded that CYP1A1 induction and DNA adducts in placental tissue could constitute useful biomarkers of early effects induced by environmental exposure to OCs (Lagueux *et al.*, 1999).

A second study was conducted to determine whether environmental exposure to PCBs induces placental CYP1A1 in Inuit women. This more recent study was designed to better control the confounding effect of smoking. Cotinine concentration in meconium and Cd concentrations in placenta had previously been validated as markers of prenatal exposure to tobacco smoke (Pereg *et al.*, 2002). Placenta, cord blood, and meconium samples were obtained from 35 Inuit women from Nunavik and 30 women from Sept-Îles (reference population). Efforts were made to sample more smokers in the Sept-Îles population and more non-smokers in the Nunavik population in order to balance the smoker and non-smoker groups. Smoking status was ascertained on the basis of cotinine concentration in the meconium and, when necessary, individuals were re-assigned to the proper smoking category based on this marker. PCB concentrations were measured in cord plasma and EROD was assessed in placenta. Despite the higher PCB exposure of the Inuit population, both groups showed similar EROD activities when the data were stratified according to the smoking status ascertained by the cotinine concentration. In the Nunavik population, EROD activity was correlated with 2,2',4,4',5,5'-hexachlorobiphenyl (CB153) plasma concentration (a marker of exposure to the environmental PCB mixture). However, cotinine concentrations in meconium were also significantly correlated with CB153 plasma concentrations and multivariate analyses failed to demonstrate a significant contribution of PCB exposure to placental CYP1A1 activity when tobacco smoking (as estimated by cotinine concentration in the meconium) was included in the analysis.

In summary, the results from this study do not support the hypothesis that low-level environmental exposure to PCBs induces an increase in CYP1A1 activity in the placenta, and leaves tobacco smoking as the major modulating factor (Pereg *et al.*, 2002).

6.7.3. Birth weight

CYP1A1 was reported to have been induced in the placenta of women who smoked during pregnancy and lower birth weights of newborns were observed for smokers with high placental aryl hydrocarbon hydroxylase (AHH) activity compared to smokers with lower AHH activity (Pelkonen *et al.*, 1979). Placental homogenates from Taiwanese mothers who developed Yu-Cheng disease (and thus had been highly exposed to PCBs and PCDFs; see section 6.8.1.5.) had 100-fold greater CYP1A1-related AHH activity levels than those measured in homogenates from non-exposed mothers (Wong *et al.*, 1985). This enzyme induction was significantly associated with low birth weights (Lucier *et al.*, 1987). A study of Swedish fishermen's wives and 1501 children supported an association between a high consumption of POP-contaminated fish from the Baltic Sea and an increased risk of low birth weight. The women

interviewed from the east- and west coast cohorts ate locally caught fish more than twice as often as their referents. Compared with the regional population, the women in the east coast (Baltic Sea) cohort gave birth to an increased number of infants with low birth weights (< 3000 g), whereas the opposite was seen in the west coast cohort. Infants in the east coast cohort had significantly lower birth weights than infants from the west coast cohort (median 3530 g versus 3610 g, $P < 0.001$) (Rylander *et al.*, 1995). Later studies have strengthened the hypothesized association between exposure to persistent OCs during childhood and adolescence and an increased risk of having an infant with low birth weight (Rylander *et al.*, 1998, 2000). A significant relationship between lower birth weight and PCB accumulation was reported in a study of newborns of mothers who had eaten fish with high PCB contents from Lake Michigan (Fein *et al.*, 1984). However, at background levels of PCBs no correlation between PCB concentration and birth weight has been observed (Rogan *et al.*, 1988).

The association of maternal smoking and blood Hg concentration with birth weight was studied in 1106 live born singletons from Greenland with a gestational period of 37+ weeks (Bjerregaard and Hansen, 1996). Smoking was significantly associated with low birth weight while consumption of marine mammals, and maternal or cord blood Hg concentration were not. In West Greenlanders a weak association was found between Hg and low birth weight. High concentration of Hg and OC substances is suspected to reduce birth weight; however, a positive influence of marine diet on birth weight due to n-3 fatty acids has been reported and may counteract the effect of POPs (Bjerregaard and Hansen, 1996).

6.7.4. Sex ratios

There have been suggestions of alteration in sex ratios following an accidental environmental exposure to dioxin in Seveso (Italy) in 1976. Of 74 births in the most heavily contaminated zone there was an excess of females; 26 males and 48 females were born (Mocarelli *et al.*, 1996). A similar occurrence has been noted for some other high occupational exposures to chemicals, e.g., dibromochloropropane (Safe, 2000). There is evidence from several countries that in the past few decades there has been a small but significant decrease in the male to female sex ratios (Safe, 2000). However, the potential role of male/female sex ratios as an indicator of environmental exposure to hormone-disrupting chemicals is still controversial and awaits further research.

6.8. The neuro-endocrine-immune system

In vertebrate species, the neuro-endocrine-immune system is responsible for many complex, inter-related physiological processes including homeostatic, reproductive and immune functions. There are four main types of hormones: polypeptides, eicosanoids, steroids, and thyroid hormones. The inter-dependency of the neuro-endocrine and immune systems is reflected by the production of hormones, neuropeptides and other neurotransmitters by some immune cells. These hormones play a role in regulation of the immune system, while endocrine and nervous tissues express receptors for many substances produced by the immune system (Marchetti *et al.*, 1995). The major focus of interest in endocrine disruption has been reproduction and sexual differentiation and development, with most attention to effects associated with steroid hormones, and to a much lesser extent, the thyroid hormones.

Gonads primarily produce sex hormones, androgens (male) and estrogens (female), which play vital roles in the control of reproductive functions. The glucocorticoid hormones, such as cortisol, are produced by adrenal glands and have fundamental effects on metabolism, as well as influencing the immune and reproductive systems (Vacchio *et al.*, 1998). Thymulin, a polypeptide hormone, is found mainly in the cortex and medulla of the thymus and is thought to be involved in the education and maturation of the immune system's T-cells. Interference with production of this hormone affects the ability of the thymus to produce mature T-cells. There are thought to be feedback mechanisms linking thymulin to testosterone, estrogen, cortisol and thyroid hormone balance (Marchetti *et al.*, 1995; Marsh and Scanes, 1994).

6.8.1. Immune system functions

The immune system includes a complex network of cells. Tissue cells involve macrophages, mast cells and dendritic cells. The lymphocytes are divided into T- and B-cells, these are subdivided into T-helper cells (Th, CD4) and T-cytotoxic cells (Tc, CD8), plasma cells (CD20) and natural killer cells (NK). The immune system cells communicate via highly regulated interleukine expressions. Macrophages initiate a non-specific immune response by phagoctytoses of allergens and then represent the antigen on their surface for the Th-cells. The Th-cells are then activated and secrete cytokines, which activates other Th-, Tc-, and B-cells. Thus the Th-cells play a central role in the immune system.

The extensive interaction between the immune and nervous systems involves common use of messengers such as neurotransmitters and cytokines (Carpenter *et al.*, 1998).

6.8.1.1. Effects of POPs and metals on the immune system

Dioxins, coplanar PCBs, and PAHs suppress the immune system (Carpenter *et al.*, 1998). Lead, however, affects the immune system differently promoting hypersensitivity, rashes, and auto-immunity. Investigations suggest that the dominance of different populations of Th-lymphocytes is a major factor in an individual's immune responsiveness. Th1-lymphocytes predominate and produce a particular profile of cytokines in individuals with normal immunity, whereas individuals with hyper-immunity (asthma, skin rashes, and auto-immunity) have predominately Th2-lymphocytes producing different cytokines (Carpenter *et al.*, 1998). Environmental exposure to Pb and Hg was shown to alter the balance between the Th1- and Th2-lymphocytes, and contaminant exposure early in life is suspected to cause prolonged abnormalities in immune function. Moreover, children exposed prenatally to DES showed an altered immune function (Carpenter *et al.*, 1998).

Studies have shown that both synthetic and natural estrogens suppress the immune system (Kendall *et al.*, 1992; Osterhaus *et al.*, 1995), and that during pregnancy, the female immune system is naturally suppressed with a decrease in thymulin and an increase in estrogen levels. The presence of estrogen receptors on thymulin producing cells indicates coordination between these two hormones (Kendall *et al.*, 1992). Increased concentration of testosterone has a positive, enhancing effect on the immune system, whereas increase or decrease in thyroid hormones results in negative effects.

6.8.1.2. Effects of POPs on the immune system of laboratory animals

Several OCs elicit immunotoxic effects in laboratory animals and humans, the most potent being substances structurally related to TCDD such as non- and mono-*ortho* chloro-substituted PCBs as well as 2,3,7,8-chloro-substituted PCDD/Fs. In almost all animal species tested, including primates, PCDD/Fs and PCBs produce myelosuppression, immunosuppression, thymic atrophy, and inhibition of immune complement system components (NRC, 1992). Exposure to TCDD during pre- and/or postnatal life results in more severe effects than if the chemical is administered during adult life and in some species it may be a prerequisite for immunosuppression (Hoffman *et al.*, 1986; Vos and Luster, 1989). In fact, available evidence in laboratory animals suggests that the maturation of the immune system is especially vulnerable to the adverse effects of dioxin-like compounds, chlordane, HCB, PAHs and possibly other endocrine-disrupting compounds such as DDT and kepone (Barnett *et al.*, 1987; Holladay and Luster, 1996).

6.8.1.3. Effects of POPs on the immune system of wild mammals

Persistent organic pollutants, such as PCBs and dioxins, can cause a broad range of immunotoxic effects in Arctic wildlife. More comprehensive information on this subject can be found in the AMAP 2002 assessment on POPs in the Arctic (AMAP, 2003c).

Exposure to POPs has been associated with effects on thyroid hormones and even low levels of PCB suppress thyroid hormone in grey seal pups in the (non-Arctic) Baltic Sea (Jenssen *et al.*, 1996). High body levels of PCBs and other OCs have been associated with suppression of the immune system (Reijnders, 1986), and it has been suggested that these compounds may be implicated in mass mortality among sea mammals (e.g., seals, porpoises, dolphins) (Osterhaus *et al.*, 1995) following infection with the phocine distemper virus, morbillivirus. In otters, environmentally exposed to PCBs, a strong negative correlation was observed between vitamin A and PCB concentrations, and a high incidence of infectious diseases was apparent in contaminated animals (Murk *et al.*, 1998).

6.8.1.4. Immunotoxic effects of mercury

Organic and inorganic Hg possess cytotoxic activities for cellular components of the immune system in several species of rodent. MeHg, a form of organic Hg, can alter non-specific defense mechanisms, such as inhibition of NK cell activity in rats and mice. It also decreases the expression of certain activation markers of T-cells (HLA-Dr, IL-2R) (NRC, 1992). Moreover, it has been well demonstrated that MeHg can affect the functions of B-cells and therefore reduce the humoral mediated response (Daum *et al.*, 1993). Exposure to inorganic Hg induces allergies and autoimmune problems in hypersensitive individuals.

6.8.1.5. Effects of POPs on the human fetal and neonatal immune system

Few data exist regarding the potential immunotoxic effects of *in utero* and lactation exposure to PCBs and dioxins/furans. In 1979, a poisoning from ingestion of rice oil contaminated with PCBs and PCDFs occurred in Yu-Cheng, Taiwan. *In utero* exposed children of highly exposed women were shown to have a higher incidence of respiratory symptoms during their first six months of life (Rogan *et al.*, 1988). An increase in the frequency of pulmonary diseases was suspected to result from a generalized immune disorder induced by transplacental or breast milk exposure to dioxin-like compounds, most likely PCDFs (Rogan *et al.*, 1988). In children and young adults accidentally exposed to PCBs and PCDFs ('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 *et al.*, 1981). In addition to a higher frequency of middle-ear diseases among 8- to 14-year old children born to Yu-Cheng mothers (Chao *et al.*, 1997), the investigation of delayed type hypersensitivity responses further indicated that cell-mediated immune system dysfunction was more frequent among patients than controls.

Studies of 207 Dutch infants (105 breast fed and 102 bottle fed) have suggested that background levels of PCB/dioxin exposure were associated with lower monocyte and granulocyte counts at three months of age and thus influence the fetal and neonatal immune system (Weisglas-Kuperus *et al.*, 1995). Follow-up studies of the children showed that perinatal background exposure to PCBs and dioxins persists into childhood and might be associated with a greater susceptibility to infectious diseases such as recurrent middle-ear infections and chicken pox, and a lower prevalence of allergic reactions (Weisglas-Kuperus *et al.*, 2000).

In Nunavik, an epidemiological study investigated whether OC exposure is associated with the incidence of infectious diseases in Inuit infants and with immune system dysfunction. The number of infectious disease episodes in 98 breast-fed and 73 bottle-fed infants was compiled during their first year of life. Concentrations of OCs 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. Otitis media was the most frequent disease with 80% of breast-fed and 81.3% of bottle-fed infants experiencing at least one episode during their first year of life. During the second follow-up period,

the risk of otitis media increased with prenatal exposure to *p,p'*-DDE, 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) increased with 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 immunological parameters. It was concluded that prenatal OC exposure can be a risk factor for acute otitis media in Inuit infants (Dewailly *et al.*, 2000b).

In 1997, an international symposium was held in Bilthoven (the Netherlands) to discuss the most appropriate effect biomarkers of immunotoxicity that could be used in epidemiological studies (Van Loveren *et al.*, 1999). Among the conclusions, one of the stronger statements was to use antibody responses to vaccination with an antigen to which no prior exposure occurred. In the scope of the ongoing cohort study on neurodevelopmental effects of Hg and POPs (Muckle *et al.*, 2001a), an immune component was added in 1998. The immune function biomarkers described in sections 6.8.1.6 to 6.8.1.9. were selected based in part on the conclusions of the Bilthoven symposium report.

6.8.1.6. Antibody response following vaccination

Acquired immunity produces a very specific response to a particular microorganism or other type of challenge. It mainly involves the activation of lymphocytes and production of antibodies. Environmental toxins may affect acquired immunity and a broad evaluation of the competence of the response provides a better picture of their effect. The development of disease represents the ultimate endpoint in evaluation of immune suppression. Antibody response to vaccination is an intermediate marker of the competence of the adaptive immunity to infections. Vaccination programmes include essentially three types of products: killed vaccine (influenza, whole cell pertussis, inactivated polio), protein-conjugated or protein-based vaccine (Hemophilus influenza type b (Hib), diphtheria, tetanus, acellular pertussis vaccine, hepatitis B), and attenuated live virus (measles-mumps-rubella, varicella, and the tuberculosis vaccine BCG). Antibody response to conjugated Hib is of great interest. Hib vaccine is important in Inuit children because, prior to immunization, Hib was the most frequent cause of bacterial meningitis in Inuit children, and was five to ten times more frequent than in Caucasian children (Ward *et al.*, 1986).

To evaluate humoral response to Hib-conjugated vaccine, two threshold values of anti-polyribosylribitol phosphate (anti-PRP), a capsule polysaccharide, have been set. An antibody titer of 0.15 µg/mL is indicative of immediate protection against Hib, whereas a titer greater than 1.0 µg/mL was found to protect for longer terms (Ward *et al.*, 1994). It should be noted that Hib vaccination is administered using two doses and that exposure to the natural antigen is used in Nunavik. It is then important to note precisely when the last dose was given prior to the blood puncture (antibodies measurement) (Raby *et al.*, 1996).

6.8.1.7. Complement system

The complement (C') system plays an important role in natural immunity against infectious agents. It is particularly important in young children for whom the acquired immune system is not yet fully developed. Deficiency of many of the C' components is associated with increased susceptibility to infections, generally of the upper respiratory tract. In a murine model, exposure to OCs increased susceptibility to *Streptococcus pneumoniae* infections, decreased C3 levels and lowered total C' hemolytic activity (White *et al.*, 1986).

6.8.1.8. Effects of POPs on cytokine production by Th1/Th2 cells

High levels of OCs and metal ions in blood and tissues are frequently related to fish intake. Fish and seal oil-supplemented diets (rich in n-3 (also called omega-3) fatty acids) have generally been shown to reduce plasma levels of some cytokines (Bonefeld-Jørgensen *et al.*, 2001b). Most human studies have shown decreased plasma levels or diminished production of IL-1 and TNFα, while n-3 fatty acids increased the production of these cytokines in mice (Blok *et al.*, 1996). Both contaminants and n-3 fatty acids alter the balance between Th1- and Th2-type cytokines, and could impair host resistance to infections. IL-1, IL-2, IL-4, IL-6, TNFα and IFNγ have been repeatedly associated with these changes and need to be measured in Arctic populations consuming seafood products. IFNγ and TNFα are known anti-viral cytokines (Zinkernagel, 1993); IL-4 enhances IgG1 and IgE, but reduces IgM production (Ada, 1993); IL-10 down-regulates Th1-cytokines and inhibits IFNγ production (Fiorentino *et al.*, 1989).

One of the principal limitations of using cytokines is their high variability due to minor (usually non-detected) infections. The extremely high incidence of minor infections in the Arctic strongly limits the use of cytokines in epidemiological studies.

Organochlorine compounds and metal ions can modulate the production of Th1/Th2-type cytokines. Two studies using murine leukocytes exposed to metal ions *in vivo* demonstrated that Hg inhibits the *in vitro* production of IFNα, IFNβ and TNFα by macrophages and induces a dose- and time-dependent increase in IL-1 activity (Ellermann-Eriksen *et al.*, 1994; Zdolsek *et al.*, 1994). High blood levels of IL-4 and IgE and low levels of IFNγ have been observed in animal studies involving treatment with Hg (Heo *et al.*, 1996). In humans, occupational exposure to inorganic Hg did not result in a significant variation of the immune response in terms of *in vitro* production of IL-1 and TNFα, whereas a prolonged low-level exposure decreased TNFα concentrations (Langworth *et al.*, 1993). Along with their effects on Th1/Th2-type cytokines, OCs and metal ions are known to alter B-cell activity and to impair host resistance to several

bacterial and viral infections (Heo *et al.*, 1996). In animals, Hg increased by 100-fold the virus titers following infection with herpes simplex virus 2 (HSV-2) and increased by 2-fold the number of macrophages in the heart of mice infected with myocardial coxsackievirus B3 (CB3) 994 (Ellermann-Eriksen *et al.*, 1994; Ilback *et al.*, 1996). Plasma levels of IFNγ in exposed animals were higher than in infected non-Hg-treated mice. In a recent preliminary *in vitro* human whole blood study of induced release of the inflammatory cytokines IL-1β and TNFα upon incubation with various OC substances, 2,3,7,8-TCDD, toxaphene, and CB180 elicited the potential to increase the level of the two cytokines in plasma (Bonefeld-Jørgensen, pers. comm., 2002).

6.8.1.9. **Vitamin A status**

Vitamin A influences the expression of over 300 genes and thus plays a major role in cellular differentiation, including that of cells related to immune response (Semba, 1994; Sommer and West, 1996). Results from different animal and human studies vary; however, almost all studies revealed that lymphopoiesis and/or maturation of lymphocytes are altered (generally reduced) in connection with vitamin A deficiency (Olson, 1994; Semba *et al.*, 1993; Sommer and West, 1996). Vitamin A deficiency could increase frequency, severity, and duration of infections. Diseases in the lower respiratory compartment were associated with vitamin A deficiency in many cross-sectional clinics and population based studies. Also, otitis media was among the first infections to be associated with vitamin A deficiency in humans (Bloem *et al.*, 1990; Semba, 1994; Sommer and West, 1996).

Vitamin A clinical deficiency has never been documented in Canadian Arctic populations. However, a recent report suggests that the daily vitamin A intake in Nunavik falls below the recommended intake (Blanchet *et al.*, 2000). Alteration of vitamin A homeostasis has been associated with PCB exposure in laboratory animals (Ndayibagira and Spear, 1999). Furthermore, POPs such as OCs have been shown to alter the vitamin A homeostasis in many species, including primates (Zile, 1992). It is thus important to better understand the relationships between vitamin A, OC levels, and infectious disease incidence in Arctic populations.

In a pilot study, retinol concentration was measured in umbilical cord plasma of newborns and the vitamin A status was assessed in four populations. The study included 55 First Nations newborns and 56 Caucasian newborns from the middle and the lower north shore of the St. Lawrence River, 135 Inuit newborns from Arctic Quebec, and 22 newborns from the general population of southern Quebec. Mean retinol concentrations in ng/mL were 175.2, 159.5, 148.2, and 242.8, respectively (Dewailly, pers. comm., 2001). These preliminary results may suggest an inverse relationship between retinol concentrations and the POPs burden. The difficulty of using vitamin A as an effect biomarker of PCB exposure is related to (1) the variability of vitamin A intake among individuals, and (2) non-systematic supplementation programmes in infants.

6.8.2. **Neurological system**

6.8.2.1. **Thyroid hormone disruption and neural development**

Thyroid hormones regulate neuronal proliferation, cell migration and differentiation including control of when differentiation begins and when cell proliferation ends (Hamburgh, 1969).

A number of organic and inorganic compounds cause toxic action in the nervous system such as abnormalities of peripheral sensory or motor nerves, resulting in either abnormal or loss of sensation, or muscle weakness (Carpenter *et al.*, 1998). In 1979 it was shown that Pb at very low concentration can cause a decrease in IQ and behavioral problems in children exposed prenatally and in the early postnatal years. Recent studies have suggested that these actions are irreversible. Moreover, several studies suggest that PCBs may have similar effects, with prenatal exposure resulting in decreased cognitive function and behavior that appears irreversible (reviewed by Carpenter *et al.*, 1998).

Although many theories exist as to how PCBs affect neurodevelopment, the main hypothesis involves PCB impact on thyroid hormone homeostasis (Porterfield and Hendry, 1998).

In addition to direct effects on neurons the thyroid system is important to nervous system function. In adults, the thyroid controls the rate of metabolism and neurological functions (Colorado State University, 2000; DeVito *et al.*, 1999; Oppenheimer *et al.*, 1995). In the developing fetus and neonate, the thyroid is essential to organ (e.g., brain) development, the development of the central nervous system, and cell differentiation and growth (Porterfield, 2000; Rodier, 1994). Congenital hypothyroidism results in minimal brain dysfunction, even if treated after birth (Carpenter *et al.*, 1998). PCBs and dioxins and their hydroxylated metabolites have some similar steric features to the thyroid hormones, which enables these compounds to interfere with normal thyroid function. The mechanisms by which PCBs can affect thyroid hormone function, and so influence development, include increase in thyroid stimulating hormone from the pituitary gland, altered structure and increased weight of the thyroid gland, decrease in thyroid hormone, thyroxine (T4) and triiodothyronine (T3), and blockage of binding of thyroid hormone to transport proteins and thyroid receptors (Carpenter *et al.*, 1998).

6.8.2.2. **Effects of POPs on fetal and neonatal neurological capabilities**

There is mounting evidence that environmental background exposure to PCBs, dioxins and furans is sufficient to affect thyroid homeostasis and neurological capability. Studies of Japanese breast-fed neonates (Nagayama *et al.*, 1998) and Dutch children (Koopman-Esseboom *et al.*, 1994b) have shown that these compounds in maternal milk affect the thyroid hormone status in children. Estimated TEQ was significantly and negatively correlated with the levels of T4 and T3 in the blood of breast-fed babies. A follow-up study of the same group of Dutch children found that exposure to high levels of PCBs and dioxins *in utero* and in maternal milk correlated negatively with the cognitive score of the children (Patandin *et al.*,

1997). This is in accordance with the findings of intellectual impairment of children prenatally exposed to PCBs through their mother's intake of polluted fish from Lake Michigan (Jacobson and Jacobson, 1996). Longnecker *et al.* (2000) did not find a significant association between *in utero* PCB exposure among 160 North Carolina children and serum thyroid measured in umbilical cord sera. Nor did a study of 182 children from the Faroe Islands, where marine food includes pilot whales, find any correlation between intellectual function and PCB levels. Maternal serum, hair, milk and umbilical cord blood were analyzed for contaminants. Levels of essential fatty acids, Se, and thyroid hormones were determined in cord blood. The neurological optimality score of each infant was determined at 2 weeks of age adjusted for gestational age, and predictors were assessed by regression analysis. Thyroid function was found to be normal and not associated with PCB exposure (Steuerwald *et al.*, 2000). However, a mild decrease in neuropsychological test scores for children 7 years of age was correlated with prenatal MeHg exposure deduced from maternal hair (10–20 µg/g) compared to controls (3 µg/g) (Grandjean *et al.*, 1997). A later study by Grandjean *et al.* (2001) reported neurobehavioral deficits associated with MeHg in 7-year old children prenatally exposed to seafood neurotoxicants. This study involved analyses of cord blood from 435 children from a Faroese birth cohort. A possible interaction between PCBs and MeHg was noted in this study (Grandjean *et al.*, 2001). In addition, MeHg neurotoxicity in Amazonian children living downstream from gold mining activities has been reported (Grandjean *et al.*, 1999b). Moreover, a cross-sectional and prospective dataset from the Maastricht Aging Study suggests that exposure to pesticides, but not metals and organic solvents, was associated with increased risk of mild cognitive dysfunction in adults (Bosma *et al.*, 2000). A developmental study involving a cohort of 7000 children carried out in the Seychelles found no clear evidence for consistent adverse effects on six developmental outcomes of pre- and postnatal study exposure to MeHg (Axtell *et al.*, 2000).

In a recent study, involving 171 healthy German mother–infant pairs, the effect of prenatal and perinatal exposure to PCBs (estimated as the sum of CB138, CB153, and CB180) on prospectively measured psychodevelopment in newborn infants at age 7, 18, 30, and 42 months was estimated (Walkowiak *et al.*, 2001). In summary, the findings showed that the PCB concentration in serum samples at 42 months increased markedly with duration of breast feeding, up to five times higher than in the group of non-breastfed children. Moreover, prenatal and postnatal exposure to European background PCB levels (1.22 µg/L serum at age 42 months) was associated with a decrease in mental and motor development up until 42 months of age. In comparison, the mean of the sum of these three congeners in the blood of women of child-bearing age from Greenland is 5.0 µg/L plasma (with a range of 1.55 to 9.4 µg/L, depending on the region, see Table 5·2).

6.8.2.3. **Animal studies**

The finding of intellectual impairment in humans is supported by animal studies on exposure to PCBs (Brouwer *et al.*, 1998; Eriksson and Fredriksson, 1998; Hany *et al.*, 1999; Hussain *et al.*, 2000). In animal experiments, several chemicals such as PCBs, flame retardants, pesticides, phthalates, and dioxins have been shown to have the capacity to lower T4 levels in blood (Brucker-Davis, 1998; Fowles *et al.*, 1994).

6.8.2.4. **Thyroid effect studies of Inuit populations exposed to POPs**

In Nunavik, a cord blood monitoring programme took place between 1993 and 1996. Measurements of thyroid hormones were performed on 466 Inuit newborn umbilical cord blood samples. Free T4, total T3, thyroxine-binding globulin (TBG) and thyroid stimulating hormone (TSH) were measured. Hydroxylated metabolites of PCBs (OH-PCBs) and other phenolic compounds were also measured in a sub-sample (n=10). As expected, birth weight was positively associated with thyroid hormones (T4, TBG). For this reason, further analyses were adjusted on birth weight. After adjustment, TBG and TSH were significantly and negatively associated with PCB congener levels (Dewailly, pers. comm., 2001).

The main mechanism for the transport of thyroid hormones to the brain requires them to pass through the blood brain barrier via a thyroid hormone transport protein called transthyretin (TTR) (Chanoine and Braverman, 1992). Although PCBs show some binding affinity for TTR (Chauhan *et al.*, 2000), OH-PCBs have much higher *in vitro* binding affinities that can be as high as 12 times the binding affinity of the natural ligand, thyroxine (T4) (Brouwer, 1991; Cheek *et al.*, 1999; Lans *et al.*, 1994). Binding to TTR is not limited to OH-PCBs. Other chlorinated phenolic compounds such as pentachlorophenol (PeCP), halogenated phenols, and brominated flame retardants (Meerts *et al.*, 2000; van den Berg, 1990; van den Berg *et al.*, 1991) also have strong affinities for TTR. Recently, PeCP was found to be the dominant phenolic compound determined in Inuit whole blood (Sandau *et al.*, 2000a). Thus, other halogenated phenolic compounds may also be important contaminants in plasma as they have been found to exhibit similar toxicological properties to OH-PCBs (Schuur *et al.*, 1998; van den Berg *et al.*, 1991).

PCBs have previously been measured in umbilical cord plasma; however, few studies have examined levels of hydroxylated metabolites in blood, especially in humans. OH-PCBs have recently been quantified in whole blood of Inuit from northern Quebec, Canada (Sandau *et al.*, 2000a), and Swedish and Latvian fish eaters (Sjodin *et al.*, 2000). One study examined chlorinated phenolic compounds in umbilical cord plasma to determine possible differences among three human populations with different PCB exposures due to cultural differences in dietary habits (Sandau *et al.*, 2002). Retinol and thyroid hormone status (triiodothyronine (T3)), free T4, TSH, and TBG were determined in most samples. An inverse association was found ($r = -0.62$; $P = 0.003$) between log-normalized free T4 and log-normalized total phenolic compounds (sum of PeCP and OH-PCBs). Total chlorinated phenolic compounds were also negatively associated with T3 ($r = -0.48$, $P = 0.03$) (Sandau *et al.*, 2002). The results indicate that PCBs, OH-PCBs and PeCP affect thyroid hormone status.

6.8.2.5. Oxidative stress induced to the nervous system by methylmercury

Methylmercury is a highly toxic environmental neurotoxin that can cause irreparable damage to the central nervous system (Choi, 1989; Clarkson, 1993, 1997). Although the underlying biochemical and molecular mechanisms that lead to impaired cell function and nerve cell degeneration are not well understood, there is abundant evidence supporting the hypothesis that a major mechanism of MeHg neurotoxicity involves an oxidative stress (Sarafian and Verity, 1991; Yee and Choi, 1996). Mercury increases production of reactive oxygen species via deregulation of mitochondrial electron transport as well as through glutathione (GSH) depletion (Lund *et al.*, 1993). The oxidative stress hypothesis is clearly supported by the finding that MeHg neurotoxicity can be inhibited by various anti-oxidants including Se (Park *et al.*, 1996) and N-acetyl-L-cysteine, a precursor of GSH (Ornaghi *et al.*, 1993).

Glutathione peroxidase (GSHPx) and glutathione reductase (GSHRd) activities were measured in blood samples from 142 Inuit from Sallummiu, Canada (Mirault and Dewailly, pers. comm., 2001). Activities of enzymes involved in detoxification of free radicals were measured in order to investigate relationships between Hg, Se and oxidative stress. It was observed that Hg was negatively correlated with GSHRd activity; an NADPH-dependent enzyme that regenerates glutathione from glutathione disulfide. In contrast, plasma Se concentration was positively correlated with GSHPx activity; a selenoenzyme that catalyses the conversion of hydrogen peroxides to water. Hence, Hg exposure may diminish defense mechanisms against oxidative stress by limiting the availability of glutathione, while Se may afford protection by favoring the destruction of hydrogen peroxide (Mirault and Dewailly, pers. comm., 2001).

Biochemical assessment of oxidative stress markers also includes three other indices. Firstly, the ratio of the reduced form of coenzyme Q10 (ubiquinol-10) to the oxidized coenzyme Q10 (ubiquinone-10) in plasma, which is now considered as one of the most reliable and sensitive indices of an oxidative stress *in vivo* (Finckh *et al.*, 1995; Lagendijk *et al.*, 1996; Yamashita and Yamamoto, 1997). In contrast to the total level of coenzyme Q10, which is reported to be associated with multiple factors including gender, age, and cholesterol and triglyceride levels (Kaikkonen *et al.*, 1999), the ubiquinol-10/ubiquinone-10 ratio index is apparently independent of these variables and thus represents the oxidative stress index of choice. Secondly, an increased level of specific F2-isoprostanes (direct oxidation metabolites of arachidonic acid) in plasma and/or urine is another index recently used to demonstrate oxidative stress in several pathological conditions involving oxygen free-radical formation (Patrono and FitzGerald, 1997; Pratico, 1999). The most easily measurable and frequently used F2-isoprostane species as a marker of oxidative stress *in vivo* is 8-isoprostaglandin F2-α (Patrono and FitzGerald, 1997; Pratico, 1999). Thus the levels of 8-isoprostaglandin F2-α in plasma samples will be measured. Finally, the level of plasmatic low-density lipoprotein (LDL) oxidation could also be assessed as a potential marker of oxidative stress (Dewailly, pers. comm., 2001).

6.9. Conclusions and unanswered questions

There is increasing evidence of adverse trends in human reproductive health, most notably testicular cancer and female breast cancer, whereas the decrease in sperm counts apparent from some studies is still being discussed. However, causal links between effects and exposure to environmental chemicals have still not been firmly established.

Environmental chemicals have been focused on because of their capacity to interfere with hormone activities and hence their possible relation to trends in hormone related health effects. In wildlife, there is more convincing evidence of links between environmental exposure and endocrine disruption. This strengthens the concerns about endocrine modulation by environmental chemicals in humans. Because the developing fetus is particularly susceptible to exposure to environmental chemicals, and because there are many different effect targets, evaluation in terms of both lifetime effects (generations) and effects on organs (time to dysfunction) is complicated. Much research and monitoring are still required, and there is a need to develop, refine, and validate test methods that can accurately predict the effects of chemicals on human health.

In this context, risk assessment must include interaction between chemicals, because in general humans are exposed to chemical mixtures. Finally, and most importantly, is the question of whether the available evidence is strong enough to warrant regulation of the chemicals concerned: Which test methods should be included for the definition of an endocrine disrupter? Is demonstrating detrimental effects in wildlife sufficient to require regulation of a chemical? International controversy will continue until commonly accepted grounds for regulation of potential hormone-disturbing chemicals are established.

After reviewing what has been done, and what is possible and desirable to do in order to obtain a better assessment of the human health impact related to the contamination of the Arctic food web, implementation of a circumpolar biomarker monitoring and research programme (based on Table 6·1) has been recommended by the AMAP Human Health Expert Group. This set of biomarkers will produce the information necessary to complement and support the determination of causality in relationships found in epidemiological studies. Some of the included biomarkers are also likely to be used in the future to improve risk assessments and to establish guidelines which, at present, are still largely based on experimental studies conducted on laboratory animals. Finally, such a programme will effectively meet AMAP requirements for monitoring human health impacts of contamination in the Arctic.

At the same time, it is important to be aware that the use of biomarkers of effects presents new and difficult challenges in relation to the communication of results to local people. The concept of biomarkers is usually difficult to understand for the lay people, and results can be hard to describe and communicate in an unambiguous manner. The fact that biomarkers are indices of subtle deleterious effects, with variable sensitivity and specificity to disease, makes their interpretation even more difficult. An analogy with the effects of alcohol con-

sumption over time might be useful in helping to illustrate the role that biomarkers of effects can play in describing the development of health impacts (i.e., the sequence from alcohol intake, liver enzyme increases, to development of cirrhosis).

There are still major gaps and deficiencies in our understanding of health effects of food chain contaminants in the Arctic. Some of these are highlighted as follows.

Exposure during the developmental period is important because it represents the most sensitive period for several health effects. However, other critical life stages such as puberty and aging can be highly relevant for effects on reproduction, the immune system, or the nervous system.

Efforts should be made to relate molecular or biological markers to adverse health endpoints at the individual and population level. Biomarkers of effect should be integrated in epidemiological studies in order to fill knowledge gaps between exposure and overt clinical effects.

Although receptor-based assays can be very useful, it is imperative to recognize that endocrine disruptive effects can also be mediated through interactions at other levels (e.g., co-activator or repressor levels, enzymes involved in hormone biosynthesis or degradation, etc.). It will be important to design assays that can be directed toward improved understanding of the mechanism(s) involved, further helping in the interpretation of the results and future prevention.

It is important to recognize that genetic variability may affect the susceptibility of individuals or populations to the effects of POPs and MeHg.

Studies on environmentally relevant mixtures (at relevant concentrations) are required to investigate possible interactions between components of the mixture.

Understanding the relationship between subtle biological effects and chronic diseases may prove to be the greatest challenge. Many potential mechanisms of action have yet to be discovered and researched.

Chapter 7

Recent Dietary Studies in the Arctic

Bente Deutch

Summary

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, organochlorine (OC) compounds and radionuclides. Dietary surveys have been performed among Arctic populations as part of the AMAP Human Health Programme and as part of independent studies. A very large body of dietary information has been accumulated in Canada over the last twenty years, especially by the Centre for Indigenous Peoples' Nutrition and Environment (CINE).

This chapter focuses mainly on recent AMAP-related dietary studies, in particular where it has been possible to make comparisons between different geographic and ethnic groups. Despite very large variations, the general tendency is clearly that traditional/country food consumption is gradually decreasing as imported foods become more available and culturally acceptable to the Arctic peoples. This is most clearly shown by dietary indicators such as human blood lipid profiles of n-3 and n-6 polyunsaturated fatty acids; the n-3 : n-6 ratio is a strong marker of traditional food intake, mainly indicating the consumption of marine mammals, but also terrestrial fish and game. The high levels of n-3 fatty acids in traditional/country food are thought to provide some protection against cardiovascular disease and diabetes. On the other hand, human blood levels of marine-acquired n-3 fatty acids are strongly associated with levels of persistent organic pollutants (POPs), because the main dietary source of POPs is fat (blubber) from marine animals.

7.1. Positive effects of traditional foods

The traditional food of the Arctic indigenous peoples can be defined as consisting of specific compositions of local products gathered and prepared in certain ways that are thereby meant to fulfill the nutritional and cultural needs of the population group concerned (Kuhnlein and Receveur, 1996). Traditional/country foods include many Arctic animals and plants. Various species of fish are caught, including salmon and trout (*Salmo* spp.), whitefish (*Coregonus* spp.), burbot (*Lota lota*), and Arctic char (*Salvelinus alpinus*). In Arctic coastal communities, marine mammals, including various species of seal, bowhead whales (*Balaena mysticetus*), beluga (*Delphinapterus leucas*), walrus (*Odobenus rosmarus*), sea lion (*Eumetopias jubatus*), and polar bear (*Ursus maritimus*) are a valuable source of food. Both coastal and inland communities fish and hunt terrestrial animals with caribou/reindeer (*Rangifer tarandus*) forming a significant part of the diet. Although caribou/reindeer is the most important terrestrial mammal, moose (*Alces alces*), muskox (*Ovibos moschatus*), brown bear (*U. arctos*), black bear (*U. americanus*), Dall sheep (*Ovis canadensis dalli*), and a number of smaller animals are also caught. Berries, mushrooms, roots, and green plants are also gathered. In addition to their importance as a source of nutrition, traditional foods serve as a focus for cultural and social activities and help to maintain the social bonds within societies through the traditional sharing of the hunt/harvest and feasting together.

The indigenous peoples are well aware of the many benefits of traditional food systems, and as such these form integral parts of their holistic concept of health. Certain benefits are repeatedly emphasized in surveys regarding attitudes toward traditional foods: well-being, health, leisure, closeness to nature, spirituality, sharing, community spirit, pride and self-respect, economy, and the education of children (Van Oostdam *et al.*, 1999; Jensen *et al.*, 1997).

The traditional foods vary from community to community according to the availability of natural resources, climatic conditions and seasonal changes, but are particularly associated with the cultural traditions and associated technological skills which form the identity of the ethnic group concerned (Van Oostdam *et al.*, 1999). In Canada for example, Dene/Métis food is quite distinct from Inuit food, but both are generally referred to as 'country food' as opposed to 'market food' or imported food.

In Greenland, the traditional Inuit food 'Kalaalimernit' literally means 'little pieces of Greenlanders' as opposed to imported food 'Qallunaamernit' meaning 'little pieces of Danes'. Thus the traditional food of the Inuit is considered necessary as building blocks for a human being and as necessary for providing health, bodily warmth (to withstand the cold climate), strength and well-being in a way that imported food cannot.

7.1.1. General changes in food consumption in the various Arctic populations

Despite their awareness of the benefits of traditional food, during the last 50 years the energy content of the diet of indigenous peoples in most Arctic communities has increasingly been met by imported food products. For Baffin Island Inuit, market food now accounts for approximately 62% of the diet; for Sahtu Dene/Métis in the northwestern Canadian Arctic it is about 70%; in Fort Resolution in the North West Territories (NWT) 90% (Kim *et al.*, 1998); and for Greenland Inuit 75% to 80% (Pars, 2000). The percentage range is very large and in all cases dependent on location, road access, infrastructure, season, gender, and age group (Jensen *et al.*, 1997; Kim *et al.*, 1998; Kuhnlein, 1995; Kuhnlein *et al.*, 1995a,b, 1996; Kuhnlein and Receveur, 1996; Pars, 2000). The change can best be illustrated by examining the differences in intake of traditional food between

older and younger generations. Three generations of adult women from Nuxalk, British Columbia, were interviewed about present and retrospective food use. Although outside the Arctic, their experience illustrates the steady decline throughout the twentieth century in the use of traditional plant food, such as berries, roots and greens, as well as a decline in the use of wildlife by indigenous peoples. The reasons given were the introduction of fishing- and game Acts, and their associated restrictions, better availability of market food, and increasing employment leaving less time for the traditional but time-consuming harvesting and hunting.

A 24-hour dietary recall survey of three generations of Baffin Island Inuit showed that traditional food accounted for an average of 30% to 40% of the daily energy intake, but was much less among younger people than older people. Among Baffin Island Inuit and NWT-Dene/Métis the average traditional food consumption varied from 200–300 g/day among the 13 to19 year age group, to 600–700 g/day among the 41 to 60 year age group (Kuhnlein *et al.*, 1996). As caribou is the main source of radiocaesium, whole body measurements of radiocaesium may be used to indicate caribou intake. Such a study on adults from the Baker Lake Area, NWT, indicated that caribou consumption had decreased from >250 g/day in 1967 to <70 g/day in 1989 (Jensen *et al.*, 1997).

Consumption of traditional Inuit food in Greenland (reported as monthly meals of seal, whale, wildfowl, and local fish) ranged from 20 meals/month among the 18 to 24 year age group to more than 40 meals/month among people over 60 years old (Bjerregaard *et al.*, 1997).

The same association between age and the intake of traditional foods was thus found in Canada and Greenland. Men generally consume traditional food more frequently than do women.

A decrease in the consumption of traditional food in the Russian Arctic, especially of reindeer meat, is less evident, despite the fact that since 1992 the quantity of market food transported to rural settlements and towns has increased considerably (Klopov, pers. comm., 2001). The continuing emphasis on traditional food relative to market food reflects tradition, low income, and the high price of imported foods. Consumption of reindeer meat by the indigenous peoples of the Taymir Peninsula is still about 400 g/day (Klopov, pers. comm., 2001). The non-indigenous peoples of Arctic Russia also eat local reindeer meat; approximately 80 to 200 g/day. The main reason for the majority of residents in the remote Russian Arctic relying on subsistence food, hunting, and fishing, is economic (Klopov, pers. comm., 2001).

7.2. Recent and ongoing dietary surveys in Arctic populations

7.2.1. Alaska

In 1987/1988, eleven indigenous communities in Alaska participated in a study of dietary intake. The study evaluated the nutritional contributions of various food items and listed some of the important sources of nutrition in traditional and imported foods (Egeland *et al.*, 1998a). More recently nutritional intake in a small number of Siberian Yupik in Alaska (29 men, 35 women) was investigated using a 91-item food frequency questionnaire (FFQ) (Nobman *et al.*, 1999). Marine mammal and fish intake, milk, syrup and pizza, and 27 different nutrients were correlated with cardiovascular risk indicators, such as the ratio between low density lipoprotein cholesterol (LDL-cholesterol) and high density lipoprotein cholesterol (HDL-cholesterol). Multiple linear regression analysis indicated a complicated situation in which the foods and nutrients that were significantly associated with LDL:HDL varied according to gender and age group.

The AMAP Human Health Monitoring Programme includes the Alaska Native cord blood monitoring programme. This aims to sample 20 to 25% of the pregnant women in the Arctic coastal and Bering Sea populations each year and will include dietary assessments, analysis of blood for POPs, heavy metals, and selenium (Se), and maternal urine analysis for radionuclides (AMAP, 2000).

7.2.2. Canada

Dietary assessments have been included in several surveys of indigenous peoples in Canada (Kim *et al.*, 1998; Kuhnlein, 1995; Kuhnlein and Receveur, 1996). Some studies focused directly on the amounts of anthropogenic substances in traditional food items while others presented comprehensive profiles of their nutritional components. Nutritional intakes and their distribution between traditional and market foods were determined for Inuit from the Baffin region based on data collected in 1987/1988 (Kuhnlein *et al.*, 1996). This study found marine mammals to represent 20 to 28% of the total energy intake, terrestrial animals 9%, fish 2%, and market foods 66%. A dietary survey of 16 Dene/Métis communities (Receveur *et al.*, 1997) and Inuit from the Baffin region (Kuhnlein, 1995; Kuhnlein and Receveur, 1996) concluded that their diets were deficient in calcium, vitamin A, and folic acid. Twelve years of data concerning the risks and benefits of food in Nunavik were integrated in the Arctic Environmental Protection Strategy Report (Dewailly, 1998). The report concluded that vitamin A intakes were insufficient due to seasonal variation in food availability; that iron deficiency was common among young women despite an apparently adequate iron intake, and that vitamin C intakes were only 25% of the recommended daily intake. The report also concluded that calcium intakes among Inuit were low, at around 50% of the recommended daily intake.

A recent survey has studied the traditional and market food intake of 426 Nunavik Inuit by 24-hour recall (Blanchet *et al.*, 2000). Habitual food intake over a year was studied in 246 women using an FFQ. Energy and nutritional profiles (only 10 different nutrients were considered) were calculated and the relative contributions of traditional and market foods were determined. Traditional food was identified as an important source of vitamin D, iron, Se, and phosphorus, and was the major source of the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Vitamin A and calcium were low in these diets. Market food was an important supplement for carbohydrates, and several other nutrients, such as vitamin A, calcium, and magnesium. The situation for vitamin C was not reported. In the same survey, the intake of fatty acids, plasma phospholipid fatty acids and cardiovascular risk indicators were

measured and compared between sexes and two age groups (below and above 40 years old) (Dewailly *et al.*, 2001b). Men and women over 40 years old had a significantly higher intake of traditional foods and n-3 fatty acids than either men or women under 40 years old, corresponding to a higher relative concentration of EPA and DHA in plasma phospholipids. No correlation studies were reported between intake of fatty acids and their levels in blood.

Canada is currently implementing the AMAP Phase II Human Health Programme. Maternal blood contaminant monitoring has been completed or is underway in the Baffin, Kitikmeot, Kivalliq and Inuvik regions, and the results to date are reported in section 5.2.1.1. Dietary surveys have been completed in nineteen Inuit communities and the data are currently being analyzed (AMAP, 2000).

7.2.3. Greenland

The use of traditional food in Greenland has been examined in a countrywide study (n=1500) in which the results of different dietary survey methods (FFQs and semi-quantitative food frequency questionnaires; SQFFQs) were compared with the results of 48-hour and 24-hour recall (Pars, 2000). Within this wider investigation, a more in-depth study was carried out focusing on Disko Bay, with a sample size of 250 persons (Pars, 2000). To date, the information on intake of traditional food items (i.e., frequency and amount or weight) has been analyzed for different gender and age groups. As in most Arctic communities, the relative and absolute intake of traditional food increased with age and was higher in settlements than in towns. The AMAP Human Health Programme includes a small, 10-item, purely qualitative FFQ; the responses to which supported the general pattern of traditional food intake (Deutch, 1999, Deutch and Hansen, 2000). There was a reasonably good correlation between consumption of marine foods and blood mercury (Hg) levels (Pearson's bivariate correlation coefficient 0.417, $P < 0.001$) and between marine food and n-3 fatty acids in plasma (0.42, $P < 0.001$) or erythrocytes (0.39, $P < 0.001$). In 1999/2000, more detailed dietary surveys were carried out in relation to the AMAP Human Health Effects Monitoring Programme. These included a 24-hour recall survey for 48 men from Uummannaq and an SQFFQ for 50 men and 50 women from Scoresbysund (Ittoqqortoormiit) and Ammassalik (Tassiilaq) (Deutch, in prep.).

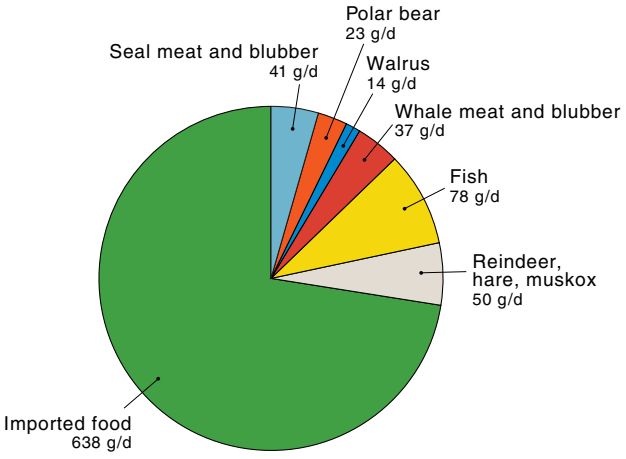

Figure 7·1. Estimated daily intake of traditional and imported foods in East Greenland in 2001 by semi-quantitative food frequency questionnaire (n=180).

Figure 7·1 illustrates the distribution of traditional and imported food intake in East Greenland and represents the outcome of a survey of 180 people (50 men and 40 women from both Tassiilaq and Ittoqqortoormiit). Traditional food represents 27% of the total solids intake, and is slightly but not significantly higher in Ittoqqortoormiit than in the more southern Tassiilaq. The intake of polar bear was higher in Ittoqqortoormiit, while fish intake was higher in Tassiilaq, which also had a more varied diet in terms of imported fruit and vegetables (Deutch, in prep.). There is currently no documented record of the dietary nutritional intake profile for the Greenland population. The data on which Figure 7·1 is based could be used to calculate nutritional intakes, however this has not been done to date.

Table 7·1. Dietary nutrient intake of pregnant women in the Faroe Islands and Finnish Lapland compared to the Nordic Nutrient Recommendations for pregnant women.

	Faroe Islands[1]	Finnish Lapland[2]	Nordic Nutrient Recommendations[3]
Sample size	150	127	
Total energy (kJ)	10200	7500	
Protein (E%)	14.7	16.3	15
Lipid (E%)	33	36	30
Carbohydrate (E%)	52	47.6	55–60
Saturated fat (E%)		16.2	10
Monounsaturated fat (E%)		11.1	10
Polyunsaturated fat (E%)		4.6	>3
Fiber (g/day)		19	
Retinol (equivalents/day)		878	800
Folic acid (µg/day)		260	400
Vitamin C (mg/day)		114	70
Vitamin D (ig/day)		3.7	10
Vitamin E (mg/day)		7.4	10
Calcium (mg/day)		1170	900
Fe (mg/day)		10 + suppl.	10[4]
Zn (mg/day)		11.5	9
Se (mg/day)		68	55
Sum of n-3 fatty acids (E%)			0.5

E%: percentage of total energy intake.
[1]Weihe (pers. comm., 2002); [2]Mussalo and Soininen (pers. comm., 2002); [3]Nordisk Ministerråd (1996).
[4]Supplement recommended.

7.2.4. Faroe Islands and Iceland

An FFQ study of the adult population in the Faroe Islands showed an average daily consumption of 72 g fish, 12 g whale muscle, and 7 g blubber (Weihe *et al.*, 2000). A detailed dietary survey by FFQ and 24-hour recall was undertaken in 2001 for 150 pregnant women in accordance with the AMAP Human Health Effects Monitoring Programme. Table 7·1 shows a provisional calculation of mean nutritional intake values, for macronutrients only, based on three interviews, 24-hour recall, six food diaries per person, and using the Dankost Nutrient database (Weihe, pers. comm., 2002). The data are presented together with data for pregnant women in Finnish Lapland obtained by a comparable method (a food diary, and by using the Nutrica Nutrient database).

No recent dietary surveys have been reported for Iceland.

7.2.5. Northern Scandinavian Saami

7.2.5.1. Sweden

In 1987, food and nutritional intake were examined in a Swedish population (indigenous and non-indigenous) by repeated 24-hour recalls. The Saami had a high intake of protein and fat and a low intake of carbohydrates. Reindeer-breeding Saami had a lower than recommended intake of vitamin C (Becker, 1995). In 1990, the nutritional intake of a group of Saami was compared to that of the local Swedish population. The Saami carbohydrate intake had increased and had become more like that of the non-indigenous Swedish population, while their intake of certain minerals (Fe, zinc (Zn), and Se) and vitamin B-12 was also higher (Håglin, 1988, 1991).

7.2.5.2. Norway

In 1999, the dietary pattern of a group of Saami living in northern Norway (n=75) was compared to that of other Norwegians by dietary history interview. Their nutritional profiles were determined and the contributions made by various food items were calculated. The findings indicated that their diet was generally adequate except for folic acid for which their intake was too low. Calcium and iron intakes were slightly below recommendations for females. The diet of the Saami group was found to be changing towards a more typical Norwegian diet (Nilsen *et al.*, 1999). Reindeer accounted for 7% of their total energy intake, relative to 1.5% for the typical Norwegian diet; their intake of lean plus fatty fish was almost the same, representing approximately 12% of energy intake.

7.2.5.3. Finland

The Finnish National Public Health Institute has monitored adult health behavior (including dietary habits) since 1978 using annual postal surveys of 5000 persons. Since 1999, data have been gathered to investigate the variability in health characteristics between Finnish provinces (Nummela *et al.*, 2000). The surveys indicate that women in Lapland eat less bread than elsewhere in Finland, and that they prefer lighter food alternatives on bread. Also, that men in Lapland drink more fatty milk, and that both sexes eat fresh vegetables less often than in other parts of Finland. Healthy dietary habits were rarer in Lapland than elsewhere in Finland. Absence of teeth was common, perhaps because dental visits were rare.

During the period 1996 to 1998, as a part of the AMAP Phase I follow-up, 147 pregnant women from seven communities in the most northern and northeastern parts of Finnish Lapland completed a questionnaire concerning information on age, occupation, lifestyle, hobbies, parity, miscarriages, illnesses, use of medicines, and diet. These women completed an FFQ during their third trimester and 124 also kept a 7-day food diary. The nutritional intakes of these women were calculated using the Nutrica nutrient calculating program from the Finnish Social Insurance Institute. Mean nutritional intake values are shown in Table 7·1 and trace element and heavy metal intakes are shown in Table 7·2. The macronutrient distribution and the nutritional intakes for pregnant women in Finnish Lapland generally fall within the Nordic Nutrient Recommendations, although intakes for folic acid and vitamins D and E are slightly below recommendations. The results also indicated that dietary Hg intake was correlated with the Hg concentration in maternal whole blood ($r = 0.293$, $P < 0.01$) (Mussalo and Soininen, pers. comm., 2001).

Table 7·2. Estimated intake of trace elements and heavy metals by pregnant women in Finnish Lapland. Mussalo and Soininen (pers. comm., 2002).

	Finland[1]	
	mean	min – max
Iron, Fe (mg/day)	10.06	4.9 – 19.0
Manganese, Mn (mg/day)	4.92	1.8 – 10.4
Zinc, Zn (mg/day)	11.45	5.8 – 20.3
Copper, Cu (µg/day)	1187.31	598.7 – 2206.9
Cobalt, Co (µg/day)	13.36	6.6 – 31.9
Nickel, Ni (µg/day)	121.72	39.1 – 357.3
Chromium, Cr (µg/day)	23.5	9.0 – 59.1
Fluorine, F (µg/day)	385.77	173.6 – 777.2
Iodine, I (µg/day)	210.09	94.2 – 413.5
Selenium, Se (µg/day)	68.18	34.4 – 123.7
Arsenic, As (µg/day)	28.71	9.2 – 221.7
Aluminium, Al (mg/day)	4.29	2.3 – 7.8
Mercury, Hg (µg/day)	3.65	0.9 – 16.4
Cadmium, Cd (µg/day)	10.38	4.5 – 19.1
Lead, Pb (µg/day)	48.25	20.4 – 118.3

[1]sample size = 127.

In general there was very good agreement between the two methods used (i.e., FFQs and food diaries) so only food diary results are reported here. Protein accounted for 16.3% of the total energy intake and was higher than the recommended intake in Finland (i.e., 10–15%). Fat accounted for 36.0% of the total energy intake and was slightly higher than recommended (i.e., about 30%). Saturated fat accounted for 16.2% of the total energy intake and was considerably higher than the recommended intake of 10% in Finland. Essential polyunsaturated fatty acids accounted for 4.6% of the total energy intake, which is less than the recommended 5% for pregnant women in Finland (Finnish national recommendation), but more than the 3% Nordic Nutrient Recommendation. The energy intake from carbohydrates (47%) was also below the Finnish recommended level (55–60%). The estimated mean fiber intake was 19.3 g/day, which is below the minimum recommended intake (25–35 g/day), and 80% of the pregnant women had a fiber intake below the recommended minimum of 25 g/day. Reported alcohol use was very low, at below 1% of total energy intake.

The mean intakes of vitamins D and E, thiamin and folic acid were below recommended levels in Finland for pregnant women. Iron intake from the diet was 10.1 mg/day, which is below the recommendation for women (12–18 mg/day), but 40% of the women increased their intake using iron supplements. Relative to the values used by the Nutrica nutrient calculating program, the mean intake of heavy metals (Hg, lead (Pb) and cadmium (Cd)) among the pregnant women in the study were low, whereas the mean intakes of Zn, copper (Cu) and Se were above the requirement levels.

7.2.6. **Russia**

As part of a mother–infant study undertaken during AMAP Phase I, FFQs were used to obtain dietary information from obstetric patients in northern Siberia, including non-indigenous mothers (Norilsk, n=49; Salekhard, n=31; Dudinka, n=27) and indigenous mothers (Taymir, n=18; Yamal, n=12). For rural indigenous mothers the intake of reindeer meat was 320 g/day; ten times higher than for non-indigenous mothers in towns. Also, their fish intake was double and game intake 3 to 5 times higher (Klopov, pers. comm., 2000). In contrast to the situation in other Arctic populations, the blood levels of anthropogenic contaminants were lower among indigenous than non-indigenous mothers (Klopov, 1998; Klopov *et al.*, 1998; see also section 5.2.1.4.).

A more general dietary survey based on indigenous and non-indigenous men and women from the Taymir Peninsula, the rural areas of Khatangskiy and Ustj-Yeniseyskiy, and the towns of Dudinka and Norilsk (Klopov, pers. comm., 2001), confirmed the outcome of the study on the obstetric patients.

The results for the Ustj-Yeniseyskiy and Dudinka districts (Table 7·3) illustrate the differences between indigenous and non-indigenous peoples versus the trend between country and town. Indigenous populations in rural Ustj-Yeniseyskiy consume more reindeer and game and less vegetables and imported meat than the non-indigenous populations. This difference is also found in the more urban area of Dudinka. At the same time the rural populations consume more traditional food, especially reindeer, than the urban populations. In addition to the items listed both indigenous and non-indigenous peoples consume equal amounts, 40 to 50 g/day, of local 'treated' meat and 380 to 400 g/day of imported bread. The total food intake was lower in the urban population than in the rural areas, probably reflecting different levels of physical activity.

In a study of dietary habits among indigenous school children in 1997 the nutritional intake and energy values were calculated for children in boarding schools in the Taymir Peninsula (Volotchanka, n=63; Dudinka, n=155; Khatanga, n=130; and Norilsk, non-indigenous, n=360). The total energy intake, and the protein, iron, and Zn intakes were sufficient but the calcium, vitamin C, and iodine intakes were below recommended levels (Panin and Kiseleva, 1997).

Further health and dietary surveys were undertaken in Russia in 2001 as part of an ongoing project on 'Persistent Toxic Substances (PTS) and Food Security of Indigenous Peoples of the Russian North'.

7.3. Changes in dietary habits

7.3.1. Impact of changes in food consumption on other lifestyle factors

The hunting, gathering, production, and preparation of traditional food uses local knowledge and skills and can serve as a full-time occupation. A successful hunt or harvest brings respect from others and increases self-esteem (Van Oostdam *et al.*, 1999).

These activities also result in many types of natural physical activity and lead to the construction of tools, weapons, and traps; and the manufacture of specialized clothes for hunting. They also provide opportunities for the learning, development, and teaching of associated skills. The catch must also be transported and processed and the animal products shared. Because these activities require hard physical exercise that occurs outdoors at low temperatures, energy requirements are very high. As a local product economy is gradually replaced by wage earning in a market economy the strenuous physical activities associated with a subsistence diet are replaced by the considerably less energy consuming tasks of picking up food items at the local markets or supermarkets. Thus, the energy requirements of the population will in general decrease.

In 1936 the diet of a young male Inuit hunter in Ammassalik, Greenland was analyzed over a six-day period. The food intake averaged 2300 g traditional food per day, with the food comprising almost exclusively meat and fish and with an estimated energy content of 16 000 kJ/day (Hansen *et al.*, 1997). In 1994 to 1996, the average energy intake for 180 men in Disko Bay was estimated at 11 000 kJ/day (Pars, 2000). Thus, energy intakes (and requirements) appear to have decreased in Greenland by more than 40% since 1936.

Among the Dene and Métis in Canada a shift away from traditional food toward market food has been characterized by a significant increase in the absolute energy intake (Receveur *et al.*, 1997), which together with a more sedentary lifestyle can lead to obesity.

Traditional foods are often high in protein and very low in carbohydrates. The imported goods are often not sufficiently healthy alternatives to traditional foods, often being higher in fat content, sugar, and other 'empty calories', and low in nutritional value; a transition that has been termed 'cocacolonization', meaning a transition to a fast-food and soft-drink consuming society. Consequently the transition can lead to obesity and nutritional deficiencies and to increases in chronic diseases such as heart disease, osteoporosis, diabetes and cancer (see also chapter 3).

Table 7·3. Food intake in the Russian Arctic for indigenous (Nenets) and non-indigenous peoples (g/day per person). Source: Klopov, pers. comm., (2001).

	Reindeer	Fish (fresh or treated)	Game	Vegetables	Imported meats	Dairy	Total
Ustj-Yeniseyskiy district							
Indigenous, male, n=77	402	511	50	180	98	118	1798
Indigenous, female, n=91	380	484	45	156	86	113	1694
Non-indigenous, male, n=81	243	417	31	311	157	111	1734
Non-indigenous, female, n=98	210	255	24	270	113	98	1381
Dudinka area							
Indigenous, female, n=64	140	361	44	168	100	100	1228
Non-indigenous, female, n=87	80	217	35	382	215	130	1411

In remote communities in Alaska, Canada and Greenland (Egeland *et al.*, 1998a) the local stores have a limited supply of goods, and these are mainly preserved, canned, or dried foods with few fresh products, such as meat, dairy products, fruit, and vegetables. These foods are also comparatively expensive. Thus the replacement costs of subsidizing subsistence food with imported food may present considerable economic burdens on local indigenous groups in Canada, Alaska (Egeland *et al.*, 1998a), and Greenland (Hansen *et al.*, 1997).

Owing to different sampling and reporting methods, or simply to a lack of data, it is not, at present, possible to make direct comparisons between the prevailing dietary habits in the various Arctic regions and their variability over time, but the overall trend is clear: among all Arctic indigenous groups diets are gradually including more and more imported foods.

7.3.2. Impacts of changes in food consumption on nutritional intake

Traditional food systems have been developed through generations, relying on many different combinations of local products each with their own unique contribution to the integrated nutritional composition of the diet. Under normal circumstances (i.e., with the exception of starvation conditions), traditional diets are nutritionally sufficient to meet a broad range of dietary requirements. During the transition toward greater use of imported foods, specific items diminish in importance or disappear from the diet and are replaced by alternatives with a different nutritional composition. Also, local knowledge and skills associated with collection and preparation of traditional foods diminish and may be lost.

In many Arctic regions fish are caught locally and shared or sold in the local market. When fish are not available locally they are often not substituted in the diet by fish products purchased from supermarkets, since these may be too expensive. Instead, miscellaneous other products are used instead of fish, and thus an important source of calcium, vitamin D and iodine is consumed less often.

In Greenland, iodine intake (measured as µg urine-iodine/g creatinine) has dropped as the degree of imported food intake has increased. In the villages it is still sufficient but in the capital of Nuuk the intake is only 50% of that recommended (Andersen *et al.*, 2000). While iodine intake is normally sufficient among ethnic groups with a high intake of marine food, it may be a problem in ethnic groups that are more reliant on terrestrial foods. In the Yamal-Nenet Autonomous Okrug in northwestern Siberia, iodine deficiency goiter is highly prevalent (Luzina *et al.*, 1998) and iodine intake among boarding school children is below recommended levels.

Iron intake and iron status is considered good among both Dene and Inuit due to the high intake of haem iron from red meat; caribou, moose, beluga, seal, and walrus etc. (Jensen *et al.*, 1997). A recent comparative autopsy study of Greenland Inuit and Danes showed that older Inuit (>50 years old) in particular have a higher hepatic iron index than the Danes (Milman *et al.*, 2000). Trace mineral status, including iron, is also satisfactory in northern Norway, the Kola Peninsula and Arkhangelsk (Odland *et al.*, 1996).

7.3.3. Dietary changes and hygiene

As local knowledge about traditional food preparation diminishes or is lost, different hygiene issues arise concerning the prevention of parasitic diseases and food poisoning due to bacterial toxins.

Some traditional methods of preparing and preserving food by anaerobic fermentation procedures are potentially dangerous because toxin-producing *Clostridium perfringens* and *C. botulinum* grow under the same anaerobic conditions. *C. botulinum* poisonings are, however, very rare.

Many predatory animals, especially bears but also walrus, and some seals, dogs, and foxes, etc., can contain *Trichinella spiralis*. If the meat from these animals is very infected and not cooked for long enough, people eating the meat can acquire trichinosis (Hansen *et al.*, 1997).

Microorganisms associated with mass production have been introduced with imported foods, e.g., *Salmonella* sp., *Campylobacter* sp. and other zoonotic bacteria, and these can cause food-borne infections if proper hygiene procedures are not followed. As an example, Table 7·4 shows diagnosed bacterial food-borne diseases reported by the Danish Food Agency for Greenland in 1996 and Denmark in 1995 (only a small fraction of the total number of cases of diarrhea are usually diagnosed by positive cultivation of pathogens). The much higher incidence of food poisonings in Greenland suggests that the understanding of hygiene issues and the standard of hygiene practices are not appropriate for dealing with imported products.

7.3.4. Risk of imbalance of certain micronutrients in traditional foods

Despite a normally high iron intake among rural Arctic populations in Alaska (Yup'ik Eskimos), high levels of iron deficiency have been observed, and are thought to result from gastrointestinal bleeding caused by *Helicobacter pylori* infections (Yip *et al.*, 1997). Gastric biopsies revealed chronic active gastritis associated with *H. pylori* among 99% of the populations studied.

Table 7·4. Food poisoning and infections in Greenland (1996) and Denmark (1994–1995) diagnosed by positive cultivation of pathogens.

	Bacillus cerus	*Clostridium perfringens*	*Campylobacter* sp.	*Salmonella* sp.	Massive microbial contamination
Greenland, number of persons affected[1]	68	20	62	128	14
Greenland, cases/100000 capita	124	36	112	232	25
Denmark, number of persons affected[2]	18	30	2177	4307	5
Denmark, cases/100000 capita	0.33	0.54	39.6	78.3	0.9

[1]Hansen *et al.* (1997); [2]Danish Food Agency.

A screening for *Helicobacter* antibodies in Greenland showed a prevalence of about 40%, equivalent to that in Canadian Inuit populations (Koch *et al.*, 2000), although possible adverse effects on iron status have not been studied.

Calcium intake is traditionally low among the Inuit, who have a low intake of dairy products (and possible lactose intolerance) and, with the exception of fish bones and skin, their diets comprise few good sources of calcium (Jensen *et al.*, 1997). In this respect it is important to retain the consumption of locally caught fish as opposed to filets from the market. The low calcium intake may favor the uptake of other bivalent metals, such as Pb and Hg.

The Se level in traditional food is very high, with the main sources being muktuk (whale skin), and meat and liver from whales, seals, and seabirds. A dietary survey of 400 adults in Disko Bay (Greenland) in 1995/1996 resulted in an estimated Se intake of >600 µg/day, but the authors considered this an over-estimate (Johansen *et al.*, 2000). An AMAP study from 1997 (Deutch *et al.*, in prep., see section 5.3.1.2.), which included 96 pregnant women from Disko Bay, found an average whole blood Se concentration of 140 µg/L. In a 1986 survey, the range in whole blood Se levels among 95 Qaanaaq Inuit was 320 to 4400 µg/L, with the average concentration over ten times higher than among local Danes (Hansen, 2000). This means that the daily intakes in northern Greenland are substantially higher than the maximum safe daily intake of 500 µg recommended by Yang *et al.* (1989).

Selenium concentrations in reindeer/caribou meat are relatively high at 24 to 30 µg/100 g meat. Thus reindeer/caribou consumers have a reasonable Se intake, at least in Finland (see Table 7·8) (Näyha and Hassi, 1993).

The question of vitamin C intake and requirements among the Inuit are very complex and recommendations for western populations may not be applicable. Because of their high iron status and Se levels, the need for vitamin C as an antioxidant is normally filled and high intakes of the vitamin may even sometimes be harmful. However among young women in Nunavik with a vitamin C intake of only 25% of the recommended daily intake (RDI), iron deficiency anemia was common despite intakes of iron at the recommended level. Vitamin C also enhances the absorption of various other metals, including Hg, from the intestinal tract (Chapman and Chan, 2000).

There are few known sources of vitamin C in Arctic diets and the local supply, which depends on wild berries and plants, seaweed, raw seafood products, and the skin and liver of fish and seals, is seasonal. Historically, therefore, low vitamin C intake has been a matter of concern. However, use of local wild green leafy vegetables, fruits, and seaweed are not sufficiently documented (Kuhnlein and Receveur, 1996), and nutrition tables do not cover all products. In addition, fresh raw meat and fish are consumed by many Arctic groups and all fresh raw products, e.g., reindeer/caribou meat and organ meats, contain some vitamin C (Näyha and Hassi, 1993; Nummela *et al.*, 2000). Thus vitamin C intake is probably underestimated, and scurvy is not usually a problem among indigenous Arctic peoples.

7.3.5. Long-chain fatty acids

For diets in which the food mainly originates from the hunting of wildlife and the gathering of wild plants, dietary composition in terms of fatty acids differs from that of diets based mainly on modern industrially produced foods. In general, the saturated fat content of traditional foods is less, and the n-3 : n-6 polyunsaturated fatty acid ratios are higher. This is particularly the case for marine wildlife in which n-3 fatty acids are biomagnified and/or elongated through the complex food webs from microalgae to zooplankton, invertebrates, fishes, marine mammals and birds. The same is true for terrestrial plants: mosses, lichens, herbs, and berries (Simopolous, 1991); as well as for the secondary producers: hare, deer, caribou/reindeer, muskox, etc. In all cases the fat composition depends on the particular food chain, and food chains can now be manipulated. For example, fish are mostly wild, however fish farming is increasing, and research indicates that farmed fish have lower n-3 : n-6 ratios than the same species living wild. In modern agricultural practice livestock are fed n-6 rich grain instead of grass, and the popular n-6 rich vegetable oils comprise a high percentage of fats, cooking oils, and other industrial products. It has been proposed that humans have evolved on a diet close to the diet of hunters and gatherers and that dietary recommendations should aim at this 'Paleolithic diet'. Thus, in addition to reducing the dietary fat content they should attempt to balance the relative fat content, in particular the n-3 : n-6 ratio. It must be emphasized that DHA (an n-3 fatty acid) is essential for fetal retinal- and neuro-development and that low birth weight, birth length and head circumference are significantly correlated with low levels of maternal and cord plasma arachidonic acid (AA) and DHA (Crawford *et al.*, 1989).

Emphasis on addressing the relative fat content, in particular the n-3:n-6 ratio, rather than focusing entirely on reducing dietary fat content is in accordance with the many beneficial effects of n-3 fatty acids reported in relation to the development of chronic diseases. Nevertheless, susceptibility to chronic diseases such as coronary heart disease, hypertension, and diabetes, is to some extent determined genetically, e.g., through the response to dietary fats, and so different populations should not simply copy each other's dietary recommendations.

Recent reviews of epidemiological and experimental studies (Bjerregaard *et al.*, 2000; Connor and Connor, 1997; Simopolous, 1999) show that the n-3 fatty acids in the marine diet have important biological effects on several pathways leading to atherosclerosis. Experimental studies show that n-3 fatty acids have antithrombotic and antiarrhythmic vascular effects etc., and modify the serum lipid pattern toward that associated with lowered cardiovascular risk, in both the normal population and in coronary heart disease patients, thereby lowering coronary heart disease mortality.

A few studies have analyzed this phenomenon within Arctic populations. During 1993/1994 a random sample of Greenlanders (n=259) participated in a health study (Bjerregaard *et al.*, 1997, 2000). Multiple linear regression analysis showed a significant inverse correlation between several cardiovascular risk factors and plasma n-3 : n-6 ratios, total Hg levels (as a dietary marker), and

seal consumption. The pattern for serum lipids was the same as that for the effects found in intervention studies using fish or seal oil in other populations, namely that n-3 significantly lowered VLDL (very low density lipoprotein) and triglyceride levels, increased HDL levels and had little effect on LDL and total cholesterol levels (Bonefeld-Jørgensen *et al.*, 2001b; Connor and Connor, 1997; Deutch *et al.*, 2000).

The diet of Yup'ik living in southwestern Alaska is based on fish and marine mammals and their EPA:AA plasma ratios are 9 to 14 times higher than in non-indigenous Alaskan adults (Ebbeson *et al.*, 1999). Based on the outcome of an FFQ for Siberian Yupik in Alaska (n=64), dietary nutritional intakes were correlated with cardiovascular risk factors. The HDL levels were higher and the triglyceride levels lower than in the general North American Caucasian population (Nobman *et al.*, 1999), however, within the population sample studied, beneficial effects of n-3 could not be demonstrated. Adipose fat and plasma lipid profiles of polyunsaturated fatty acids indicate that the diets of Alaskan Natives are already more 'Americanized', with considerably lower n-3 levels than the Inuit population of Greenland (Deutch *et al.*, 2000; Ebbeson *et al.*, 1999; Pedersen, 2000). Their diets are basically similar to those of north Europeans (Danes) and non-indigenous Canadians (see Tables 7·5 and 7·6).

Prevalence of diabetes was relatively low among the Alaskan Yup'ik and Canadian NWT/Nunavut Inuit compared to other Natives in North America (Young *et al.*, 1992). This could be explained by lower fasting insulin and lower insulin resistance. However, the prevalence of diabetes has increased over the last 30 years (see chapter 3). Insulin resistance increases with increasing obesity (Schraer *et al.*, 1998). The reasons for the rapidly increasing prevalence of non-insulin demanding diabetes mellitus and impaired glucose tolerance among Alaskan Yup'ik is only partly understood, but there is some evidence to suggest that they are associated with a lower intake of fish and marine mammals, lower plasma n-3 levels and higher levels of saturated fat (Ebbeson *et al.*, 1999). In the Greenland health study, fasting blood glucose was significantly correlated with the plasma n-3:n-6 ratio and the intake of seal (Bjerregaard *et al.*, 2000). While n-3 polyunsaturated fatty acids may protect against thrombogenesis and diabetes, very high levels (as occur in Greenlanders) may be a risk factor for hemorrhagic strokes (Pedersen *et al.*, 1999). Canadian standardized mortality statistics indicate 70 and 34 deaths per 100 000 person-years due to cerebrovascular events among Nunavik Inuit and Quebec citizens, respectively, and 96 and 246 deaths per 100 000 person-years, respectively, due to ischemic heart disease plus myocardial infarction (Dewailly, 1998). Thus the benefits of an n-3 rich diet appear to be greater than the risks, but this may depend on the level of n-3 intake. The incidences of diabetes and cardiovascular disease in northern areas are confounded by other dietary factors, drinking water composition, lifestyle, latitude/climate, and genetics; and thorough consideration of all these factors is a vast area of research, beyond the scope of this report.

Although single food items have been analyzed for fatty acid content (Kuhnlein *et al.*, 1991), for most Arctic populations there are no studies providing comprehensive information about the total dietary content of n-3 and n-6 fatty acids except for Canadian Sahtu Dene/Métis (Kuhnlein, 1997; Kuhnlein *et al.*, 1995b).

Several studies have indicated that adipose fat and blood levels of fatty acids are good biomarkers of the dietary polyunsaturated fatty acids and good indicators of the intake of marine mammals and fish (correlation coefficients: 0.4–0.5) (Andersen *et al.*, 1999; Marckman *et al.*, 1995; Willet, 1998). Adipose tissue polyunsaturated fatty acids show good correlation with long-term dietary intake. Plasma fatty acids occur in different lipid fractions and with different half-lives; total plasma fatty

Table 7·5. Polyunsaturated fatty acid profiles for subcutaneous adipose tissue from recent population studies. Fatty acids are expressed as a percentage of total lipid content.

	18:2, n-6 linoleic acid	20:4, n-6 AA	20:5, n-3 EPA	22:6, n-3 DHA	Σ n-3 fatty acids	Σ n-6 fatty acids	n-3:n-6 ratio
Greenland[1], n=99	7.57	0.14	0.2	0.56	1.74	7.71	0.23
Denmark[2], n=77	11.88	0.3	0.06	0.16	1.18	12.7	0.09
Alaskan natives [1], n=129	12.27	0.16	0.11	0.3	1.28	12.5	0.10
Alaskan non-natives[1], n=115	13.06	0.2	0.05	0.13	0.95	13.3	0.07

[1]Pedersen (1999); [2]Deutch *et al.* (2000a).

Table 7·6. Polyunsaturated fatty acid profiles for blood lipids (phospholipids) from recent population studies. Fatty acids are expressed as a percentage of total lipid content.

	18:2, n-6 linoleic acid	20:4, n-6 AA	20:5, n-3 EPA	22:6, n-3 DHA	Σ n-3 fatty acids	Σ n-6 fatty acids	n-3:n-6 ratio
Inuit, Nuuk[1], n=15	14	5.24	4.9	7.89	14.6	21.4	0.68
Inuit, Uummanaq[2], n=48	14.2	4.68	5.5	5.89	13.4	21.5	0.62
Alaska, Yup'iks[3], n=436	24.8	5.4	5.05	4.3	15.3	36.4	0.42
Inuit, Canada[4], n=426	19	6.22	3.01	4.95	9.7	28.4	0.34
Indigenous, Koryaks, Russia[5,6], n=74	28.6	6.13	0.98	1.92	3.7	36.2	0.10
Indigenous, Koryaks, Russia[3,7], n=57	23.6	3.32	4.67	3.24	9	28.3	0.32
Denmark[8], n=42	29.9	6.3	0.82	2.53	4.5	36.2	0.13
Canada (general population), n=16	18.4	10	1.3	4.23	6.9	32.7	0.21

[1]Stark *et al.* (1999); [2]Deutch *et al.* (2002); [3]Ebbeson *et al.* (1999); [4]Dewailly *et al.* (2001b); [5]Klopov, pers. comm. (2001); [6]reindeer breeders; [7]coastal population; [8]Deutch *et al.* (2000a).

acids represent intake within the last few weeks, whereas erythrocyte or phospholipid fatty acids represent intake within the last month or so.

A recent dietary study of 426 Nunavik Inuit (Dewailly *et al.*, 2001b), based on 24-hour recall and using measurements of plasma phospholipid fatty acids and several cardiovascular risk indicators (total-cholesterol, LDL, HDL, and triglycerides), showed that plasma n-3 was negatively correlated with the cholesterol:HDL ratio and with the triglycerides:HDL ratio. These risk factors were low among the study group. Plasma n-3 fatty acids were positively correlated with plasma glucose but there was no significant association with plasma insulin or with diastolic and systolic blood pressure. However, Dewailly *et al.* (2001b) do not report the correlation factors between individual fatty acid intakes, plasma fatty acids, and the various cardiovascular risk factors.

7.3.6. Genetic aspects of metabolism

In addition to reflecting dietary composition, the fatty acid profiles of adipose tissue and blood lipids in Tables 7·5 and 7·6 depend on the ability to elongate and desaturate dietary fatty acids such as linoleic and linolenic acids. Linoleic acid levels are high in almost all types of diet since linoleic acid is ubiquitous. Among Caucasian populations linoleic acid is a major substrate for the formation of the essential fatty acid AA by elongation and desaturation.

Both AA and DHA are essential for the development of the fetal brain and visual function (Innis, 2000), and selective partitioning appears to exist between the developing fetus and its mother, namely a magnification of the two essential fatty acids from maternal to cord blood (see Figure 7·2). Furthermore, within the fetus DHA is selectively partitioned between the liver and brain (Crawford *et al.*, 1989).

The ratio between linoleic acid and AA in plasma phospholipids or erythrocytes is much higher among the Inuit of Chukotka, Alaska, Canada and Greenland, than among Caucasians. This indicates that the desaturation

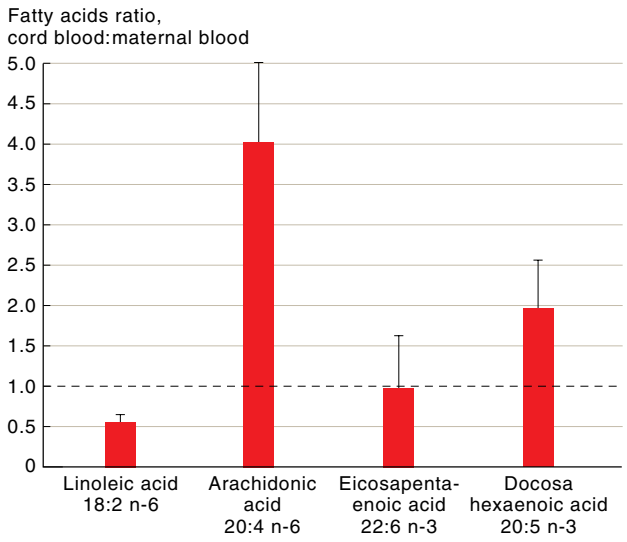

Figure 7·2. Selective partitioning of essential fatty acids from maternal to cord blood. The ratio of essential fatty acids in cord blood: maternal blood is based on 50 mother–infant pairs from the Disko Bay area in 1996 to 1997.

of linoleic acid is not optimal, with possible inhibition of the metabolic pathway regulated by δ-5 and δ-6 desaturases (Young *et al.*, 1999), and that AA is supplied directly by the diet from the same sources which supply EPA. It is thus fortunate that AA is high in traditional diets consisting of mammals and fish (see Table 7·6). This highlights the importance of retaining these diets to supply the essential fatty acids for fetal development.

7.4. Traditional food as a source of anthropogenic substances

It has been known for more than twenty years that a range of anthropogenic substances bioaccumulate and biomagnify in the higher trophic levels with older and more predatory fish, mammals and birds containing the highest concentrations. These animals comprise the bulk of the traditional diet of Inuit and other indigenous peoples of the Arctic. A substantial amount of literature highlights an association between a diet high in traditional food and high body burdens of anthropogenic substances (AMAP, 1998), such as POPs and heavy metals. Epidemiological investigations, especially regarding exposure parameters, are best supported by long-term diet surveys. However, almost all dietary surveys concern present daily intakes using methods such as 24-hour recall or food diaries covering a number of days, although some do attempt to cover longer periods, e.g., for up to a year, through retrospective FFQs. If their purpose is to estimate exposure from persistent OCs or metals then it is generally assumed that present day dietary intakes are the same, or similar to the long-term intake, which may not actually be the case. For example some individuals may have changed their dietary habits in response to contaminant information and also most diets exhibit day-to-day and seasonal variations (Willett, 1998). In Arctic areas, seasonal variations may be more extreme because of the influence of climatic conditions, supply problems, and extent of hunting and gathering seasons. In Greenland, for example, seal consumption is constant throughout the year, but the consumption of other species such as walrus and birds varies seasonally. The same is true for consumption of whales, with baleen whales (e.g., bowhead whale) more commonly taken in the fall and toothed whales (e.g., beluga, narwhal) in the spring (Pars, 2000). Thus associations between reported dietary intakes and human blood levels of contaminants should be accepted with caution unless supported by other techniques such as biomarkers.

7.4.1. Heavy metals

Contaminant databases for wildlife have recently been established for several Arctic areas: Canada (Berti *et al.*, 1998; Chan, 1998; Kim *et al.*, 1998) and Greenland (Dietz *et al.*, 1996; Johansen *et al.*, 2000). Such data may be combined with dietary survey data, concerning relative and absolute intakes of traditional food, to estimate the average habitual intake of heavy metals or other contaminants and to indicate the major sources of intake. Heavy metal concentrations in wildlife products vary widely between species, and for the same species by geographical location (Egeland *et al.*, 1998a), as well as by age, gender and size of the animal, tissue or organs.

In general, fish liver and liver and kidney of large marine and terrestrial mammals contain higher metal concentrations than muscle (meat). Caribou/reindeer and moose liver contains very high concentrations of Pb, Cd, and Hg; seal and toothed whale liver and kidney contain very high concentrations of Cd and Hg (resulting in an 'allowable lifetime weekly intake' (ALWI) of 40 to 140 g of the food source for Cd) (Egeland *et al.*, 1998a). However, most of the Hg in liver is not methylated and has low bioavailability (Egeland *et al.*, 1998a). Thus seal meat and toothed whale meat are the most important sources of Hg. Marine birds and bird liver can be important sources of Pb (Berti *et al.*, 1998; Chan, 1998; Johansen *et al.*, 2000).

Tables (7·7 and 7·8) show estimates of dietary exposure to heavy metals from traditional food for indigenous peoples in Greenland and Canada. These estimates are based on the contribution from traditional food items only and do not include the contribution from market food. Since traditional food represents 20% to 30% of the total energy intake, market food (from Denmark or Canada) adds to the total contaminant burden, most significantly for Pb.

In Greenland, contamination of waterfowl by lead shot is considered the most important single dietary source of Pb. The intake of one murre (*Uria* spp.) boiled in soup could yield as much as 50 µg of Pb (Johansen *et al.*, 2000).

In Finland the nutritional and trace element intakes of 147 pregnant Lappish (Saami) women were estimated by FFQ and a 7-day food diary. The results of the two methods showed good agreement. Table 7·1 shows the food diary results together with comparable data for pregnant women in the Faroe Islands. A Nutrica database was used to estimate daily trace element intakes (see Table 7·2). The estimated weekly mean intakes in Finland were: Pb 337 µg, Cd 73 µg, Hg 26 µg, and Se 476 µg (Mussalo and Soininen, pers. comm., 2002). These are shown in Table 7·8 together with the estimated heavy metal intakes in other Arctic/ Nordic and Canadian populations.

All populations have additional Cd exposure from smoking (Egeland *et al.*, 1998a) and there are particularly high rates of smoking among the Inuit (Bjerregaard *et al.*, 1997).

The total Hg intake of 850 µg estimated for Greenland and Canadian Inuit includes a contribution of about 500 µg from seal and whale liver. However, in fatty tissue such as liver, inorganic Hg makes up than 90% of the total Hg (Egeland *et al.*, 1998a). The bioavailability of inorganic Hg, which is Se-bound, is low and the estimated exposure should be modified accordingly (Hansen, 1990), resulting in an estimate closer to 450 µg. Other dietary components (e.g., calcium, Se and fatty acids) interact with the uptake, metabolism, and probably the toxicity of Hg and *vice versa*. Thus to evaluate the possible health impacts of Hg many factors must be considered (Chapman and Chan, 2000).

Table 7·7. Estimated heavy metal intakes (µg/person/week) from marine food in the Disko Bay region, West Greenland 1995–96 (Johansen *et al.*, 2000).

	Pb	Cd	Hg	Se
Fish meat	1.7	26	24	34
Fish liver	0.5	63	1	75
Seal meat	6.2	62	147	129
Seal liver	2.0	693	507	212
Whale meat	1.7	7	52	36
Whale liver	0.03	7	6	6
Whale skin	0.8	11	60	3833
Bird meat	1.1	34	29	152
Bird liver	0.6	101	20	92
Total	15	1004	846	4569

7.4.2. Persistent organic pollutants

Diet is the main source of human exposure to organic xenobiotic compounds, chemicals foreign to the biosphere, although their transport to the Arctic is mainly via winds and water currents. These lipophilic chemicals accumulate in the fatty tissues of all biota, they accumulate with age due to their slow metabolism, and some are biomagnified in food chains. They are therefore prevalent in large Arctic mammals, especially those at the top of the food chains, and are concentrated in their fatty tissues and organs, such as blubber, liver, brain, and kidney. Almost without exception, OC levels are lower in the terrestrial environment than the marine environment due to the longer food chains and higher fat content of marine mammals and large fish. But birds, especially bird liver, can contain high concentrations of OCs due to their high metabolic rate. Analyses of the OC content in a growing list of wildlife species have been published

Table 7·8. Provisional tolerable weekly intake of heavy metals and the estimated weekly intake of heavy metals from traditional food (µg/week) for a 60 kg person. The data are based on wildlife contaminant databases for Greenland Inuit and Canadian Arctic populations and estimated daily food intakes. The Finnish data are based on a dietary survey and calculated heavy metal data from the Nutrica database.

	Pb	Cd	Hg	Se
PTWI (World Health Organization unless otherwise indicated)	1500	420	200	2800[1] 4000 (Canada) 2400 (United States)
Greenland, Inuit[2]	15	1000	850	4500
Canada, Inuit[2]	470	1000	850	
Canada, Dene/Métis[3,4,5]	< 42	32 (240[6])	42	
Denmark, general population[2]	162	100	35	340
Canada, general population[2]	168	88		
Finland, Saami[7]	337	73	26	476

[1]Yang *et al.* (1989); [2]Johansen *et al.* (2000); [3]Berti *et al.* (1998); [4]Chan (1998); [5]Kim *et al.* (1998); [6]traditional food + market food + smoking; [7]Mussalo and Soininen (pers. comm., 2002).

Table 7·9. Estimated daily intake of OCs by Inuit in towns and villages in south-western Greenland. Estimates based on a semi-quantitative food frequency questionnaire for 410 adults with traditional food intakes (Pars, 2000) and contaminant concentrations in Greenland species (Johansen *et al.*, 2000). Canadian TDI guideline values are given for comparison (Berti *et al.*, 1998).

	Chlordanes	ΣDDT	HCHs	HCB	ΣPCB_{10}
18–24 years, n=50 ng/day	9190	24765	5998	1759	21270
35–59 years, n=175 ng/day	11553	27095	6026	1737	22159
All, n=410 ng/day	9920	23992	5446	1578	19862
All, n=410, µg/kg/day	0.165	0.399	0.09	0.026	0.331
Canadian TDI, µg /kg/day	0.05	20	0.3	0.27	1 (Arochlor) 0.3 ΣPCB_{14}

for Canada (Berti *et al.*, 1998; Kuhnlein and Receveur, 1996) and West Greenland (Johansen *et al.*, 2000). Berti *et al.* (1998) combined a regionally adjusted contaminant database with a nutritional database and dietary survey based on 24-hour recall for 1012 Dene/Métis and compared the 99th percentile values with the present Canadian guideline values. Only chlordane and toxaphene intakes approached the guideline values, with three and five people, respectively, exceeding the guideline values. For the estimated intakes of all other OCs the 99th percentiles are below 20% of the guideline values. Compared with the Inuit, however, the Dene/Métis are not consuming such large quantities of marine foodstuffs.

Johansen (in prep.) presents concentrations of polychlorinated biphenyls (PCBs) and DDT on a 5-decade logarithmic scale, on which the lowest concentrations occur in Arctic hare (*Lepus arcticus*) muscle and liver and the highest in ringed seal (*Phoca hispida*) and minke whale (*Balaenoptera acutorostrata*) blubber. In general, the prevalence of the various OCs in the environment strongly coincides although there may be minor differences from tissue to tissue. The distribution pattern is also similar to that of total Hg.

Table 7·9 shows the estimated dietary POP exposure for a 60 kg person from towns and villages of south western Greenland (Disko Bay). The estimate was derived using:

1. estimated dietary intakes in g/day of 25 different local traditional food items (for which contaminant levels are available) yielding a total intake of 200 g traditional food per day (Pars, 2000); and
2. POP concentrations in Greenland animal species determined by Johansen (in prep.).

Contaminant levels have not been analyzed in reindeer, and have only been determined in one species of saltwater fish from West Greenland (Aarkrog *et al.*, 1997). Also, only one whale species, minke whale, has been included, even though the concentrations of contaminants in toothed whales, e.g., beluga and narwhal (*Monodon monoceros*) are known to be higher (Kuhnlein and Receveur, 1996). Whale blubber was analyzed but not whale meat. The contaminant level in whale meat was estimated for the calculations based on the relative fat content of whale meat and was estimated to be 10% of the content in whale blubber.

The estimated contaminant intakes from the traditional food for Greenland Inuit are slightly lower but of the same order of magnitude as for Baffin Inuit (Kuhnlein, 1995; Kuhnlein and Receveur, 1996), but are higher than for Sahtu Dene/Métis by factors of 10 to 20 (Berti *et al.*, 1998). Traditional food intake in Greenland varies by district and is lower on the southwest coast than on the east and northwest coasts. This is consistent with measured blood levels of POPs in younger men and women from seven districts in Greenland (Deutch and Hansen, 2000; and section 5.2.1.2).

The estimated contributions from various traditional food items to daily β-HCH, total chlordanes, hexachlorobenzene (HCB), ΣPCB_{10}, and DDT exposure are shown in Figure 7·3. These data are based on relatively few species. However, the relative contributions from seal blubber and meat are so predominant that the missing food items can be considered of minor importance.

Seal is the most important source of dietary POP exposure because it is the most common traditional food item and its intake is greater than that of whale products. Traditional food intake in rural communities (30%)

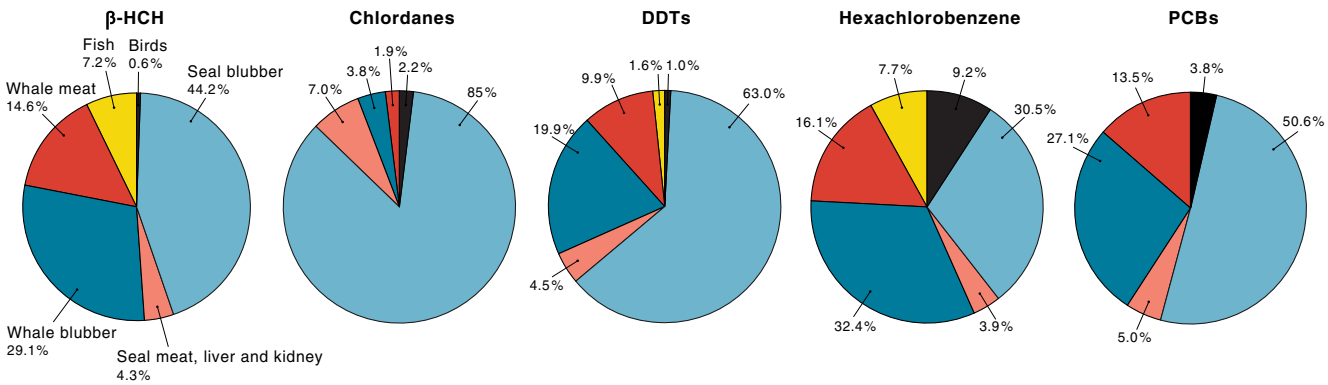

Figure 7·3. The contribution of different traditional foods to dietary exposure to organochlorines in southwestern Greenland. Relative OC contributions from different food groups are based on estimates of daily food intake by Pars (2000) multiplied by contaminant levels reported by Johansen *et al.* (2000). The relative contributions from terrestrial animals are not shown but are below 0.5%.

Table 7·10. Average concentration of OCs (ng/g) in 0–3 year old male ringed seal blubber from four districts in Greenland (AMAP, 1997).

	ΣPCB	ΣDDT	ΣHCH	HCB
Avernarsuaq, NW Greenland	505	4218	1636	116
Qeqertarsuaq, Disko Bay, W Greenland	275	4408	1256	116
Nanortalik, S Greenland	573	7464	1182	141
Ittoqqortoormiit, NE Greenland	706	9649	1805	163

is greater than in towns (19%), especially regarding seal. However, whale intake is higher in towns and accounts for some of the difference in exposure to POPs. Traditional food accounts for 22% of the total energy intake. The remaining 78%, from imported food, also adds to the total contaminant burden (Pars, 2000). This additional contribution has not been measured directly, but based on human blood levels of PCBs and DDT in northern Europe and Canada it is estimated at 25% to 35% (AMAP, 1998). This implies that previous estimates (based on traditional food alone) are too optimistic and should be at least 25% to 35% higher. The mean intakes of chlordanes and PCBs already exceed the Canadian guideline values and the mean β-HCH intakes represent one third. This means that a large proportion of people exceed the guideline intake values as supported by measured blood levels of contaminants from another study (Deutch and Hansen, 2000). Organochlorine concentrations were analyzed in several marine animals from four locations in Greenland, Table 7·10 (Aarkrog *et al.* 1997). The data for ringed seals clearly illustrate the general geographical distribution of pollutants. Blood levels of OCs measured in 1997 in a small geographical survey (Deutch and Hansen, 2000) follow approximately the same pattern. The urban population in southwest Greenland has the lowest pollution burden and Ittoqqortoormiit in the northeast the highest, with >60% of men exceeding the Canadian PCB guideline level for action (100 µg PCB-Arochlor 1260 per liter plasma).

The estimated PCB intake of Inuit in southwestern Greenland exceeds the TDI value (Table 7·9). If seal blubber were the only source of PCB (and compared to the TDI value it is the most critical), the daily intake of ringed seal blubber should not exceed 300 g in Disko Bay or 100 g in Ittoqqortoormiit. However, seal blubber contributes about 50% of the PCB intake, which changes these limits to 150 g and 50 g respectively. In Disko Bay the average daily intake of seal blubber is about 30 g (Pars, 2000).

Taking another example, locally grown and produced farm products were collected in Arkhangelsk, northern Russia, in 2000 and analyzed for pesticides and PCBs. All the grain- and vegetable products had very low concentrations of POPs, except for HCH which was high. The meat and fats from farm animals had considerably higher concentrations and were 3 to 10 times higher than the corresponding levels in Norway (Polder *et al.*, 2002b). This applied particularly to pig meat and fat, for which the DDT concentrations were 10 and 130 ng/g respectively. A 60 kg person consuming a pork chop per day (170 g meat and 30 g fat) would consume 0.1 µg DDT/kg/day, however this is still only 25% of the estimated intake in Greenland (Table 7·9).

7.4.3. Dietary intakes, anthropogenic blood levels and dietary indicators

A correlation between the intake of traditional food items measured by dietary surveys and blood levels of xenobiotic substances has been demonstrated on a group and population basis for heavy metals (Hansen, 1990) and OCs (Van Oostdam *et al.*, 1999). However, to describe and analyze dietary risk behavior in more detail it would be extremely useful to be able to demonstrate this correlation at the level of an individual. This is obviously more difficult to achieve owing to the large day-to-day variation concerning dietary behavior and to the seasonal variation in traditional food availability. Also, individuals may accumulate contaminants at different rates owing to genetic causes and other lifestyle factors modifying their metabolism.

Organochlorine compounds are metabolized by a number of enzymes: CYP1A1, CYP1A2, phenobarbital-CYP, etc., which are part of the P-450 cytochrome oxidase system (Lagueux *et al.*, 1999). Different OCs are metabolized by the same enzyme systems and may compete or interact with each other in terms of uptake and excretion. These same enzymes metabolize nicotine and its breakdown products, which may also influence enzyme expression. Tobacco smoking has been correlated with higher OC levels in plasma (Deutch, 1999; Deutch and Hansen, 1999, 2000). In residents of Nunavik, northern Quebec, with a high marine food intake and OC exposure, CYP1A1 activity in placenta tissue was

Table 7·11. Correlations between reported monthly intake of marine food items (based on a food frequency questionnaire), plasma phospholipid n-3:n-6 ratios, whole blood Hg (µg/L) and lipid adjusted plasma PCB levels (µg/kg lipid) in male Inuit hunters from Uummanaq, northwest Greenland, n=48 (bivariate Pearson correlation coefficients) (Deutch *et al.*, 2002).

	Marine food intake	n-3 : n-6 ratio	Whole blood Hg	Plasma PCB
Marine food intake		0.39**	0.26 ns	0.22 ns
n-3 : n-6 ratio	0.39**		0.72**	0.63**
Whole blood Hg	0.26 ns	0.72**		0.65**
Plasma PCB	0.22 ns	0.63**	0.65**	

ns: not significant; * $P < 0.05$; ** $P < 0.01$; *** $P \leq 0.001$.

statistically correlated with DDE, PCB congeners and HCB levels, as well as with levels of smoking (Lagueux *et al.*, 1999). Therefore, to identify individuals at risk of high OC burden is a multi-factorial issue, and is not just a question of diet.

Thus, although it is well documented that marine mammals in the traditional diet contain high levels of OCs (AMAP, 1998; Chan, 1998; Johansen *et al.*, 2000; Kuhnlein, 1995; Kuhnlein and Receveur, 1996) at the present time it is only possible to demonstrate:

1. the overall correlation between self-reported high intakes of traditional food and selected dietary biomarkers such as blood Hg (Bjerregaard and Hansen, 2000; Deutch, 1999) or n-3 fatty acids in plasma, phospholipids, erythrocytes or adipose tissue (Bjerregaard *et al.*, 2001; Deutch and Hansen, 1999, 2000); and
2. the correlation between these dietary indicators (fatty acids, blood Hg levels etc.) and OC levels.

In the Canadian reports (Chan, 1998; Kuhnlein, 1995; Kuhnlein and Receveur, 1996) the question of direct associations between self-reported marine food intake and blood levels of OCs is not considered. In other reports such associations are described as being weak or non-significant (Bjerregaard and Hansen, 2000; Deutch, 1999; Deutch and Hansen, 1999, 2000; see also Table 7·11).

7.5. Conclusions and recommendations

Within the last five years most countries have performed one or more dietary surveys among their Arctic indigenous populations. However, these have been undertaken for different reasons, with different target groups, and using different sampling and reporting methods. It is difficult to make direct comparisons between dietary survey data obtained by different methods, e.g., interviews versus recording or food frequency questionnaires. Also, some studies report results as intake frequency or weight of listed food items whereas others calculate nutritional profiles. Some dietary surveys report traditional food intake only, whereas others consider total diet. Therefore, in most cases, only qualitative comparisons can be made between countries, or between ethnic groups within countries. This should be considered when planning sampling methods for future dietary surveys and when considering more standardized means of reporting. The aim should at least be to report both daily intakes, e.g., g/day (rather than portions), and daily nutritional intakes in absolute and relative units, e.g., per 10000 kJ.

The diet of Arctic indigenous peoples includes traditional food and imported (market) foods. Although varying by country, location, gender, and age group, traditional food currently yields 10% to 40% of the total energy intake; a considerably smaller percentage than 30 to 40 years ago. Traditional foods are the main sources of protein, fat, most minerals (iron, Zn, Se, iodine), vitamin D, and particularly the essential long-chain n-3 fatty acids, which supply some protection toward heart disease and diabetes. The ratio between n-3 and n-6 fatty acids in human lipid fractions serves as an indicator of the relative intake of traditional food.

Imported foods are the main sources of carbohydrate, water-soluble vitamins, vitamin A, and calcium. Composite diets are sufficient in terms of most nutritional requirements. However, those elements of most importance in relation to meeting required intakes in Arctic populations 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.

Analyses of food items of animal origin have provided ample proof that traditional food is a major source of heavy metals (Hg, Cd and sometimes 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 POPs have so far only been compared with human body burdens of POPs on a population basis. Correlations between estimates of individual dietary intakes and individual blood levels of xenobiotic substances 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 a connection between intake of marine mammal fat (e.g., blubber) and organic pollutants highly probable. It is also evident that POP concentrations in animal fat vary with the age, gender and geographical location of the animals.

Uptake, metabolism, and excretion of OCs are influenced, among others, by genetic factors. Tissue levels are influenced by various lifestyle factors such as smoking (Deutch, 1999; Deutch and Hansen, 1999, 2000; Lagueux *et al.*, 1999) and body mass index (Deutch *et al.*, 2002). Therefore, identification of individuals at risk of accumulating high POP burdens 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.

Chapter 8

Lifestyle Factors as Determinants of Health in Arctic Communities, with Emphasis on Pregnant Women and Adverse Pregnancy Outcome

Jon Øyvind Odland

Summary

This chapter discusses lifestyle factors as determinants of health, with emphasis on pregnant women and adverse pregnancy outcome. An important issue is how to extract reliable information on these very complex problems with multi-factorial origins in modern, Arctic communities. Questionnaires and biomarkers are two possible tools, both currently valuable for assessment of, e.g., smoking frequency and alcohol consumption. However, the development of new and better biomarkers will possibly change this in favour of biomarkers in the years to come.

Strategies to reduce smoking frequency through information campaigns and/or by increasing the price of tobacco have not been particularly successful. The concept 'engineering of consent' is more promising, using the tobacco industry's own strategy, but creating an image of non-smoking rather than smoking as the attractive lifestyle standard for women and youth. Different national programmes to address alcohol problems by community action also exist, mostly reflecting national and cultural differences. Medical professionals and medical arguments generally play a secondary role when it comes to the definition of the alcohol problems. Engineering-of-consent is also relevant in the struggle to reduce the general alcohol consumption in Arctic populations.

Pregnant women in often harsh working environments are especially vulnerable. All Arctic countries have tried to offer special benefits for working in the north. Particular attention is now focused on the health of workers in heavy industries of the Arctic, and a general trend is to try to prevent fetal exposure to environmental pollutants by removing pregnant women from unhealthy work places when (and if possible before) a pregnancy is recognized.

8.1. Effects of tobacco smoking on human health

Cigarette smoke contains a number of substances with known or potential negative effects on pregnancy endpoint factors such as gestational age, birth weight, newborn body mass index, and congenital malformations (Odland, 2000; Odland *et al.*, 1999a,b,c, 2001; Shu *et al.*, 1995). It is causally associated with cardiovascular disease; chronic obstructive lung disease; cancer of the respiratory system, pancreas, renal pelvis, and urinary bladder; and is also associated with cancer of the liver, uterine cervix and myeloid leukemia (Hoffmann and Hoffmann, 1997).

8.1.1. Contaminants in tobacco

Nicotine is recognized to be the major inducer of tobacco dependence (Hoffmann and Hoffmann, 1997). More than 50 carcinogens have also been identified in tobacco, including polycyclic aromatic hydrocarbons (PAHs), aromatic amines, and N-nitrosamines, especially the tobacco-specific N-nitrosamines. Owing to changing manufacturing methods, the nitrate content of tobacco has changed, causing enhanced combustion of the tobacco, decreased carcinogenic PAH concentrations, but increased formation of carcinogenic N-nitrosamines.

Cadmium (Cd) is a component of tobacco and a known human carcinogen (Shaham *et al.*, 1996). Animal data suggest that oral exposure to Cd results in reduced birth weight and more severe effects on the fetus, including placental damage (WHO, 1992), and embryotoxic and teratogenic effects (Hauptman *et al.*, 1993; Luo *et al.*, 1993). However, in humans it is difficult to separate the impact of Cd from the impact of smoking on birth weight. The human placenta serves as a selective barrier to Cd with an average attenuation of 40% to 50% (Baranowska, 1995; Lauwerys *et al.*, 1978; Roels *et al.*, 1978). Individual variability related to metallothionein induction in the placenta may occur. Animal data support this conclusion, with free transport of Cd through the Wistar rat placenta, while the hamster placenta is totally blocked (Hanlon and Ferm, 1989; Tsuchiya *et al.*, 1987). In humans, Cd accumulation is detectable in follicular fluid. It accumulates in the ovaries of smokers in a dose-dependent manner, and may reduce the quality of human eggs (Zenzes *et al.*, 1995). Milnerowicz (1997) has documented a three-fold increase in Cd concentrations in amniotic fluid of active smokers. A comprehensive study of a British national cohort has revealed that smoking is independently related to an earlier menopausal transition, although the effect was particularly marked among underweight women (Hardy *et al.*, 2000).

Several interactions of toxic substances related to tobacco smoke are documented in human studies. Ellingsen *et al.* (1997) suggest that Cd depresses the concentration of selenium in blood, but smoking alone cannot be regarded as a true predictor for this effect.

Recent Arctic studies also document associations between smoking frequency and Cd concentrations in human fluids, as well as increasing concentrations of mercury (Hg) and Cd with the consumption of marine mammals (Bjerregaard and Hansen, 2000; Van Oostdam *et al.*, 1999). Deutch and Hansen (1999, 2000) have reported highly significant positive associations be-

tween maternal smoking status (never, previous, present), cotinine, and plasma concentrations of organic pollutants in both maternal blood and umbilical cord blood. Traditional food is believed to be the source of the contaminants, but smoking may influence the enzymatic turnover of toxic substances.

8.1.2. Smoking frequency in the Arctic

Smoking cessation among pregnant women may reduce the number of fetal and infant deaths by 11% (Cnattingius *et al.*, 1988). Even so, a large proportion of women continue to smoke after they have become pregnant (Madeley *et al.*, 1989). A Norwegian study of pregnant women in 1987 showed that 35% to 39% of pregnant women smoked daily, and that 82% of the smokers continued to smoke throughout their pregnancies (Peen *et al.*, 1991). A study from southern Norway of a large non-selected population showed a more optimistic reduction from 34% to 22% during pregnancy in 1994 (Eriksson *et al.*, 1996). Eriksson *et al.* (1998) undertook a study of 4766 pregnant women living in northern Norway in 1994/1995. The point prevalence of self-reported daily smoking among the women three months before pregnancy was 34%; at 18 weeks of pregnancy 21% of the women reported smoking daily. A multiple logistic regression analysis revealed that a low number of cigarettes smoked per day during the last three months before pregnancy was the best predictor for smoking cessation. Educational level, maternal age, parity and civil status were also significant positive contributors to smoking cessation. Eighty percent of the women who were unable to stop smoking reported a reduction in smoking frequency, from 13.9 cigarettes per day to 7.3 in the eighteenth week of pregnancy. In a Finnish study, 12% of the delivering women reported daily smoking, while 11% were ex-smokers (Luopa *et al.*, 2002). Odland *et al.* (1999a,b,c) documented a significantly higher self-reported smoking frequency in Arctic Norwegian pregnant women compared to Russian population groups, independent of self-reported ethnic relationship. Of the Norwegian pregnant women, 22.7% smoked 1 to 10 cigarettes per day, while 13.5% smoked more than 10 cigarettes per day; the reported Russian results were 20.5% and 2.6%, respectively. The highest Arctic smoking frequency in pregnancy was registered in Greenland by Deutch and Hansen (1999, 2000); 58% (78 out of 134) of pregnant Greenlandic women reporting daily smoking.

The results by Odland *et al.* (1999a,b,c) from 1994/1995 seem to reflect the increasing smoking frequency of Arctic Russian pregnant women since perestroika. Concurrent with the opening of the country to western imports, and the advent of western-style advertising, the smoking frequency of Russian pregnant women appears to have approached the rates for Norwegian pregnant women mentioned earlier (Eriksson *et al.*, 1996; Odland *et al.* 1999a; RFCSES, 1998). This was also observed in a Polish study, which showed an increase in smoking frequency in the adult female population of 4% between 1990 and 1995 (Jokiel, 1996). The women with the highest smoking frequency had a high university level education and high socio-economic status, possibly indicating a tendency to associate smoking with high social status in the new market economy of Eastern Europe.

According to a national Finnish study, 16% of 2769 mothers of 14-year old school children, smoked during pregnancy in 1981. In the same study, 22% of the fathers and 21% of the mothers of these children smoked in 1995 (Pekkanen *et al.*, 1996).

The smoking status of school children in all schools in Lapland was assessed in a recent report (Luopa *et al.*, 2002): 29% of boys and 30% of girls under 15 years of age smoked daily. In the age range 15 to 16 years, 47% of the boys and girls smoked, and in the age range 17 to 18 years, 22% of boys and 27% of girls smoked.

8.1.3. Methodological problems, self-reporting and biomarkers

A well-known epidemiological problem is the validity of self-reported smoking status based on questionnaires. Biomarkers of tobacco smoke introduce new and important approaches to the problem. In a recent Swiss study, the validity of tobacco questionnaires was evaluated using a single biomarker or a combination of two biomarkers (Morabia *et al.*, 2001). A comparison of the questionnaire data with simultaneous measurements of salivary thiocyanate and expired carbon monoxide positively indicated that valid responses can be obtained for self-reported, current smoking habits in population-based surveys.

Using a self-administered questionnaire, Jaakkola *et al.* (1994) assessed the role of a smoking parent's education and socio-economic status, and their child's health, as determinants of a child's exposure to environmental tobacco smoke at home. The risk of exposure to environmental tobacco smoke was higher when the parents had no professional education, compared to having had a university or college education, although socio-economic status was not associated with exposure level, contrary to recent studies from Eastern Europe (Jokiel, 1996). The exposure risk was higher with a single parent. The risk decreased significantly for atopic children, indicating that knowledge of a child's illness affects the smoking behaviour of its parents.

In a study of 429 Spanish women, Pichini *et al.* (2000) investigated the association between biomarkers of fetal exposure to cigarette smoke at the end of pregnancy, which involved measurements of cotinine in cord serum and in maternal and newborn urine samples, and quantitative measurements of smoking intake and exposure employing a self-administered questionnaire. The questionnaire was completed in the third trimester of pregnancy and on the day of delivery. Cord serum cotinine appeared to be the most accurate biomarker of fetal exposure to smoking at the end of pregnancy, distinguishing active smoking from passive smoking, and environmental tobacco smoke from non-exposure.

Cotinine was also studied by Willers *et al.* (2000) in a non-pregnant study group. In this case the detailed questionnaire gave only a rough picture of the environmental exposure to active or passive smoking. It was more strongly indicated by the cotinine levels in urine, saliva and plasma. Children with a history of asthmatic symptoms had significantly lower median cotinine levels in urine and saliva compared to referent children, probably owing to the anti-smoking information received by their parents. This factor must obviously be considered

in any epidemiological assessment of environmental tobacco smoke risks.

Cotinine has also been employed as an indicator of children's exposure to passive smoking in British population surveys (Jarvis *et al.*, 2000). The conclusions were that exposure to passive smoking among children has been approximately halved since the late 1980s. This reduction might be explained by parental reduction in smoking frequency, as well as by the reduction of smoking in public places. Another valuable biomarker is urinary 1-hydroxypyrene. Li *et al.* (2000) found that urinary 1-hydroxypyrene concentrations are strongly correlated with the number of cigarettes smoked.

Thus, new and promising biomarkers such as cotinine and 1-hydroxypyrene are now available. Verkerk *et al.* (1994) concluded that information bias is not likely to have a large influence on effect estimates in studies using current and retrospective information on both alcohol and cigarette consumption. Thus, biomarkers and questionnaires are both valuable for evaluating health risks connected to cigarette smoking.

8.1.4. Information, intervention, and cultural aspects

The classic approach to reducing smoking frequency is to increase the cost of tobacco products through higher excise taxes (Nakamura, 1996). Local networks of health workers and politicians in Alaska have also partly succeeded in reaching at-risk groups with relevant information campaigns. The Alaskan programme of education on health risks of smoking has also been introduced in the Russian Far East, with special emphasis on information programmes in schools (Holder, 1998). A World Health Organization programme, WHO CINDI (Countrywide Integrated Program for Disease Prevention), has also been introduced widely throughout Siberia (Alekseeva, 1998). The results are not yet evaluated. Brandt (1996) introduced the concept of 'engineering of consent'. The tobacco industry, together with advertising and public relations experts, has created a specific image of smoking, designed to make cigarette smoking appeal to women; smoking being associated with independence, glamour, seduction, and sexual motives. The same idea can be adapted to create sets of negative associations for the cigarette as well (unhealthy, smelly, premature aging, etc.). In general, neither propaganda nor 'objective public information', have succeeded in reducing smoking frequency in most countries (Eriksen, 1999). From a public health perspective, the only solution to the physical dependence on smoking is to lower the nicotine concentration in cigarettes to a level at which there is no induction of dependence on tobacco (Hoffmann and Hoffmann, 1997).

8.2. Effects of alcohol consumption on human health

Alcohol use, or abuse, is a very controversial subject. One related problem is that self-reported alcohol consumption estimates are significantly influenced by under-reporting (Verkerk *et al.*, 1994). As described in section 8.1.3., however, Verkerk *et al.* (1994) also noted the view that information bias is not likely to have a large influence on effect estimates in studies using current and retrospective information on alcohol and cigarette consumption.

8.2.1. Alcohol in pregnancy

Consumption of alcohol during pregnancy can result in damage to the developing fetus, including cognitive impairment, small stature, poor growth, and altered development of facial bones (Stratton *et al.*, 1996). In its most severe form, the combination of poor prenatal or postnatal growth, poorly developed mid-facial bone structure, and a variety of brain function impairments is referred as to Fetal Alcohol Syndrome (FAS). Lesser degrees of prenatal alcohol exposure can result in brain dysfunction without growth impairment or altered facial features.

Active surveillance for FAS carried out in the Alaska Native health care system from 1988 to 1994, documented a rate of 4.2/1000 live births, compared to rates of 0.3 to 1.0/1000 live births in the U.S. population. Among Alaskan Natives, FAS is the most common cause of preventable congenital mental retardation. It is quite possible that rates of FAS are elevated in other Arctic populations. An ongoing human health study, which is being coordinated by the AMAP Human Health Expert Group in the Russian Arctic as a sub-component of a large scale project on 'Persistent Toxic Substances (PTS), Food Security and Indigenous Peoples of the Russian North' will add new knowledge to this issue. Delivering women consuming excess alcohol during pregnancy need extensive help and professional care. Heavy maternal alcohol consumption during pregnancy is consistently linked to decreased birth weight (Faden and Graubard, 1994). The main controversies of alcohol and pregnancy outcome are connected to moderate alcohol consumption during pregnancy.

Polygenis *et al.* (1998) have recently conducted a meta-analysis of moderate alcohol consumption during pregnancy and the incidence of fetal malformations. The definition of moderate alcohol consumption was from 2 drinks/week to 2 drinks/day and the abstainer group included those who drank 0 to 2 drinks/week. A total of 130 810 pregnancy outcomes were evaluated, with 24 007 in the moderate alcohol group and 106803 in the abstainer group. The relative risk for fetal malformations was 1.01 (0.94–1.08). Thus, no association was found between moderate alcohol consumption and increased risk of fetal malformations.

For birth weight, results are less consistent (Faden and Graubard, 1994). A non-significant trend was seen in the direction of greater numbers of low-birth-weight babies born to mothers who drank more frequently during pregnancy. A significant interaction between drinking and smoking was found in which the negative effects of smoking on birth weight were less for those women who drank more heavily.

A connection between moderate alcohol consumption and spontaneous abortion has not been verified (Cavallo *et al.*, 1995). These authors found a significant increase in spontaneous abortion in the age group >30 years and in the higher parity category. As for premature rupture of membranes, no association has been found, in contrast to the situation for heavy smoking (Myles *et al.*, 1998). A comprehensive European multi-center study

on infertility and sub-fecundity concluded that any causal effect is restricted to females with a high (close to daily) intake of alcohol within the range of normal consumption reported in European countries (Olsen *et al.*, 1997).

Growth retardation in the first two years of life has been found to be significantly associated with maternal moderate alcohol consumption during pregnancy (Day *et al.*, 1994). Behavior, however, is more difficult to measure and poorly defined in relation to teratogenic exposure. For that reason, only children who are clearly affected (i.e., dysmorphic or growth retarded) or those who are participating in well-controlled prospective studies have shown effects on global developmental tests during this period (Jacobson *et al.*, 1993).

Excess alcohol consumption during pregnancy has serious and well-documented effects on pregnancy outcome. Also, it is often linked to a variety of other factors, such as social and economic problems, nutritional factors, and smoking. For this reason, alcohol abuse is discussed in more detail under section 8.3.

8.2.2. Contaminants and alcohol

Sallsten *et al.* (2000) have studied Hg in end-exhaled air and the influence of ethanol on Hg exhalation in subjects with long-term Hg exposure from diet, amalgam fillings, or the work environment. They concluded that low levels of Hg could also be detected in end-exhaled air in individuals without amalgam fillings, probably due to the alcoholic oxidation of Hg. A five-fold increase was seen 30 minutes after alcohol intake, the relative increase independent of the body burden of Hg. However, exhalation of Hg represents only a small percentage of the total elimination of Hg.

8.2.3. Assessing consumption, and methodological problems

In the studies of Odland *et al.* (1999a,b,c) on pregnant women in the Norwegian and Russian Arctic, self-reported alcohol consumption was difficult to assess in the Russian group. The topic appears to have been avoided by the interviewers and interviewees. In the Norwegian group, the results were considered partly reliable and partly under-reported. In addition to the previously described information on smoking frequency, Verkerk *et al.* (1994) collected prospective as well as retrospective information on alcohol consumption for 2806 women in all provinces of the Netherlands who gave birth in 1978 and 1979. Outcome measures were stillbirth, small-for-gestational-age, congenital malformations, preterm birth and low birth weight. The only statistically significant result was found for smoking and small-for-gestational-age. The results also indicated that information bias was unlikely to have a large influence on effect estimates.

Many biomarkers are now introduced in the assessment of alcohol consumption (Sarkola *et al.*, 2000). Mean cell volume (MCV), g-glutamyl transferase (GGT), carbohydrate-deficient transferrin and hemoglobin-acetaldehyde adducts are some of the most explored. These authors compared the usefulness of these four biomarkers in a follow-up study of alcohol abuse during pregnancy. The study concluded that MCV and GGT appeared to be the most efficient laboratory markers for detecting excessive alcohol consumption and the adverse effects of alcohol on the fetus.

8.2.4. Information or intervention?

A number of prophylactic measures have been tried, from the most alarming propaganda to much more casual approaches, as described by Koren *et al.* (1996). These researchers characterized women's perception of the teratogenic risk of alcohol by studying the reactions of 30 adult non-pregnant women to a videotape containing alarming information. Most subjects had a strong impression after being exposed to the most alarming propaganda that even one drink during pregnancy could harm the fetus. The conclusion from this research was that it is preferable to refrain from making unfounded statements about fetal risks from mild alcohol consumption. In the worst case, it was considered that an alarmist approach might even lead to termination of otherwise wanted pregnancies.

Another important aspect concerns the poor information given by a substantial group of medical doctors to their patients about risks related to alcohol consumption during pregnancy (Leversha and Marks, 1995). Doctors' attitudes to alcohol consumption in pregnancy do not reflect their reported clinical practice. Only 53% of obstetricians and 48% of general practitioners in this study routinely advised women about alcohol consumption at the first antenatal contact.

The complexity and incomplete nature of existing information about causes of women's drinking habits, including ethnicity, socio-economic class, occupation, and even job category, has been documented by Ames and Rebhun (1996).

Dejin-Karlsson *et al.* (1997) have tested the impact of psychosocial resources on pregnant women in relation to continued alcohol consumption. All women included in the study (n=692) reported alcohol consumption in the year before pregnancy. Almost a third (32.8%) continued to drink during pregnancy, even though their alcohol intake was moderate. Despite the official Swedish alcohol recommendation of total abstinence during pregnancy, more socially active and more highly educated women continued drinking alcohol, with wine as the alcoholic beverage of choice. Younger women, or women with fewer years of education, tended to stop drinking to a higher degree, but those who continued drinking mostly consumed beer. Grimstad *et al.* (1998) reported that alcohol and/or tobacco use during pregnancy may be associated with a history of substance abuse.

Different national programmes to prevent alcohol problems by community action are described and summarized by Larsson and Hanson (2000), showing very different approaches, mostly reflecting national and cultural differences. A Baltic study on alcohol misuse as a health and social issue concluded that the medical profession and medical and epidemiological arguments play a secondary role in most of the countries when it comes to the definition of the problem (Simpura *et al.*, 1999). A national experiment was performed in conjunction with the legalization of strong beer in Iceland in 1989 (Olafsdottir, 1998). Total alcohol consumption peaked the year after the drinking of strong beer was allowed, but

leveled off very rapidly as real income in society declined due to other economic factors. The survey data indicate that almost all socio-demographic groups ultimately moved from consumption of strong traditional distilled spirits to weaker beverages. The groups contributing most to this change were those living in the Reykjavik area, women, people in academic professions, and men employed in the service professions. Different results are described in a report on Poland's 'anti-alcohol campaign', which effectively ceased in the early 1990s, with no significant change in people's drinking behavior (Moskalewicz, 1993).

8.3. The influence of cultural change on alcohol and substance abuse

8.3.1. Influence of cultural change on alcohol consumption, and related problems

Alcohol consumption is closely associated with social, economic and cultural factors. In the Russian Arctic, alcohol consumption is a major problem in society; a problem that increased considerably in the years following perestroika (RFCSES, 1998). Clearly this constitutes a serious risk of adverse pregnancy outcome (Odland, 2000; Paschane, 1998; RFCSES, 1998). However, based on fragmentary information, alcohol abuse is much less of a population problem among women of child-bearing age compared to adult men. In indigenous culture and tradition, alcohol abuse during pregnancy is rare, and typically connected to malnutrition and pregnancy related infections.

8.3.2. Influence of high latitude on lifestyle and health determinants

Paschane (1998) suggested that factors associated with high latitude, such as winter depression (or Seasonal Affective Disorder, SAD), and a variety of socio-economic factors may present unique risk indicators for substance abuse. Environmental factors include extreme light and dark cycles and long periods of cold harsh conditions. Climatic patterns can be highly inconsistent, but the light and dark cycles are very consistent. Another characteristic is geographical remoteness, resulting in greater isolation. Variation in alcohol consumption appears more pronounced in northern climates (Levine *et al.*, 1994) and might therefore be partly explained by seasonal changes (Lemmens and Knibbe, 1993). Studies of isolated northern communities demonstrate a low frequency of alcohol-related homicides and suicides, which is attributed to cultural homogeneity and environmental adjustment of the population (Stenback and Saukko, 1996). Risk of injury, however, is greater in northern communities because work and recreational activities are often dangerous (see chapter 3). Combined with alcohol, these activities can be life threatening (Landon and Saylor, 1997).

One possible method in the further assessment of the risk indicators associated with latitude is to use the alcohol-attributable proportions of injuries (Shulz *et al.*, 1991). Global data on three types of mortality have been compared in six Arctic northern areas (Norway, Sweden, Canada, Finland, Alaska, and Russia) and the United States as a whole (Paschane, 1998), including chronic liver disease, motor vehicle traffic accidents, and homicide. For chronic liver disease, the relative risk was twice as high in Finland compared to Norway. For motor vehicle traffic accidents, there was no difference between Norway and Sweden, the risk in Finland was slightly higher, the risk in Canada almost twice that of Norway, and the risk for both men and women in Alaska and men in Russia the most serious. The most dramatic risk differences were observed in comparisons of alcohol-attributable mortality for homicide, with men in Finland, Alaska, and Russia at the top. The overall conclusion of these comparisons is that there is a high degree of variability among northern areas and that alcohol-related problems are serious in northern areas (Paschane, 1998).

Geographically isolated indigenous groups have mostly adapted well to environmental conditions that may affect their health status. However, changes in environmental conditions, combined with dramatic social and cultural change may destroy a group's ability to adapt and survive (Young, 1994). Such changes may affect an epidemiological transition in health. For example, a decline in infectious diseases, but increases in chronic, non-communicable diseases, accidents, and violence have been reported. Abuse problems in indigenous populations may affect adaptation skills and mask unique historical problems facing the populations. Although some indigenous groups appear to experience serious substance abuse problems, this is not indicative of a cultural or biological problem (Waldram *et al.*, 1995). It is only a minority inside the groups who experience problems with substance abuse and the ability to adapt to environmental hazards (e.g., homogeneity in a community, communal responsibility, behavioral cohesiveness) (Landon and Saylor, 1997).

In conclusion therefore, northern areas show substantial differences in their alcohol-related mortality data, pointing to very complex underlying causes for the patterns of variability.

8.3.3. Drug abuse

Cocaine and marijuana use represent major problems in many Alaskan and Canadian Arctic communities (WHO, 1995). Seasonal variations in their use have been identified, with the highest levels in the fall and winter (Romberg *et al.*, 1992). Cocaine use may be linked to seasonal depression (Sandyk and Kanofsky, 1992). Significant links have also been found between cocaine use and seasonal affective disorder (SAD) (Satel and Gawin, 1989).

Injection drug use appears to be as common in northern areas as in other areas (Fisher and Booker, 1990). There is, however, evidence that sharing of drug injection equipment may be greater in northern communities. Registered HIV-infections increased almost exponentially in northwest Russia in 2000, probably related to drug addiction and needle contamination in 90 to 95% of cases (RFCSES, prelim. data).

Studies in Ontario First Nations communities report that as many as 25% of children aged 5 to 15 years inhale solvents (Remington and Hoffman, 1984). This behavior seems to be strongly correlated with parental alcohol abuse (Barnes, 1979).

8.4. Working conditions and adverse pregnancy outcome

8.4.1. Work and pregnancy

In a recent meta-analysis, working conditions and pregnancy outcome for 160 988 women participants in 29 individual studies have been extensively discussed (Mozurkewich *et al.*, 2000). Outcomes of interest were preterm birth, hypertension in pregnancy, pre-eclampsia, and small-for-gestational-age. Physically demanding work was significantly associated with preterm birth, small-for-gestational-age, and hypertension or pre-eclampsia. Other occupational exposures significantly associated with preterm birth included prolonged standing, shift and night work, and high work fatigue score (Luke *et al.*, 1999). No association was found between long work periods and preterm birth.

In Norwegian communities, Wergeland and Strand (1998a,b) and Wergeland *et al.* (1998) have reported that strenuous work increases the risk of low birth weight, particularly in non-smokers. The strongest factor was a lack of influence on the pace of the work. The preventive effect on pregnancy complications of job modification during pregnancy is just as important as smoking cessation. Strand *et al.* (1996, 1997a,b), from the same research group, reported that fertility among employed women (based on time-to-pregnancy calculations) was 17% higher than the general fertility rate. They suggest that work status and occupation should be included among the variables of birth registries, in order to facilitate routine presentations of fertility rates and pregnancy outcome for women in paid work; the same conclusions were drawn from a U.S. study by Gabble and Paige Turner (1997) who observed an association between specific working conditions and first-birth fertility. Wergeland *et al.* (1996) and Wergeland and Strand (1997) also reported that abstention from smoking during pregnancy increased with opportunities to limit total work load, and that control of working conditions reduced the risk of pre-eclampsia. They concluded that women with power to control their own work pace, reduced their sick leave in general (Wergeland and Strand, 1998b) and had better pregnancy health than women without such possibilities (Wergeland *et al.*, 1998). General working conditions in the Scandinavian countries have improved since the 1960s, and thus results from these countries cannot be generalized to situations where there is a higher exposure to contaminants or more extreme working conditions (Ahlborg *et al.*, 1989). Nordstrøm and Cnattingius (1996) found that practically all social differences in birth weight are related to differences in maternal age, parity, height, and smoking habit. No general pattern could be seen for work environment characteristics.

Female health workers are found to have a high risk of pregnancy complications in many studies, probably owing to many factors, e.g., exposure to contaminants and very stressful working conditions (Ortayli *et al.*, 1996; Saurel-Cubizolles *et al.*, 1991a,b). Even occupational noise can be considered a form of risk during pregnancy (Hartikainen *et al.*, 1994). Pregnant immigrant women are a special risk group in the European society; generally they have more heavy occupational activity and duties at home (Stengel *et al.*, 1986). This observation also reflects the rapid changes in the new Eastern European states (RFCSES, 1998).

8.4.2. Working conditions and cultural change

Latitude offers unique risk etiologies in connection with working conditions. Extreme light and dark cycles and long periods of cold harsh conditions, geographical remoteness and resulting isolation, etc., require special working arrangements and special adaptations to prevent stress and burnout in general. Pregnant women are especially vulnerable under harsh working conditions. All Arctic countries have, to a greater or lesser degree, tried to allocate special benefits for working in the north, such as longer vacations, free breaks in the south, higher salaries, tax incentives, subsidized accommodation, cultural activities, and special educational programmes for children. However, the reduction in the quality of medical care associated with economic downturns has been a great threat to these programmes in the last ten years, especially in the Russian Arctic (Odland, 2000).

In the Russian Arctic, special attention is now focused on the health of workers in heavy industries, such as the nickel, cobalt and aluminum refining industries, and power plant workers. These are all working places associated with high risk of accidents, as well as occupational exposure to toxic substances (Chashschin *et al.*, 1994; Nieboer *et al.*, 1997, 2000; Odland *et al.*, 1999d; Thomassen *et al.*, 1999). In a preliminary study, Chashschin *et al.* (1994) reported increased risk of spontaneous abortion, premature birth and congenital malformations in the offspring of women working in the nickel industry of the Kola Peninsula. Subsequently, Odland *et al.* (1999d) evaluated the medical, statistical, and occupational data sources of the Kola Peninsula, and concluded that a comprehensive epidemiological study of reproductive and environmental health is feasible. International funding is now in place for such studies, and these have been initiated.

8.5. Early onset of puberty, obesity, and exposure to xenohormones

Obesity has started to become a serious health problem in Arctic communities. Recently, a steep rise has occurred in the prevalence of obesity among boys and men in Denmark, in two phases related to the birth cohorts of the 1940s and of the mid-1960s and later. This rise suggests that environmental influences operating early in life might lead to indirect effects, such as early onset of puberty (Sorensen, 2000).

Gladen *et al.* (2000) have studied whether prenatal or lactational exposure to background levels of PCBs or DDT are associated with altered puberty, growth, and development in a cohort of 594 North Carolina children. They found that the height of the boys increased with transplacental exposure to DDE, as did body mass index. No effect was documented on the ages at which pubertal stages were attained. No effect was shown of lactational exposure to DDE or transplacental/lactational exposure to PCBs. Girls with the highest transplacental PCB exposures were heavier for their heights than other girls by 5.4 kg, but the difference was significant only if the analysis was restricted to girls of Caucasian ethnicity. The authors concluded that prenatal exposure at background levels might affect body size at puberty.

8.6. Conclusions and recommendations

Both questionnaires and biomarkers provide valuable tools for assessing smoking frequency and alcohol consumption. However, the development of new and better biomarkers will possibly change this in favor of biomarkers in the years to come.

Increasing the cost of tobacco products through higher excise taxes is a well-documented and tested solution, often resulting in the unintended side-effect of illegal import and distribution of cigarettes. Educational information on health risks associated with smoking has also been widely used, but with limited success. Propaganda, as well as 'objective public information' seems to fail in most countries. The engineering-of-consent approach appears to be more promising. There is an urgent need for public authorities to try this approach, especially in areas where smoking frequency in the female population, especially the pregnant female population, is very high (e.g., Greenland), and in areas where female smoking frequency is rapidly increasing (e.g., the Russian Arctic).

The only solution to physical dependence on tobacco, from a public health perspective, seems to be a lowering of the nicotine concentration in cigarettes to a level at which there is no induction of dependence on tobacco.

National programmes to prevent alcohol problems through community action are adapted to national and cultural differences. Medical professionals and medical arguments mostly play a secondary role when it comes to the definition of the problem. However, some lessons can be learned: the legalization of strong beer in Iceland led to a general decrease in alcohol consumption and a change to weaker beverages. A confounding factor for this process was the decline in socio-economic standards over the same period. In Poland, the anti-alcohol campaign disappeared almost completely in the early 1990s, but with no associated significant change in drinking behavior.

The engineering-of-consent, discussed in the context of tobacco consumption, is just as relevant in relation to strategies aiming to reduce the general level of alcohol consumption in Arctic populations.

Pregnant women are a vulnerable group, especially under the generally harsh working conditions often found in the Arctic. All Arctic countries have, to a greater or lesser degree, tried to allocate special benefits for working in the north. Recent economic changes are posing threats to these programmes. Special attention is now being focused on the health of workers in heavy industries in the Arctic, with a general trend towards prevention of fetal exposure by removing pregnant women or women of child-bearing age from contaminated working places at the moment (or where possible before) a pregnancy is recognized.

Chapter 9

The Effects of Arctic Pollution on Population Health

Eric Dewailly and Pál Weihe

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).

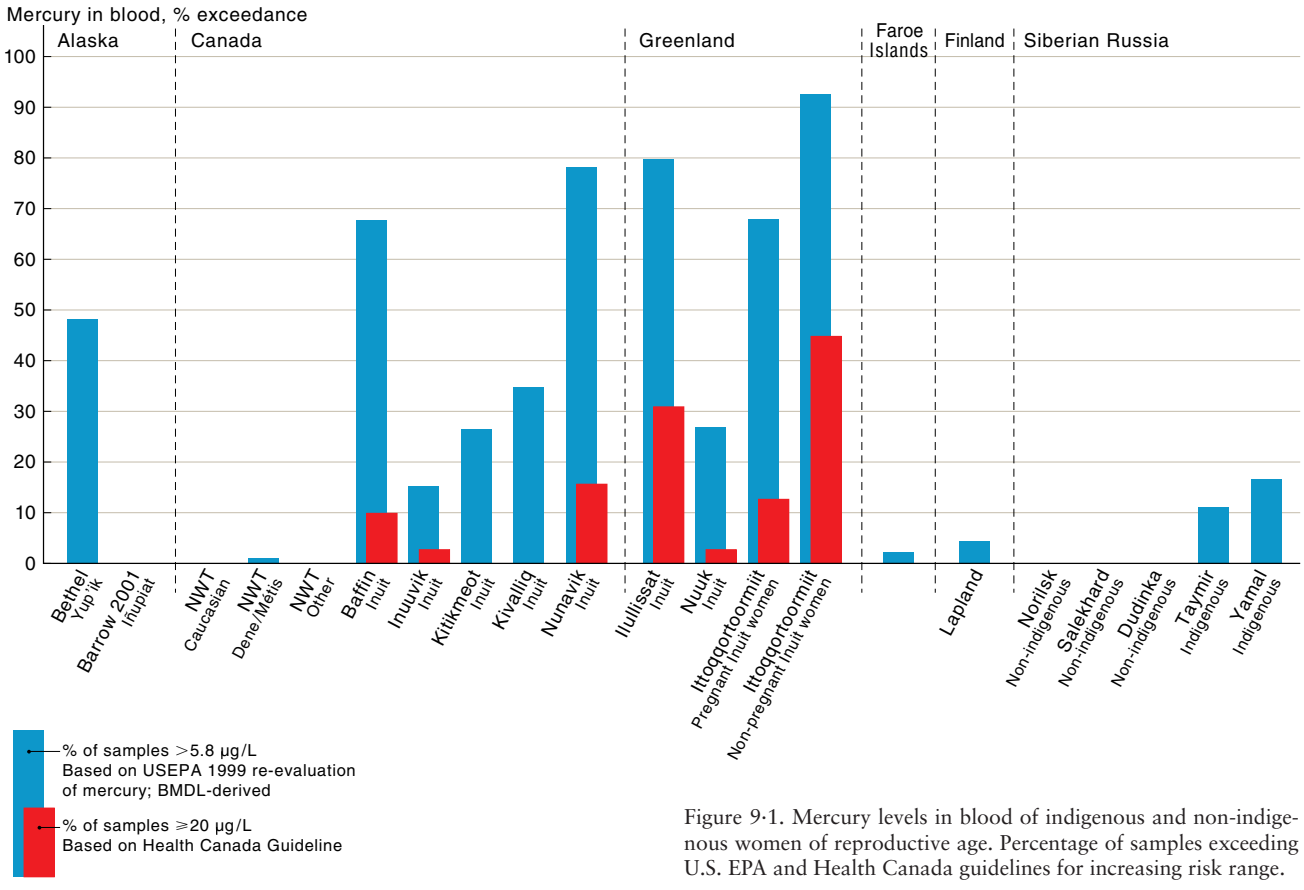

Figure 9·1. Mercury levels in blood of indigenous and non-indigenous women of reproductive age. Percentage of samples exceeding U.S. EPA and Health Canada guidelines for increasing risk range.

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

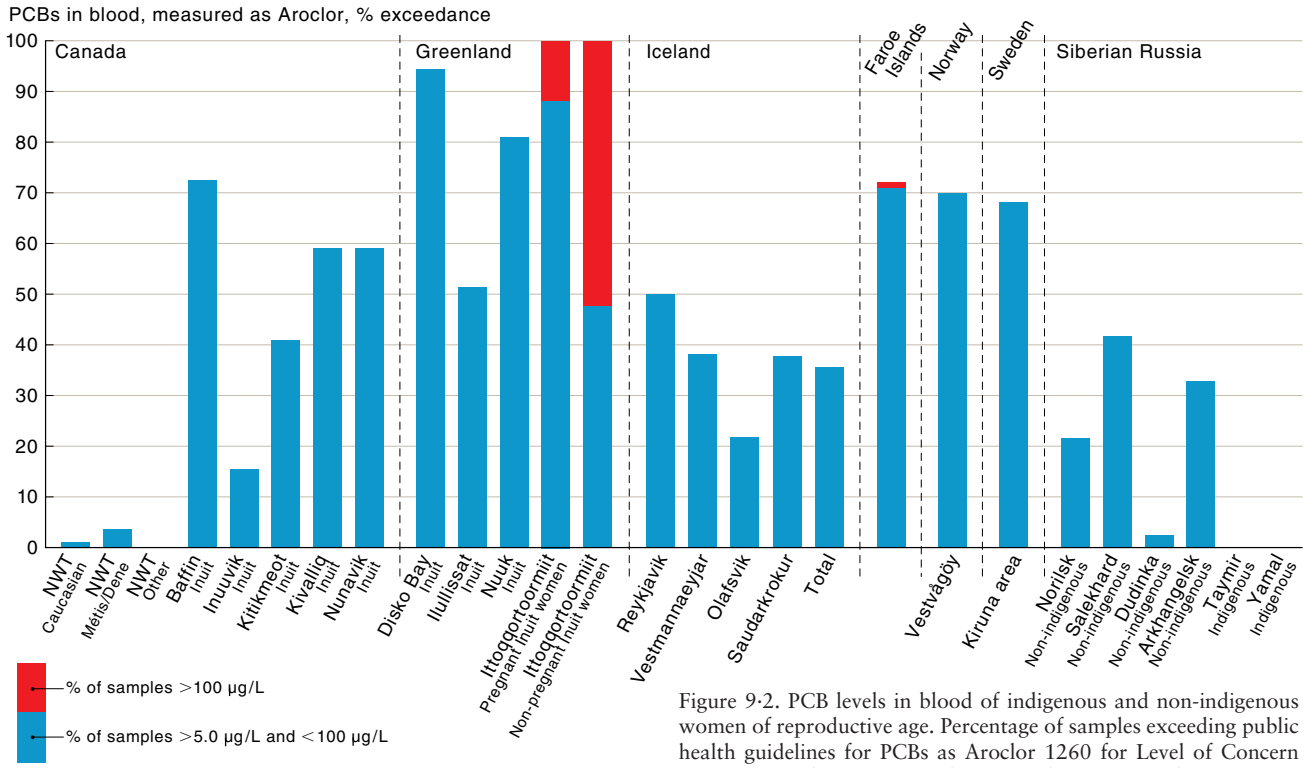

Figure 9·2. PCB levels in blood of indigenous and non-indigenous women of reproductive age. Percentage of samples exceeding public health guidelines for PCBs as Aroclor 1260 for Level of Concern (LOC, >5 and <100 µg/L plasma) and Action Level (>100 µg/L plasma).

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.

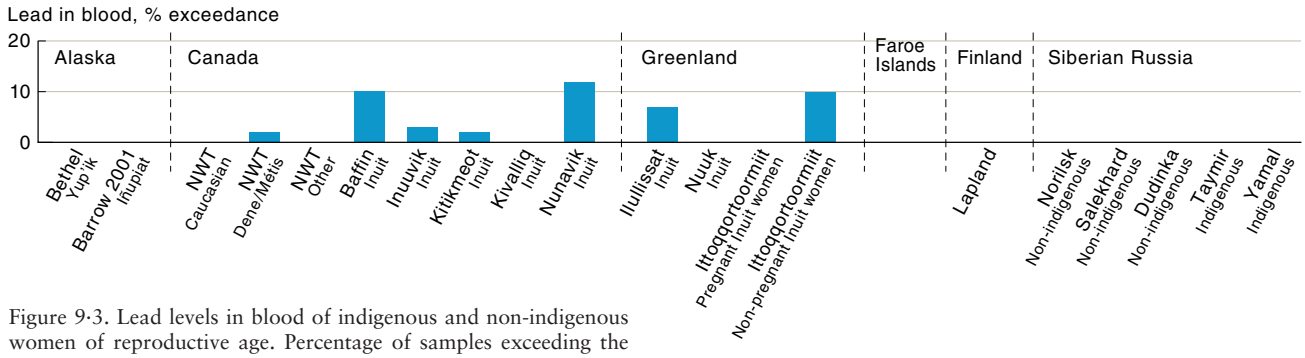

Figure 9·3. Lead levels in blood of indigenous and non-indigenous women of reproductive age. Percentage of samples exceeding the blood guideline Action Level of 100 µg/L.

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.

Chapter 10

Risk Reduction Strategies for Arctic Peoples

Andrew Gilman

Summary

The Arctic region and its peoples are extremely sensitive to global environmental pollution. The levels of persistent organic pollutants (POPs) and metals in Arctic peoples and their traditional food supply vary considerably throughout the circumpolar region and there remains a need for local risk reduction strategies in some regions of the Arctic where current levels of POPs and/or metals are above levels of concern. In general, it has been most effective when local public health authorities, working in concert with the community at risk and experts from a variety of disciplines, develop risk reduction strategies that address the risks and benefits components for a specific concern. However, the global nature of contamination by some POPs and metals and their capacity to travel to the poles from the mid-latitudes also requires international, regional and national risk management approaches to control their manufacture, use, transportation, storage, and disposal. Based on current global trends, and various activities to manage risks, there are likely to be minor decreases in POPs in the tissues of Arctic populations in Greenland, the Faroe Islands, eastern Canada, western Alaska, and eastern and western Russia by 2010, and minor increases in mercury (Hg) levels in Greenland and eastern Canada. There are likely to be major decreases in both POPs and Hg levels in these same populations by 2030. In general, levels of most POPs and metals in populations in western Canada, Iceland, Norway, Sweden, Finland, and central Russia are already reasonably low and are only likely to decline marginally by 2030. These predictions will be heavily influenced by prompt ratification and implementation of the Stockholm Convention on POPs and other multinational environmental agreements.

10.1. Introduction

The global nature of contamination by POPs and some metals, and their capacity to travel from the mid-latitudes to the poles requires risk management approaches that encompass international, regional, and national strategies to control their manufacture, use, transportation, storage, and disposal. Currently there are several international agreements that have been negotiated to address regional pollution (e.g., the Århus Protocols on Persistent Organic Pollutants and Metals under the United Nations Economic Commission for Europe's (UN ECE) Convention on Long-Range Transboundary Air Pollution (LRTAP), and the North American Agreement on Environmental Co-operation (NAAEC), which is the side agreement to the North American Free Trade Agreement), and others to address global pollution issues (e.g., the Stockholm Convention on POPs, the Basel Convention on Wastes, and the Rotterdam Convention on Prior Informed Consent). When ratified and fully implemented, these Conventions, Agreements and Protocols should significantly reduce new circulating sources of some of the most dangerous POPs to which Arctic populations are exposed. Considering the steady movement of these compounds over months and years into the Arctic, and their persistent nature, especially in polar regions, it could take many years for significant reductions to be observed in Arctic media, and especially in the fish and wildlife which serve as the primary food supply for indigenous populations.

The levels of POPs in Arctic peoples vary considerably throughout the circumpolar region (chapter 5). Based on current data on physiological, biochemical and genotoxic effects of POPs (chapter 6) and their impacts on population health (chapter 9) there remains a need for local risk reduction strategies in some regions of the Arctic where current levels of POPs and/or metals are above levels of concern. In general, it has been most effective for local public health authorities working in concert with the community at risk and experts from a variety of bio-medical, biological and physical disciplines to develop risk reduction strategies that address each specific concern. These local strategies are able to take account of the nature of the problem, the at-risk group(s) most in need of protection, the primary exposure route(s), the different levels of education and understanding in the community, and the social and cultural needs of the exposed group(s). Where a risk reduction strategy involves decreasing exposure to contaminants found in food, local advice can be extremely specific, focusing on where and when animals are caught, what normally consumed parts of the animal are best avoided (chapter 7), how food can be prepared to lessen contaminant intake, how much can be safely consumed while still ensuring that nutritional benefits are maintained, and when it is wise to decrease consumption because of age or fertility status. The likelihood that local advice is implemented is enhanced because the governance (e.g., the local legal authority) and support structure (e.g., public health support staff, phone information system, news media, etc.) are almost always in place prior to the issuance of the public health strategy. As environmental, social, cultural, and economic conditions change (due to a variety of interrelated factors such as climate change, the appearance of new contaminants or changing levels of existing contaminants, changes in local, regional and national governance policies, behavioral changes in the population, habits or genetics, etc.) so local risk reduction strategies need to be developed that are more able to adapt promptly and effectively to meet these changing local conditions and needs.

10.2. Risk reduction case studies

This section discusses some recent risk reduction strategies that have been applied in the Arctic countries. The information is based on material submitted by the individual countries and where possible describes the effectiveness of the strategies employed.

10.2.1. Alaska

Following the issuance of national fish advisories by the U.S. Environmental Protection Agency (EPA) and the U.S. Food and Drug Administration (FDA), the latter recognized that Hg levels in Alaskan fish were lower than average levels in other fish consumed in the United States and amended their original advisory; recommending that Alaskan consumers contact their local health and food safety authorities for specific consumption advice. The Alaskan Division of Public Health has determined that Hg levels are very low in most of the frequently consumed fish species and that there are documented health, social, cultural, and economic benefits associated with fish consumption. This Agency through a consensus process involving a variety of scientists, health policy experts and community leaders concluded that 'the known benefits of fish consumption far outweigh the theoretical and controversial potential adverse effects from mercury found in Alaska fish' and that 'substitution of other less healthy, less nutritious food for Alaska fish would result in far greater harm to health'. It is strongly recommended by the Alaskan Division of Public Health (and endorsed by ten partner organizations) that all Alaskans, including pregnant women, women who are breast feeding, women of child-bearing age, and young children continue unrestricted consumption of fish from Alaskan waters (SOA, 2001).

10.2.2. Canada

A number of experiences in Canada have lead to an approach where scientists, health policy makers, and community leaders work together to develop specific advice pertaining to specific findings in a manner that is respectful of cultural and social issues and of maximum benefit to the health of local consumers.

10.2.2.1. High levels of persistent organic pollutants in marine mammals

In 1995, Health Canada and Environment Canada officials presented research results on the levels of organochlorine compounds in Arctic marine mammals to the Northwest Territories (NWT) Technical Committee on Arctic contaminants. This committee comprised northern indigenous representatives, government health and research representatives, as well as representatives from the national Inuit organization, the Inuit Tapiriit Kanatami (ITK) (previously the Inuit Tapirisat of Canada (ITC)). The research indicated the presence of a number of organochlorine compounds, including toxaphene, dieldrin and polychlorinated biphenyls (PCBs), in high concentrations in ringed seal (*Phoca hispida*) fat and beluga whale (*Delphinapterus leucas*) fat and skin. The Committee's discussion of the data with regional representatives, the evaluation processes and decision-making responsibilities lead to consensus building on necessary future action. The regional representatives wanted to ensure that the release of the contaminant information was well coordinated, that the approach of providing 'advice' be used rather than a restrictive advisory or warning, and that the communication of any message must come from regional Inuit leaders in an easily understood local language. The following national press release was issued by the President of the ITK: "So far as we are aware, the risks to public health from continuing to eat beluga and seal blubber are very small and are outweighed by the benefits to you of these foods. However, Inuit must judge for themselves what is an acceptable risk for themselves and their families". Regional leaders presented the information to their communities in a coordinated fashion and through the ITK. They supported the basic message that the benefits of consuming these foods outweighed the risks and that food consumption decisions were ultimately individual decisions.

10.2.2.2. Mercury in Arctic waterfowl

In 2001, Health Canada released a health hazard assessment for Hg and selenium (Se) levels determined by the Canadian Wildlife Service in livers from waterfowl harvested in northern Canada between 1988 and 1994. The evaluation of the data led to a recommendation that "…it would be considered prudent to limit consumption of the livers…" of some waterfowl species. The evaluation information was immediately provided to the Yukon Contaminants Committee, the NWT Contaminants Committee, the Nunavut Contaminants Committee, the Nunavik Nutrition and Health Committee, and the Labrador Inuit Association. The diverse membership of these environmental contaminants committees provided the fora and perspectives necessary for a balanced discussion about the importance of the results for northerners. Dietary survey information on consumption of waterfowl livers was also of value in the discussions because it provided information on frequency and seasonal consumption of duck livers, as well as on economic, spiritual, cultural, and social benefits. Based on the discussions, the groups made the risk management decision not to issue advice to limit consumption of waterfowl livers, but to update current communication materials and to provide a fact sheet discussing the elevated levels of Hg found in some of the bird livers.

10.2.2.3. Lead shot in traditional foods

The results of studies on cord blood lead (Pb) carried out between 1993 and 1995 show that 7.6% of Nunavik newborns (n=238) had blood Pb levels of 100 µg/L and over, compared to 0.2% for babies from the southern part of Quebec (n=955). Subjects with high concentrations were uniformly distributed across the territory. Moreover, 2.1% of the samples from Nunavik showed blood Pb levels of >150 µg/L. These data, together with data collected in Nunavik during the 1992 Santé Québec survey, revealed that 24% of women between 18 and 39 years had blood Pb levels of >100 µg/L. While Pb exposure through contamination from industrial activities, from vehicle emissions, from ingestion of old Pb-based

paint or through drinking water was unlikely in the Inuit communities of Nunavik, the consumption of contaminated game was a plausible source of exposure. Relatively high levels of Pb have been reported in caribou (*Rangifer tarandus*) and many species of waterfowl that are key elements of the traditional Inuit diet. Caribou pick up Pb via the consumption of lichens, which in turn receive lead from the atmosphere. However, Pb levels observed in waterfowl are generally thought to be due to the ingestion by birds of lead shot used by hunters. Isotopic analyses of the Pb in the blood of infants from Nunavik and southern Quebec revealed that the source of Pb found in the infants from the two regions is different. Based on analyses of various brands of lead shot it has become clear that elevated levels of Pb in Nunavik infants come primarily from the direct ingestion of lead shot, lead fragments and lead dust in hunted game and less from airborne sources (as was the case in children from southern Quebec). Furthermore, X-rays of the abdomen of Nunavik Inuit reveal the presence of lead shot in the digestive system, thus supporting the hypothesis that lead shot ingestion is the main source of contamination. This problem was also observed in Cree communities from northern Ontario. These findings in Nunavik support the current bans in place in many countries on the use of lead shot (for the protection of waterfowl). They also suggest that less toxic shot, such as steel shot, be used by hunters wishing to protect themselves and their families from the health impacts of Pb exposure. Currently discussions are underway with hunters associations and the regional Health Board on a complete ban on lead shot and retailers are being asked to purchase only non-lead shot.

10.2.2.4. Mercury exposure in Nunavik women and the Arctic char promotion programme

Studies in Nunavik have indicated elevated levels of Hg in women of reproductive age. Most concentrations reported were in the range of a 'level of concern' and some at or above the 'action level', using Canadian terminology (see chapter 9, Figure 9·1), and may pose a risk to the health of the fetus. However, local public health authorities took into consideration the high level of intake of Se (which may counteract methylmercury-induced toxicity) in the diet of these same women, and consequently did not recommend a reduction in seafood consumption. Recently, a project to reduce risks among pregnant women exposed to food chain contaminants has commenced in Nunavik. This programme promotes the consumption of Arctic char (*Salvelinus alpinus*) among pregnant women living in three selected communities in Nunavik. Arctic char contain very few contaminants and are very nutritious. The evaluation of this project will include how extensively and consistently pregnant women participate in the programme and how efficient the programme is at reducing contaminant intake (especially Hg) while maintaining or improving nutritional status. Results of this project will help regional public health authorities decide whether or not to recommend this moderate change in eating pattern among a broader number of communities in Nunavik.

10.2.2.5. Seabird egg intervention on the lower north shore of the St. Lawrence River

Traditional consumption of seabird eggs in communities along the lower north shore of the St. Lawrence River has led to a pattern of contamination in human tissue that is very similar to that observed in the eggs themselves. Evaluation of the temporal trends of several persistent contaminants in umbilical cord plasma of newborns in these remote Canadian coastal populations, following advice to reduce seabird egg consumption, revealed reductions of between 25% and 69% over a seven-year period. No monthly or seasonal pattern was detected. Using n-3 fatty acid concentrations in umbilical plasma phospholipids as a surrogate for long-term fish consumption, the decrease in tissue concentrations of OCs could not be explained by a reduction in fish consumption. These results suggest that prenatal exposure to POPs has declined in this population. This decline seems to be due to a decrease in the contamination levels in the eggs themselves and a reduction in the consumption of seabird eggs following the public health advice provided to the communities.

10.2.3. Greenland

10.2.3.1. Lead levels

As in other countries, levels of blood Pb have declined as a result of the global reduction in use of leaded gasoline. To further reduce human exposure to Pb, discussions are underway with hunters associations to replace lead shot with less toxic alternatives.

10.2.3.2. Consumption of traditional foods

Greenland health authorities encourage the consumption of traditional foods for nutritional and cultural reasons. Despite documented high intakes of several contaminants through some dietary components, no advice has been given to reduce consumption of any specific traditional food items.

10.2.4. Iceland

Levels of POPs and metals in the Icelandic population are among the lowest in the Arctic. No risk management initiatives related to reduction in exposure to POPs and metals through food exposure are in place or contemplated at this time.

10.2.5. Faroe Islands

10.2.5.1. Consumption of pilot whale meat and blubber

Since 1989, research results from the Faroe Islands have shown that dietary intakes of Hg, the primary source of which is pilot whale (*Globicephala melaena*) meat and organs, is likely to slightly impair neurological development in children. It is also suspected that dietary PCBs, the main source of which is whale blubber, affect the central nervous system and sexual organs of the developing fetus. Based on the demonstrated effects of Hg exposure and on a general assessment of PCBs, the following dietary recommendation, which placed special em-

phasis on protection of women of child-bearing age, was issued in 1998.

Blubber – High PCB levels in blubber lead to a recommendation that adults eat pilot whale blubber only once to twice a month. However, the best way to protect the fetus against the potential harmful effects of PCBs is for girls and women not to eat blubber until they have given birth to their children.

Meat – The mercury content of pilot whale meat is high and is one of the main mercury sources. Therefore it is recommended that adults eat no more than one to two meals [based on pilot whale] a month. Women who plan to become pregnant within three months, pregnant women, and nursing women should abstain from eating pilot whale meat.

Organs - Pilot whale liver and kidneys should not be eaten at all.

These recommendations are still considered by the Faroese Public Health Authority to be the most appropriate advice at the present time. This dietary recommendation may be revised as new information is acquired.

Recent examinations have demonstrated that, on average, the Faroe Islands population has a PCB intake which is five to ten times higher than that of Danes. In addition it has been established that the PCB content of breast milk of Faroe Island women is very high compared to average breast milk PCB concentrations in most other Western European countries. Pilot whale meat and blubber have for many years been considered healthy for human consumption, and in recent years it has been stated again and again that marine fats, as found in whale blubber, can prevent cardiovascular disease. Public heath authorities in the Faroe Islands do not claim that pilot whale meat and blubber are unhealthy, but rather point out that pilot whale meat and blubber contain substances which international authorities consider capable of causing health problems. Remarkably, levels of Hg have declined by approximately 80% in the adult population over the last nine years. Similar declines have not been seen in the PCB levels. The decline in Hg levels appears to be based on reduced consumption of pilot whale products as proposed in the original public health advisories, and the short biological half-life of Hg.

10.2.6. Norway

10.2.6.1. Blood lead reductions

Blood Pb concentrations have declined in the general population in Norway over the last three decades, mainly due to the change from leaded to unleaded gasoline. Concentrations of Pb in blood reported in the first AMAP Assessment Report (AMAP, 1998) are some of the lowest ever reported or determined. In 2001, Norway decided to ban lead shot, based on the recent knowledge of Pb impacts on reproductive health and child development, even at relatively low levels.

10.2.6.2. Organic contaminants in fish

Fish taken from some coastal areas and fjords of southern Norway have been found to contain concentrations of POPs that exceed health guidelines. The same species are often regularly consumed by coastal populations. Women in these areas have been advised to avoid consumption during their child-bearing years and especially during pregnancy and nursing. The same high concentrations have not been documented in coastal areas and fjords north of the Arctic Circle.

10.2.6.3. Flame retardants in bird eggs

In early 2002, Norwegian health authorities announced a severe restriction on the consumption of gull (*Larus* spp.) eggs in northern regions because of findings of high levels of persistent flame retardants in these eggs. Gulls and other fish-eating birds are known to bioconcentrate most POPs, sometimes as much as one million times relative to levels in water. This is the first human consumption advisory based on flame retardants.

10.2.7. Sweden

The Swedish National Food Administration revised its advice on fish consumption in 1995 as a result of contamination levels determined in the Baltic Sea and some inland lakes and recommended as follows.

All consumers – A maximum of one meal per week of pike (*Esox lucius*), Baltic herring (*Clupea* spp.), Baltic salmon (*Salmo salar*), and eel and only occasional meals of cod (*Gadus morhua*) livers.

Girls and women of child-bearing age – No cod livers, a maximum of one meal per week of pike, eel and halibut (*Hippoglossus hippoglossus*), and a maximum of one meal per month of Baltic herring. For salmon the recommendation is a maximum of one meal per month regardless of whether it comes from the Baltic or inland lakes.

Lactating women – No consumption of pike, halibut, eel, or cod livers.

Pregnant women – No consumption of pike, halibut, eel, or cod livers, a maximum of one meal per month of herring from the Baltic and salmon from either the Baltic or inland lakes.

10.2.8. Finland

10.2.8.1. Food and fish advisories

Finland has set national limits for commercial food contamination and applies these to all food sold in the country, including the Arctic regions of Lapland. Levels of contaminants in sport fish are also monitored and there are no restrictions on fish consumption due to contaminants. There are also no restrictions on the consumption of reindeer meat from Finnish herds. Radionuclide contamination from the Chernobyl reactor accident in Russia in 1992 did not lead to contamination of reindeer in Finland.

10.2.9. Russia

10.2.9.1. Blood lead levels

Blood Pb concentrations in populations of the bigger cities of the Kola Peninsula are moderately elevated compared to levels in populations from neighboring areas in Norway. This is probably due to the continuing

use of leaded gasoline. Elevated blood levels (up to concentrations that are of medical concern) have been documented in children living in remote areas of the Kola Peninsula, with a diet based on natural, local products. This has recently been linked to the use of lead shot. The authorities are now working to prepare new guidelines on the use of lead shot.

10.2.9.2. Social and cultural impacts of modernization in the Kola Peninsula

The pollution problems associated with the nickel (Ni) smelters and refineries of the Kola Peninsula present a significant Arctic regional dilemma. Modernization of the Ni producing facilities, which will also help to reduce environmental pollution in the area, is likely to benefit the health of the workers and the general population of the area. However, modernization may also result in up to 50% of the workers losing their jobs. This level of job loss in remote regions is likely to have dramatic social consequences for communities and for the well-being of workers and their families. The political solution to date has been to slow the rate of the needed industrial rehabilitation, to give people the chance to retire, to retrain or to find other types of work. Authorities believe that remediation of the environment is of secondary importance to maintaining social cohesion during rapidly changing economic conditions. Recent new economic development in the area is promising and may enable more rapid environmental rehabilitation. A number of guidance documents for environmental health risk evaluation have been published by Russian public health authorities to promote the safety of populations in these and other parts of Russia.

10.3. Long-term impacts of risk reduction strategies and scenarios for changing global conditions

This section discusses the long-term implications of current and future risk management strategies on the exposure of Arctic populations to pollutants, and the influence of changing global conditions on health in the circumpolar region.

10.3.1. The influence of Arctic food on health risk management decisions

As omnivorous consumers, humans act as predators in the food chain. As a result they become exposed to ever increasing amounts of contaminants the higher up the food chain they feed. It is clear that food is the primary source of exposure to most POPs and a significant source of most metals, especially methylmercury. We are what we eat.

Strong evidence to support this reality occurs in recent findings provided in this report (see chapters 5 and 7).

Example A. In Canada, the Inuit consume fish and marine mammals as part of their traditional diet whereas the Dene/Métis consume fish and terrestrial mammals. Because marine mammals have significantly higher concentrations of POPs and metals than terrestrial mammals, the PCB and Hg levels in Inuit are approximately five times higher than the corresponding levels in Dene/Métis.

Example B. In Greenland, a recent study of contaminant levels among the Inuit living on the east and west coasts, both groups consuming a traditional diet high in marine mammals, indicated that while Hg levels in adults were similar, PCB levels were almost five-fold different between the two groups. Dietary evidence revealed that Greenlanders living on the east coast consumed polar bear (*Ursus maritimus*) fat which has very high PCB levels and moderate Hg concentrations, whereas the Greenlanders on the west coast eat more seals and walrus (*Odobenus rosmarus*) which are moderate in both PCBs and Hg.

Example C. Comparisons of non-indigenous and indigenous groups in Siberian Russia reveal that the non-indigenous group has a three-fold higher concentration of DDT even though it is consuming lesser amounts of traditional food than the indigenous group. These data indicate either contamination of the domestic food supply or a local source as the most significant contributor of DDT to population exposure in the region.

Examples A and B, and to the extent that food contamination is the cause, Example C, illustrate both the primary role of food in determining human body burdens and the importance of understanding local dietary patterns and contaminant levels in the dietary components when evaluating exposures and developing risk reduction strategies.

The health chapter of the first AMAP Assessment Report (AMAP, 1998) introduced the concept of the 'Arctic Dilemma' (i.e., vigorously supporting the consumption of traditional foods with their known nutritional, social, cultural and spiritual benefits while recognizing that these same foods are the primary source of environmental contaminants). Data in the present report strengthen this concept. The weight of evidence for harmful effects of POPs and metals has been augmented through epidemiological investigation (chapter 9) and biomarker studies (chapter 6). Yet knowledge of the nutritional value of traditional foods and the links they have with social, cultural, and spiritual integrity are also enhanced. Overall, the evidence is still compelling that traditional food is more nutritious than market food, reduces risk factors for several disease conditions such as heart disease and diabetes, and can bind communities together in ways that market foods do not. It is also clear that, in some areas of the Arctic, there is a need for some groups such as women who are fertile or pregnant to substitute their intake of the most contaminated food items with less contaminated but similarly nutritious items in order to minimize the risks for their babies. The AMAP Human Health Expert Group affirms that, despite the presence of contaminants in human milk, breast feeding is the best and safest form of infant nutrition, essential for optimal mother–child bonding, and critical for proper development of the infant immune system, and should therefore continue.

10.3.2. Global change and risk management

The development of risk reduction strategies for population groups must take account of changing global conditions and also changes in or surrounding the at-risk populations themselves. These changes may impact social,

cultural, spiritual, physical, or economic underpinnings of life in the circumpolar region. Some examples follow.

The availability, quality and delivery of healthcare can vary by region, size and location of community, and as a consequence of competing governmental and public health fiscal priorities. These factors can affect necessary monitoring of population trends (e.g., diseases, contaminant exposure, food consumption patterns, etc.), medical intervention and the availability of local advice from health professionals. Nevertheless, there are encouraging trends in health statistics that indicate overall population health is improving in many areas.

The emergence of new contaminants in the Arctic food chain (chapter 4), and, e.g., temperature changes that affect the permafrost, wildlife movements, disease vectors, food availability, water quality and other physical factors can significantly affect where communities live or how communities live.

Changes in the diet of indigenous communities toward consumption of less traditional food is, whilst lowering contaminant intakes, also leading to increased intake of carbohydrates, saturated fats and food additives, probably lower levels of intake of essential dietary components, and increased incidence of diabetes and heart disease (chapter 7).

Levels of smoking undoubtedly vary among population groups in the Arctic; however the rate is generally high and increasing in children and adolescents (chapter 8) as has been seen in southern regions of the circumpolar countries. Empowerment of communities to continue to address smoking rates (greater than 35% of pregnant mothers smoke in many areas) and a high intake of alcohol (rates of fetal alcohol syndrome up to five times national averages) will be essential to reduce these significant stressors of individual and community health.

Economic recession, natural resource development, increased immigration and tourism, low self-esteem among individuals and within communities, and the growing need for money to purchase commodities and food associated with a changing way of life can also affect community integrity and responses. These factors and other social pressures are likely to be partially responsible for high suicide rates, increasing substance abuse and the growing sense of poor self-worth associated with a lack of income (previously far less essential for traditional community life).

The Arctic peoples appear to be extremely sensitive to global pressures, supporting the need for ongoing monitoring of social and ecosystem changes and population health and well-being.

10.3.3. Future scenarios in the Arctic

Evaluating the combined effects of global pressures and local and global risk management strategies is speculative and can only be qualitative. There are, however, some significant international initiatives and also some scientific aspects that can be applied to speculation on future outcomes related to POPs, metals, and disease rates.

10.3.3.1. Speculation factors for POPs

1. The UN ECE Protocol on POPs is ratified by 2003 and primary sources of sixteen POPs are severely reduced or eliminated in Europe, Canada and the United States by 2010 and in Russia by 2020.
2. The Stockholm Convention on POPs is ratified by 2004 and primary sources of several POPs are severely reduced or eliminated throughout the Northern Hemisphere by 2020.
3. Secondary sources (environmental sinks) continue to yield POPs that are transported to the Arctic through 2030, however, the extent of the airborne transport from secondary sources declines by 20% by 2030.
4. Biological half-lives for POPs (the time it takes for POP levels to decline to 50% of their starting value) in human tissues are between one and seven years depending on the POP. If there are no additional exposures, and a mean half-life of five years is applied to existing tissue concentrations, then current levels of POPs in the Arctic population will decline by approximately 70% by 2010 and 98% by 2030.
5. Human intake of contaminants declines as the trend toward less consumption of traditional food (especially marine mammals) continues over the next ten years. In addition, human intake of contaminants declines as levels of contaminants in food slowly begin to decline after 2015 as a result of speculation factors 1 to 3.

Conclusions. Overall levels of POPs currently found in the tissues of Arctic residents may decline by 5% to 10% by 2010 and by 30% to 50% by 2030 (Figure 10·1). These changes will be most noticeable for PCBs, toxaphene, hexachlorobenzene, chlordane, DDT and DDE. The Arctic regions that will be most affected by reductions will be western and eastern Greenland and the Faroe Islands, followed by eastern Canada, western Alaska, and western and eastern Russia. Lesser reductions will be observed in western Canada, Iceland, Norway, Swe-

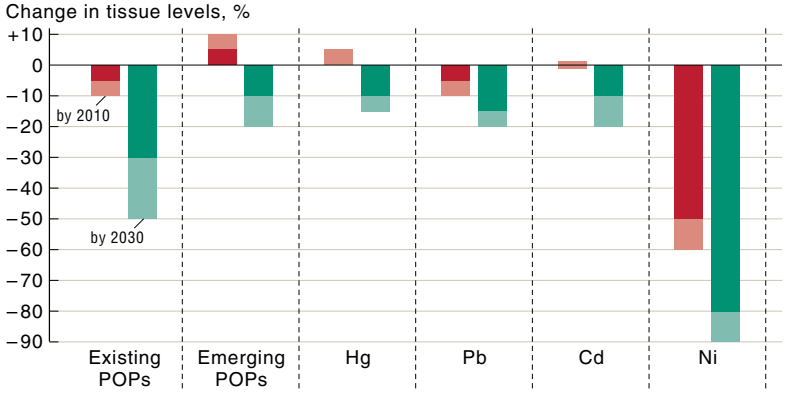

Figure 10·1. Predicted percentage change in levels of POPs and metals in the tissues of Arctic residents by 2010 and 2030 relative to 2000 levels. Speculation factors and assumptions taken into account in the predicted changes in tissue levels are described in sections 10.3.3.1, 10.3.3.2, and 10.3.3.3.

Aggregated estimates for all existing POPs in tissues are based on most affected Arctic areas (eastern/western Greenland, Faroe Islands, eastern Canada, western Alaska, eastern/western Russia). Hg: Greenland and eastern Canada only. Pb: All areas. Cd: Combined reductions (smokers and non-smokers). Ni: Russian nickle refinery areas only. Darker and lighter portions of columns show minimum and maximun predictions, respectively.

den, Finland, and central Russia (except for β-HCH) where the levels are already low and there is almost no reliance on marine mammals as a regular food source.

10.3.3.2. Speculation factors for metals

1. The UN ECE Protocol on Metals, which covers Hg, Pb and cadmium (Cd), is ratified by 2005. A global agreement is reached on metals emissions by 2010.
2. Total emissions and long-range transport of Hg continue and even increase from North America and southeast Asia through 2010 with continued reliance on fossil fuels (especially oil and coal) for energy. Traditional food consumption continues to decline over the next ten years. Unlike POPs, it is established that the half-life for mercury in human tissues is relatively short.
3. Global use of leaded fuels continues to decline and is absent in the Northern Hemisphere by 2015. Lead shot is replaced by less toxic alternatives in the circumpolar region by 2010, reducing Pb levels in the environment and Pb fragments in food portions collected through hunting. Traditional food consumption continues to decline over the next ten years. Unlike POPs, it is established that the half-life for lead in human tissues is relatively short.
4. Smoking, which is the single largest contributor to Cd levels in human tissues, decreases only marginally in Arctic populations by 2010 and significantly by 2030.
5. Industrial emissions of Ni and other metals from large smelting operations in the Arctic decrease significantly in western Russia by 2010.

Conclusions. Mercury levels in populations living in the eastern Canadian Arctic and Greenland will remain at current levels or increase by 5% through 2010 and will decline by 10 to 15% by 2030 (Figure 10·1). Lead levels measured in blood will continue to be low and will decline by 5% to 10% by 2010 and 15% to 20% by 2030. The currently small proportion of individuals exposed to lead shot fragments will reduce almost to zero by 2010, eliminating blood Pb levels above 50 µg/L across the Arctic by 2030. The percentage of the population with high levels of Cd will decline by 30% by 2030 as the proportion of smokers declines. Cd levels in individuals who continue to smoke will only decline marginally by 2030 as the number of cigarettes smoked per day per smoker gradually declines. The reduction in Cd levels in the general population (smokers and non-smokers) will be minimal by 2010 and between 10% and 20% by 2030. Ni levels in individuals living near Russian smelters will decline by 50% to 60% by 2010 and 80% to 90% by 2030.

10.3.3.3. Speculation factors for emerging POPs

1. National and international attention focuses on emerging POPs, such as polybrominated diphenylethers (PBDEs) and perfluorooctane sulfonate (PFOS) (see chapter 4), and on the current use pesticides such as lindane, and others, leading to severe restrictions or elimination of these chemicals under the UN ECE Protocol on POPs or the Stockholm Convention on POPs by 2010.

Conclusions: Levels of PBDEs, PFOS and β-HCH (resulting from use of lindane) will continue to increase by 5% to 10% through 2010 and will decline marginally by 10% to 20% by 2030 (Figure 10·1). Fewer POPs will be detected in the Arctic after 2010, and those found will be at lower levels, as most European and North American counties have been screening chemicals prior to their entry into commerce and those ratifying the Stockholm Convention on POPs will be developing screening systems.

10.3.3.4. Speculation factors for population morbidity and mortality

1. Globalization through to 2010 leads to more immigration, tourism, resource development, and pressure for income to afford commodities advertised globally and increasingly in the Arctic. The number and range of products consumed in the Arctic increases steadily as does the potential for introduction of infectious diseases.
2. Less traditional food and more commercial food are consumed by Arctic populations through 2010 followed by stabilization in the balance of traditional and commercial food consumption by 2030.
3. Increased awareness of globalization and contaminant issues and higher levels of attained education among Arctic populations through to 2030, leading to greater awareness of risks and benefits of lifestyle and diet choices.
4. Better healthcare and availability of services region-wide by 2010 and greater emphasis on and acceptance of disease prevention and management and health promotion by 2030.
5. Lower levels of exposure and body burdens of POPs and metals by 2030, as described in sections 10.3.3.1 to 10.3.3.3.
6. New and/or changing disease vectors associated with climate change.

Conclusions. Throughout the Arctic, disease rates for circulatory disorders, diabetes and some cancers will increase through 2010 as a result of globalization pressures, poorer dietary components including changes away from traditional foods, smoking and alcohol consumption, less exercise and, for cancers, current levels of POPs (Figure 10·2). These rates will begin to stabilize by 2030 as a result of lower levels of contaminants, greater public awareness and acceptance of healthy lifestyle at-

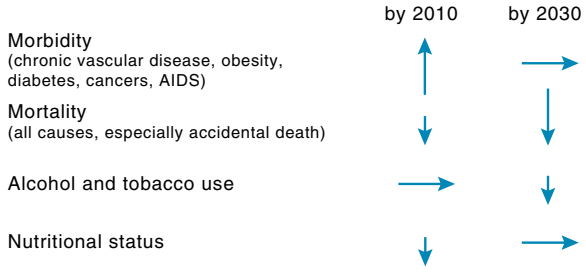

Figure 10·2. Qualitative future changes in morbidity, mortality, alcohol and tobacco use, and nutritional status among Arctic residents. Speculation factors and assumptions taken into account in the predicted changes are described in section 10.3.3.4. Orientation of the arrows and length of the shaft indicate direction of change and relative magnitude of change, respectively.

tributes and better healthcare and disease management approaches. Mortality rates will decline marginally by 2010 and significantly by 2030 as deaths due to accidents are reduced and prevention and management of diseases improves. Alcohol and tobacco use will continue unchanged through 2010 and decline by 2030 as awareness and understanding of the driving forces behind these lifestyle choices and greater community empowerment increase. Nutritional status will decline through 2010 and stabilize by 2030 as Arctic populations return to consumption of nutritious traditional foods that have lower levels of contaminants.

10.4. Conclusions and recommendations

The most effective and rapid risk management strategies are those developed locally with the community that 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 key success factors for these strategies will be based on how and when the people most affected are 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, especially the Protocols on POPs and metals to the LRTAP Convention, and the Stockholm Convention on POPs as these are 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 various activities to manage risks, there are likely to be minor decreases in POPs in the tissues of Arctic populations in Greenland, the Faroe Islands, eastern Canada, western Alaska, and eastern and western Russia by 2010 and minor increases in Hg levels in Greenland and eastern Canada. There are likely to be major decreases in both POPs and Hg levels in these same populations by 2030. In general, levels of most POPs and metals in populations in western Canada, Iceland, Norway, Sweden, Finland and central Russia are already reasonably low and are only likely to decline marginally by 2030. These predictions are heavily dependent on prompt ratification and implementation of the Stockholm Convention on POPs and other multinational environmental agreements.

There remains a key need to fill in data gaps in order 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 and who are most vulnerable to a range of change agents, e.g., POPs, metals, early childhood nutrition, education, availability of health care, tobacco and alcohol use, etc.

Serious consideration by all Arctic countries should be given to eliminating the use of lead shot as one relatively simple means of reducing the small number of excursions in blood Pb among consumers (especially children) of hunted game.

Chapter 11

Conclusions and Recommendations

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In this chapter the conclusions and recommendations from the report on AMAP Phase I (AMAP, 1998) are repeated (shown in italics) in order to allow comparisons with the conclusions and recommendations resulting from AMAP Phase II (shown in bold). This chapter also reviews progress since AMAP Phase I and provides concluding remarks on the combined effects 'multiple environmental stressors'.

11.1. Conclusions

In some areas, the indigenous peoples enjoy the same level of health as the non-indigenous populations, but in most areas their health is significantly poorer. Among indigenous peoples, lifestyle-related conditions such as obesity, diabetes, and circulatory disease have been more frequent than previously reported. Suicides and injuries also remain a significant cause of death in some parts of the circumpolar region.

11.1.1. General

(1) Contaminants of anthropogenic origin, such as POPs, metals and radionuclides, are spread globally, and contaminate the Arctic. The combination of environmental conditions and biomagnification in the marine and freshwater aquatic food webs results in accumulation of certain persistent contaminants in local food at levels which are often in excess of contaminant concentrations in the mid-latitudes where these contaminants originate. Consumed fish, marine mammals, terrestrial mammals, and birds are the major sources of human exposure to environmental contaminants in the Arctic and, as a consequence, several Arctic population groups are much more highly exposed through the diet than most populations in the developed world.

Conclusion (1) is still valid.

(2) The social, cultural, spiritual and physical health of Arctic indigenous peoples depends on the collection and consumption of country foods. A diet based on traditional foods is of high nutritional benefit. Consumption of n-3 fatty acids found in marine mammals and fish has been suggested as the component responsible for the lower incidence of cardiovascular disease in Alaska, Greenland, Canada and Japan. However, other nutrients may also influence the rate of cardiovascular disease. The consumption of local fish, meat, wild greens and berries provides the necessary dietary intake of most vitamins, essential elements and minerals. When market foods are purchased to supplement current country food diets, they should be selected for their nutrient quality. It is unlikely that market foods currently available to most Arctic indigenous populations can provide the nutritional equivalent of traditional food.

Conclusion (2) is still valid. In addition, there is still difficulty in scientifically comparing the benefits and risks of consuming a traditional or subsistence diet. These are important to quantify as dietary intakes are changing across the Arctic due to social pressures, perceived threats of contaminants, the availability of traditional food, and the availability and acceptability of store-bought foods.

(3) The influence of contaminants on fetal and neonatal development is of special concern. Preliminary results indicate that POPs and methylmercury concentrations are two- to ten-fold higher in breast milk and cord blood in some Arctic areas than in breast milk and cord blood from regions south of the Arctic. The fetus and the neonate are very vulnerable to the effects of many of these contaminants during this critical period of development.

Conclusion (3) is still valid and has been strengthened by new findings. For mercury, studies in the Faroe Islands indicate an association between fetal and neonatal exposure on the one hand and neurobehavioral deficits in children or development of hypertension in later life on the other. Similarly, preliminary findings from a larger cohort study comparing breast-fed with bottle-fed babies have strengthened concern for fetal and neonatal exposure to POPs in relation to respiratory infections in highly exposed children.

There is still a paucity of population health effects data (reproductive health outcomes, neurobehavioral development, immune system response, hypertension and cardiovascular diseases, etc.) for the Arctic. It is essential to complete the current cohort studies in Quebec, the Faroe Islands, Greenland and Finland. Meta-analyses of these studies may be possible and this would considerably increase the power of the individual cohort studies. Additional studies may be warranted when these are completed.

Fetal exposure to environmental contaminants may also result from occupational exposure experienced by the mother. All Arctic countries have, to a greater or lesser degree, tried to give special benefits for working in the north. Special attention is now focused on the health effects of workers in heavy industries of the Arctic, and the general trend is to decrease fetal exposure to harmful substances by removing pregnant women from difficult and contaminated working places when (or even before) a pregnancy is recognized.

11.1.2. Persistent organic pollutants

(4) There is both scientific and public concern about the possible adverse effects of POPs on pregnancy outcome, fetal development, child development, reproduction, male and female fertility, and the immune system. Sev-

eral of these effects may be mediated through endocrine disrupting properties of some POPs. DDT and its metabolites and some dioxin and PCB congeners have been implicated.

Conclusion (4) is still valid. In addition there is strong evidence from analyses of banked blood samples from Norway (non-Arctic donors) of an exponential increase in polybrominated diphenylethers since 1977. It is necessary to include these compounds and other 'new chemicals of concern' in future studies in order to evaluate concentrations in relation to findings on biomarkers.

(5) Despite the number of controls on several POPs imposed during the 1970s and 1980s, there is no evidence that levels in Arctic peoples have decreased. The persistence of POPs, their presence throughout the ecosystem, and the continued use of some POPs for disease vector control, all contribute to the constant influx of POPs into the Arctic environment and sustained levels of human exposure. There is very little information on temporal trends of POPs in Arctic populations. Monitoring of POPs in blood over the next decade is essential to establish whether or not risk management strategies for POPs are effective.

Conclusion (5) is still valid. Continued monitoring has provided new data, but significant temporal trends can not yet be observed due to the short period of observation. There are also few available banked (archived) Arctic population samples for retrospective studies. Further prospective monitoring of blood (and other biological samples as per AMAP protocols) and tissue banking are essential to establish these time trends in various Arctic populations. To assess changes in dietary patterns, information needs to be obtained from continued dietary surveys.

(6) Elevated levels of toxaphene and chlordane, coupled with current intake scenarios, suggest some indigenous groups are exposed to levels of these contaminants significantly above the Tolerable Daily Intake (TDI). Information on the levels of toxaphene in human tissues is limited.

No new information on dietary intake of toxaphene has appeared since Phase I. Conclusion (6) is still valid. New information on toxaphene concentrations in blood and breast milk confirms a high dietary intake of toxaphene.

(7) There is insufficient information to conclude whether the TDI for dioxins and furans and dioxin-like PCBs is being exceeded in Arctic populations. Also, there is as yet little conclusive scientific information directly linking harmful human effects to low levels of exposure to these contaminants.

New calculations of dioxin toxic equivalents from data provided in Phase I indicate that human intake of substances with dioxin-like effects (dioxins/furans, dioxin-like PCBs, and some organochlorine pesticides) is a matter of concern. Analyses of dioxin and dioxin-like compounds should be included in future human effect studies in order to enable a further assessment of the risks posed.

(8) While current levels of exposure to POPs in the Arctic are unacceptable, it is not always clear what public health measures should be taken to reduce the exposure of Arctic populations who rely on traditional foods for spiritual, cultural, physical, and nutritional benefits. Decision-making would be greatly aided by studies of the interactive effects of current levels of mixtures of POPs found in the traditional food supply. In the interim, the risks associated with a shift in dietary preference need to be considered along with the risks associated with the presence of contaminants in Arctic wildlife consumed as traditional food. Weighing the uncertainty in some of the TDI values (e.g., toxaphene) against the benefits of traditional food gathering and consumption, it has been recommended in most Arctic jurisdictions that consumption continue.

Although far from complete, progress has been made in studies on the interactive effects of current levels of mixtures of POPs in the traditional diet. Also, information on concentrations found in species used for food and in their various organs has improved. These scientific findings have improved the basis for dietary advice aimed at reducing exposure. Communication of public health advice and information differs in different areas of the Arctic due to different exposures, cultures, and public health practices, and is not commonly evaluated for its effectiveness. There is a need for an evaluation of the type, role and impact of public health advice or interventions.

(9) The concentrations of some POPs in breast milk have raised justifiable concern among mothers in the Arctic. The health benefits to newborns of breast feeding are substantial, e.g. mother-child bonding, immunological benefits transferred from mother to child, nutritional value, and reduced risk of bacterial contamination from poorly prepared formulas. Breast feeding should continue since the benefits of breast feeding outweigh the currently known risks attributed to infant exposure to contaminants through breast milk.

The substantial health benefits of breast feeding justify the development of programmes to inform mothers how adjustments within their traditional diets can significantly reduce levels of some contaminants in their milk without compromising nutritional value.

(10) Existing epidemiological evidence on the adverse effects of POPs in human is inconclusive and needs to be replicated because of the specific context in the Arctic in which there are differences in genetics, climate, food consumption patterns, and lifestyle among population groups.

Epidemiological evidence on the adverse effect of POPs on humans is emerging in Arctic and non-Arctic regions. The high exposure levels found in some Arctic communities are suspected to have a negative influence on human health. At the population level there is still no direct evidence of adverse effects on health status (mortality and morbidity). However, based on the weight of all available evidence within and outside the Arctic, there is reason for concern and a need to continue to reduce human exposure.

11.1.3. Heavy metals

(11) Existing data from the literature do not allow a valid estimate of spatial and temporal trends of exposure of Arctic peoples to mercury and cadmium, while for lead, a declining trend is observed. There is some evidence that the general decline in lead exposure parallels the decline in lead levels in industrialized areas.

Conclusion (11) is still valid for temporal trends during the period of review by AMAP (1997 to 2002). However, analyses of historical human and animal hair samples from the Arctic have shown a three-fold increase in mercury concentration and a ten-fold increase in lead from the 1400s to 2000.

(12) The high exposure of indigenous peoples to methylmercury in some Arctic areas is a matter of concern because of its neurotoxic effects on the fetus. Further investigation of both the levels and the influence of mercury on fetal development is warranted.

Dose-related, subtle neurotoxic effects of methylmercury have been observed in children in some regions of the Arctic. This emphasizes the concern for methylmercury exposure *in utero* and warrants local public health strategies in some regions to reduce the exposure of women of child-bearing age and especially those that are pregnant. The success of carefully developed public health strategies has been demonstrated in the Faroe Islands where interventions related to consumption of pilot whale meat have resulted in an 80% reduction in mean mercury body burdens.

(13) Lead levels in Arctic indigenous peoples have declined since the implementation of controls on lead emissions. Concentrations of lead in blood currently reported are below a level of concern, however, continued monitoring is warranted because of the potent effects of lead on neurological development in the fetus and children.

Conclusion (13) is still valid. In addition, recent data have shown that lead shot can be a significant source of human lead exposure.

(14) As elsewhere in the world, cadmium intake in the Arctic is mostly through smoking. However, as with mercury, the dietary exposure level will vary according to choice of food. Recent research indicates that kidney tubular dysfunction may occur at lower levels than previously considered.

The main source of cadmium exposure is smoking. Depending on food consumed, dietary intake in some Arctic regions is above the WHO provisional tolerable weekly intake (PTWI) and adds significantly to blood cadmium concentrations. The health consequences are at present unknown. Reduced smoking among Arctic residents will significantly reduce cadmium exposure.

(15) Arsenic and nickel exposures are mainly related to local industrial activities. The impacts on health of organo-arsenicals in marine food is at present not well understood. Studies of speciation of the naturally-occurring arsenicals in various animals and organs and their potential interactions with essential trace elements are needed.

Conclusion (15) is still valid. Ongoing epidemiological studies of occupationally exposed populations working in the nickel industry of the Kola Peninsula might reveal new information about the impact of nickel on fetal malformations and pregnancy outcomes in general.

11.1.4. Essential elements

(16) In general, ample supplies of selenium are provided through the diet in populations depending on marine food. Muktuk (whale skin) is the richest source. Populations predominately depending on food of terrestrial origin may have a marginal deficit in selenium supply. While animal experiments indicate selenium protects against the effects of some heavy metals (i.e., mercury, lead, and cadmium), its role as an antidote for metal toxicity in humans is at present hypothetical. The role of selenium as a protective factor against lipoprotein peroxidation and its purported beneficial effects in protecting against cancer and cardiovascular disease remain to be elucidated.

Most essential elements are amply supplied through food of marine origin while populations predominantly depending on food of terrestrial origin may have a marginal deficit. Recent data have shown that transition from a marine food to a market food diet reduces the intake of most trace elements to a level below the recommended daily intake.

11.1.5. Radiation

(17) The level of human exposure to anthropogenic radionuclides such as radiocesium in the Arctic has declined dramatically since the cessation of above-ground weapons testing. However, some Arctic populations still have higher exposures from anthropogenic radionuclides in the environment than those in the temperate zone because of unique features of Arctic terrestrial and freshwater ecosystems and the people's use of traditional foods. The cumulative dose to which a population is exposed must also include an estimate of the natural radionuclides. In some geographical areas, levels of natural radionuclides (derived from, e.g., radiolead and radiopolonium) have resulted in certain indigenous peoples being exposed to higher levels of radiation than the general population.

Human health effects associated with radioactivity are not addressed in this report – readers should consult the AMAP 2002 assessment on radioactivity in the Arctic (AMAP, 2003a).

(18) Increased UV radiation due to ozone depletion is not a major concern in terms of skin cancer because of the amount of clothing worn in Arctic environments. The primary health concern is the reflection of UV from snow and ice causing snow blindness. In addition, there is growing concern about the development of cataracts.

Conclusion (18) is still valid but this issue has not been further considered in this report.

11.1.6. Estimates of exposure and effects

(19) Food is the major exposure route for contaminants in the Arctic. The type and amount of human exposure to environmental contaminants varies throughout the circumpolar region according to the level of contaminants in the food, the amount and type of food consumed, and the method of food preparation. For these reasons, wildlife monitoring data provide a very uncertain basis for precise human exposure estimates. However, they are of great value for risk characterization as they identify the contaminants present in wildlife used as traditional food, and the most contaminated species, and can, therefore, contribute to the basis for dietary recommendations. Uniform methodology for dietary intake studies applied across the circumpolar region would greatly assist risk assessment.

Conclusion (19) is still valid. However, in addition to dietary intake, recent studies have shown that uptake, metabolism, and excretion of xenobiotic substances are under genetic influence, also lifestyle factors, e.g., smoking and body mass index influence the body burden. These factors should be considered in future studies.

(20) Determining adverse health effects in human populations due to the presence of contaminants in traditional foods and human milk is extremely difficult for methodological and ethical reasons. Results are also difficult to interpret because of a wide range of confounding factors (socio-economic, lifestyle and gender/age related). Monitoring contaminant concentrations in human tissues and using these data to estimate exposures will continue to be necessary as will a general reliance on animal studies of the effects of mixtures of contaminants and nutrients found in Arctic foods. Tissue banks would greatly assist the requirements for retrospective comparative studies of contaminant levels and effects.

Conclusion 20 is still valid. Progress in molecular biology has provided tools to identify biomarkers of effect for contaminants in human samples. Implementation of the human health effects programme combined with continued monitoring of exposure (including new contaminants of concern) would allow identification of early effects at the molecular level. It will also act as a warning system to signal increases in exposure to levels where overt signs of poisoning may appear. Little attention has been paid to the possible variation associated with the collection of blood samples from fasted versus non-fasted individuals. There is a need to set clear protocols for the collection and analysis of human tissue samples to minimize biological and analytical variability.

(21) Risk assessments are, in general, conducted for individual contaminants and not mixtures of contaminants. They are based upon extrapolations from single compound animal studies combined, when possible, with data from occupational exposure or accidental intoxication events. These assessments do not adequately account for the metabolic transformations of contaminants in the food chain, the possible interactions between contaminants concomitantly present in the environment, or the modifying influences of nutrients, such as trace elements and antioxidants, naturally present in Arctic traditional food. Consequently, the accepted guidelines for exposure are not necessarily applicable to Arctic communities.

Risk assessments have in general been conducted for individual contaminants and not mixtures of contaminants. New methodologies can integrate epidemiological and mechanistic biomarker effect studies on human samples making it possible to estimate the effects of current exposure levels of the actual mixture of contaminants (and metabolites), possible interactions, and the modifying effects of nutrients (combined effects). Guidelines on exposure levels in the Arctic should be based on recommendations from national or regional public health authorities.

(22) Very few studies of the effects of environmental contaminants on Arctic populations have been completed, therefore, existing literature does not provide convincing evidence of adverse health effects. On the other hand, the health-promoting effects of traditional diets have been well documented. This has lead to a reluctance to recommend changes to current patterns of traditional food consumption. Based on this review, there may be a need to consider providing food consumption advice to some people in some areas in order to protect the fetus from exposure to mercury and some POPs. It would be prudent for local health care providers to consider giving dietary advice to young women and pregnant women in order to help them reduce exposure levels prior to and during pregnancy. The consumption of less contaminated traditional food items that provide the nutritional needs of women of childbearing age should be promoted.

Conclusion (22) is still valid. Evidence of subtle effects of contaminants in traditional food is emerging in some Arctic populations. On the other hand, the nutritional and physiological benefits of traditional diets are well known. This supports the need for dietary recommendations to be based on risk-benefit analyses. Carefully considered and balanced dietary advice that takes risks and benefits into account is needed for children and adults of reproductive age for both genders.

(23) Contamination of the Arctic is part of a global process. While human exposures in the Arctic can be moderately reduced with some dietary modifications (provided these are culturally, socially and nutritionally suitable for the specific communities involved), it must be recognized that long-term exposure reductions can only be accomplished through international conventions resulting in bans and restrictions on production and use of the most toxic chemicals.

Conclusion (23) is still valid. There has been substantial effort to evaluate the weight of evidence for effects on human populations exposed to POPs and metals (from cellular effects to epidemiological outcomes) through various AMAP and national activities. There is a need to continue this process and to conduct the research needed to support this approach. Now that two international agreements on POPs (the Stockholm Convention on POPs and the POPs Protocol to the LRTAP Convention) and one on metals (the Metals Protocol to the LRTAP

Convention) have been successfully negotiated, it is essential that they be promptly ratified and so enter into force. These agreements will only succeed in reducing environmental burdens and human exposures if they are implemented and monitored. In addition, the global assessment of mercury initiated by UNEP in 2000 provides an opportunity to ensure that Arctic concerns are reflected in the considerations for global action on mercury.

11.2. Recommendations

11.2.1. At the scientific assessment level

(1) Continue monitoring contaminants in human blood and tissues in order to reveal temporal and spatial trends.

Recommendation (1) is still valid. It has been five years since the completion of most of the original circumpolar blood monitoring survey. Re-sampling during AMAP Phase III would enhance the ability to determine whether or not human exposures are declining.

(2) Combine experiences from the rapidly expanding disciplines of biomarker research and molecular epidemiology with existing monitoring programs.

Recommendation (2) is still valid. The AMAP Human Health Expert Group has developed a human health effects programme that should be more extensively applied.

(3) Develop uniform methods and initiate studies which will allow objective dietary assessments and exposure estimations.

Continue the process and apply uniform methods for the objective assessment of diets and estimation of exposure. In addition, promote studies on the nutrient content of traditional food items.

(4) Complete human populations studies of contaminant-related effects on reproduction and fetal and child development.

Continue to support human population studies of contaminant-related effects on reproduction and fetal and child development, immune and hormone status, and cancer.

(5) Revise existing guidelines for tolerable intakes of contaminants based upon studies of interactions among individual contaminants present in Arctic foods, and between contaminants and nutrients.

Guidelines for tolerable intakes of contaminants should be based on regional and local needs and should strike a balance between benefits from traditional foods and potential negative effects from exposure to contaminants.

(6) Create and manage tissue/specimen banks in the circumpolar region.

Recommendation (6) is still valid. In addition, support is necessary for the implementation of laboratory harmonization programmes to enhance the inter-comparability of data; and to ensure the collection of blood samples that are based on standard protocols, including the collection of samples from fasted subjects.

11.2.2. At the public health policy level

(7) Apply communication and consultation approaches that enhance the development of local information and advice for indigenous peoples about contaminant exposures and effects.

Apply communication and consultation approaches that enhance the development of local information and advice for indigenous peoples about benefits of traditional food, contaminant exposure and effects.

(8)Advise Arctic peoples to continue to eat traditional food and to breast feed their children, and develop dietary advice for girls, women of child-bearing age and pregnant women which promotes the use of less contaminated food items while maintaining nutritional benefits.

Advise Arctic peoples to continue to eat traditional food and to breast feed their children taking dietary recommendations into consideration. Where necessary, as a means of reducing exposure, ensure that the combination of traditional food and market food provides similar nutritional value to the original diet.

11.2.3. At the national and international policy level

(9) Initiate measures to reduce and control regional industrial emissions of contaminants.

Recommendation (9) is still valid. Strengthen international efforts to control production, use and emissions to the environment of persistent organic pollutants and mercury. Support the UNEP Global Mercury Assessment.

(10) Strengthen international effort to control production and use of persistent organic pollutants.

Ratify and implement the Århus Protocols on POPs and Heavy Metals and the Stockholm Convention on POPs, including participating in the global monitoring of human exposure to be established under the latter.

Support a global assessment of the linkages between health and the environment.

11.3. Progress since AMAP Phase I

During AMAP Phase I the Human Health Expert Group prepared a comprehensive review of existing information on the health implications of exposure to a defined list of priority contaminants and included evidence of exposure in various parts of the Arctic. Exposure was predominantly dietary. The objectives of the first phase of the AMAP Human Health sub-programme, developed in Nuuk in 1992, were however not fully met due to logistical and financial problems. Thus the first phase of the programme effectively became a pilot programme, i.e., the first study of blood contaminant levels for most of the eight Arctic countries in which sampling proce-

dures and analyses were standardized to allow comparisons between countries and regions.

During AMAP Phase II a more extensive human health programme was undertaken. The outcome of the Phase II programme confirms the exposure levels found during the pilot study and has extended the geographical coverage such that it is almost circumpolar. Owing to the length of the monitoring period (1994 to 2001) temporal trends in human exposure to contaminants can not yet be established. Statistically significant trend estimates will require a sustained monitoring programme over several decades. Such a programme is important as current exposure levels in certain areas and for certain contaminants exceed existing health guidelines.

During AMAP Phase II more information on contaminant concentrations in species relevant to human diets was obtained from data produced by the AMAP Heavy Metal and POPs Assessment Groups. This allows more detailed and more specific dietary guidance. Progress in procedures for dietary assessment and validation of dietary indicators (e.g., n-3 : n-6 fatty acid ratios) has also improved the basis for advice.

The mandates of AMAP Phases I and II defined the priority contaminants to be monitored. However, as described in chapter 4, new contaminants of concern have since appeared. There is an urgent need to include such contaminants in future monitoring programmes.

The main achievement of Phase II has been the development and implementation of a human health effects monitoring programme (see chapter 6). Although implementation is now almost circumpolar, the process should be continued and expanded in a continuous, coordinated programme.

11.4. Concluding remarks on combined effects

Human health status is determined by an interaction between genetic endowment and the influence of environmental factors. Genetic factors can exert an influence through entire ethnic populations, in families, and at an individual level. As a consequence, studies of genetic susceptibility (genetic epidemiology) are important for assessing the impacts of environmental exposure at all levels of the population.

In terms of health, environmental factors may be either positive (e.g., nutrients) or negative (e.g., contaminants and radiation). While the genetic determinants of health at the level of the individual are stochastic, the environmental influences are dose-related and as such include both qualitative and quantitative aspects. As a consequence, a holistic approach to describing the health–environment relationship is a huge task and one which the current state of scientific knowledge cannot support, despite considerable progress in this field over the last ten years. Although the problems are mainly of a methodological nature, it is the current lack of understanding within the scientific community of the need for a multidisciplinary approach that is of most importance.

Environmental health determinants are chemical, physical, biological, psychological, and societal in nature. This means that besides geneticists, epidemiologists and toxicologists, natural scientists, sociologists, psychologists, medical experts and anthropologists must also be involved if a holistic approach to the description of the health–environment relationship is to be developed.

During AMAP Phase I the mandate was to monitor the specified priority contaminants and to evaluate the potential risks to human health. In Phase II the mandate was expanded through the Alta Declaration to an evaluation of the influence on human health of 'multiple environmental stressors'. This expanded mandate has been the focus of the present report. As the scientific background required to fulfill the Alta mandate is currently insufficient, the work is not yet complete. Nevertheless, it is generally agreed that significant progress has been made and the work is headed in the right direction.

Recent scientific advances have improved the ability to address the impacts of multiple stressors. Classical epidemiology can identify the combined effects of environmental exposures in a given population. However, this is insufficient under Arctic conditions owing to small population sizes, the lack of specificity concerning which exposure causes which effect, and its capacity to measure only overt effects. An improvement has been the coupling of epidemiological methods to subclinical endpoints, e.g., neurophysiological effects such as evoked nerve potentials (see chapter 9). In this manner, lower exposure levels can be related to effects. Further resolution of low-exposure related effects will come from a coupling of epidemiological methods with the experience obtained in molecular biology and genetics (see chapter 6). While the effect that is measured may be of decreasing immediate clinical significance, its early detection will, in the long-term, be of increasing significance for the development of disease prevention policies.

The identification of new contaminants in the environment often complicates and confounds efforts to identify causal agents. Many of these new contaminants have poorly defined acute, chronic and multi-generational toxicity. These uncertainties notwithstanding, the finding of effects at a sub-clinical level is a strong rationale for immediate reduction of the actual exposure level. They also call for a more intensive focus of the AMAP Human Health Effects Programme on the nature and extent of the adverse effects that may already be present in Arctic populations.

Exposure to contaminants in Arctic populations is almost exclusively the result of consuming traditional food. This food, at the same time, is of great importance to sustained physical health and cultural and spiritual integrity. Therefore, there is an essential need to balance risk assessments with evaluations of the nutritional benefits of traditional food.

The main conclusion of this report is that current human exposure to the existing level and mixture of contaminants in the Arctic influences the health of some Arctic populations in a negative manner. Subtle effects have been demonstrated to be present at a sub-clinical level. In relation to potential effects on future generations, efforts to reduce the input of persistent substances to ecosystems world-wide should be accelerated. Furthermore, the process initiated through AMAP Phases I and II should be continued and expanded to include all relevant disciplines with the aim of pursuing a more holistic assessment of the health of Arctic peoples.

Personal communications

Berner, J., 2001. Alaska Native Tribal Health Consortium, Alaska, United States.

Bjerregaard, P., 2001. National Institute of Public Health, Copenhagen, Denmark.

Bonefeld-Jørgensen, E., 2001, 2002. Department of Environmental and Occupational Medicine, University of Aarhus, Denmark.

Dewailly, É., 2001. National Institute of Public Health, Laval University, Quebec, Canada.

Deutch, B., 2001. Department of Environmental and Occupational Medicine, Aarhus University, Denmark.

Hansen, J.C., 2001. Department of Environmental and Occupational Medicine, Aarhus University, Denmark.

Klopov, V., 2001, 2002. Regional Centre 'Monitoring of the Arctic', St. Petersburg, Russia.

Middaugh, J., 2001. Section of Epidemiology, State of Alaska.

Muckle, G., 2000. Department of Social and Preventive Medicine, Laval University and Public Health Research Unit, CHUQ Research Centre (CHUL), Beauport, Quebec.

Mussalo, H., 2002. State Provincial Office of Lapland, Rovaniemi, Finland.

Odland, J.Ø., 2000. Tromsø Universitet, Institute of Community Medicine, Tromsø, Norway.

Olafsdottir, K., 2001. Department of Pharmacology and Toxicology, University of Iceland, Reykjavik, Iceland.

Prinz, S., 2001. Behavioral Health Consultant, Alaska Native Tribal Health Consortium.

Soininen, L., 2001. State Provincial Office of Lapland, Rovaniemi, Finland.

Weber, J.-P., 2002. L'institute nationale de sante publique du Quebec, Sainte-Foy, QC, Canada.

Weihe, P., 2001, 2002. Department of Occupational and Public Health, Tórshavn, Faroe Islands.

Vlasov, S., 2001. Regional Centre 'Monitoring of the Arctic', St. Petersburg, Russia.

References

Aarkrog, A., P. Aastrup, G. Asmund, P. Bjerregaard, D. Boertmann, L. Carlsen, J. Christensen, M. Cleemann, R. Dietz, A. Fromberg, E. Storr-Hansen, N.Z. Heidam, P. Johansen, H. Larsen, G.B. Paulsen, H. Petersen, K. Pilegaard, M.E. Poulsen, G. Pritzl, F. Riget, H. Skov, H. Spliid, P. Weihe and P. Wåhlin, 1997. Environmental Project No. 356, 1997. Ministry of Environment and Energy, Danish Environmental Protection Agency, Copenhagen. 792 pp.

Ada, G.L., 1993. Vaccines. *In*: Fundamental Immunology. 3rd ed. pp. 1309–1352. New York, Raven Press, Ltd.

Adami, H.O., R. Bergstrom, M. Mohner, W. Zatonski, H. Storm, A. Ekbom, S. Tretli, L. Teppo, H. Ziegler, M. Rahu, R. Gurevicius and A. Stengrevics, 1994. Testicular cancer in nine northern European countries. *International Journal of Cancer*, 59:33–38.

Ahlborg, Jr. G., C. Hogstedt, L. Bodin and S. Barany, 1989. Pregnancy outcome among working women. *Scandanavian Journal of Work Environment & Health*, 15:227–233.

Alcock, R.E. and K.C. Jones, 1996. Dioxins in the environment: A review of trend data. *Environmental Science & Technology*, 30: 3133–3143.

Alekseeva, N.V., A.L. Molokov and T.I. Astakhova, 1998. New approaches to smoking prevention in the north. *International Journal of Circumpolar Health*, 57:489–492.

AMAP, 1997. Arctic Pollution Issues: A State of the Arctic Environment Report. Arctic Monitoring and Assessment Programme, Oslo, Norway, xii+188 pp.

AMAP, 1998. Hansen J.C., A. Gilman, V. Klopov, and J.O. Odland (eds.) Pollution and Human Health. *In*: AMAP Assessment Report: Arctic Pollution Issues, pp. 775–844. Arctic Monitoring and Assessment Programme, Oslo, Norway.

AMAP, 1999. AMAP Trends and Effects Programme: 1998–2003. AMAP Report 99:7. Arctic Monitoring and Assessment Programme, Oslo, Norway.

AMAP, 2000. AMAP Report on Issues of Concern: Updated Information on Human Health, Persistent Organic Pollutants, Radioactivity, and Mercury in the Arctic. AMAP Report 2000:4. Arctic Monitoring and Assessment Programme, Oslo, Norway, 69 pp.

AMAP, 2003a. AMAP Assessment 2002: Radioactivity in the Arctic. Arctic Monitoring and Assessment Programme, Oslo, Norway.

AMAP, 2003b. AMAP Assessment 2002: Heavy Metals in the Arctic. Arctic Monitoring and Assessment Programme, Oslo, Norway.

AMAP, 2003c. AMAP Assessment 2002: Persistent Organic Pollutants in the Arctic. Arctic Monitoring and Assessment Programme, Oslo, Norway.

AMAP, 2003d. AMAP Assessment 2002: The Influence of Global Change on Arctic Contaminant Pathways. Arctic Monitoring and Assessment Programme, Oslo, Norway.

Ames, G.M. and L.A. Rebhun, 1996. Women, alcohol and work: interactions of gender, ethnicity and occupational culture. *Social Science and Medicine*, 43:1649–1663.

Amin-Zaki, L., S. Alhassani, M. Majeed, T.W. Clarkson, R. Doherty and M. Greenwood, 1976. Perinatal methylmercury poisoning in Iraq. *American Journal of Diseases of Children*, 130: 1070–1076.

Andersen, L.F., K. Solvoli, L.R.K. Johansson, I. Salminen, A. Aro and C.A. Drevon, 1999. Evaluation of a food frequency questionnaire with weighed records, fatty acids and alpha-tocopherol in adipose tissue and serum. *American Journal of Epidemiology*, 150:75–87.

Andersen, S., B. Hvingel, K. Kleinschmidt, T. Jørgensen and P. Lauberg, 2000. Jodindtagelse blandt ældre i vest- og øst Grønland. Proceedings from Nuna Med 2000 conference, pp. 61–63.

Andersen, H.R., A.M. Vinggaard, T.H. Rasmussen, I.M. Gjermandsen and E.C. Bonefeld-Jørgensen, 2002. Effects of currently used pesticides in assays for estrogenicity, androgenicity and aromatase activity *in vitro*. *Toxicology and Applied Pharmacology* 179(1):1–12.

Angerer, J., C. Mannschreck and J. Gundel, 1997. Biological monitoring and biochemical effect monitoring of exposure to polycyclic aromatic hydrocarbons. *International Archives of Occupational and Environmental Health*, 70:365–377.

Arnold, S.F., D.M. Klotz, B.M. Collins, P.M. Vonier, L.J. Jnr. Guillette and J.A. McLachlan, 1996. Synergistic activation of estrogen receptor with combinations of environmental chemicals. *Science*, 272:1489–1492.

Arnold, S.F., J.M. Bergeron, D.Q. Tran, B.M. Collins, P.M. Vonier, D. Crews, W.A. Toscano and J.A. McLachlan, 1997a. Synergistic responses of steroidal estrogens *in vitro* (yeast) and *in vivo* (turtles). *Biochemical and Biophysical Research Communications*, 235:336–342.

Arnold, S.F., P.M. Vonier, B.M. Collins, D.M. Klotz, L.J. Guillette Jr. and J.A. McLachlan, 1997b. *In vitro* synergistic interaction of alligator and human estrogen receptors with combinations of environmental chemicals. *Environmental Health Perspectives*, 105(3):615–618.

Asplund, L., B.G. Svensson, A. Nilsson, U. Eriksson, B. Jansson, S. Jensen, U. Wideqvist and S. Skerfving, 1994. Polychlorinated biphenyls, 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane (*p,p'*-DDT) and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)-ethylene (*p,p'*-DDE) in human plasma related to fish consumption. *Archives of Environental Health*, 49:477–486.

ATSDR, 1994. Toxicological profile for alpha-, beta-, gamma- and delta- hexachlorocyclohexane. U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

ATSDR, 1995. Toxicological profile for polyaromatic hydrocar-

bons. U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

ATSDR, 1996. Toxicological profile for selenium. U.S. Department of Health and Human Services, Public Health Service, Atlanta.

ATSDR, 1999a. Toxicological profile for pentachlorophenol (Draft). U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

ATSDR, 1999b. Toxicological profile for cadmium. U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

ATSDR, 1999c. Toxicological profile for mercury. U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

ATSDR, 2000a. Toxicological profile for endosulfan. U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

ATSDR, 2000b. Toxicological profile for arsenic. U.S. Department of Health and Human Services, Public Health Service Agency for Toxic Substances and Disease Registry, Washington DC.

Auger, J., J.M. Kunstmann, F. Czyglik and P. Jouannet, 1995. Decline in semen quality among fertile men in Paris during the past 20 years. *New England Journal of Medicine*, 332:281–285.

Autrup, H., 2000. Genetic polymorphisms in human xenobiotica metabolizing enzymes as susceptibility factors in toxic response. *Mutatation Research*, 464:65–76.

Axmon, A., L. Rylander, U. Stromberg and L. Hagmar, 2000. Time to pregnancy and infertility among women with a high intake of fish contaminated with persistent organochlorine compounds. *Scandanavaian Journal of Work Environment & Health*, 26: 199–206.

Axtell, C.D., C. Cox, G.J. Myers, P.W. Davidson, A.L. Choi, E. Cernichiari, J. Sloane-Reeves, C.F. Shamlaye and T.W. Clarkson, 2000. Association between methylmercury exposure from fish consumption and child development at five and a half years of age in the Seychelles Child Development Study: an evaluation of nonlinear relationships. *Environmental Research*, 84:71–80.

Ayotte, P., S. Giroux, E. Dewailly, M. Hernandez Avila, P. Farias, R. Danis and C. Villanueva Diaz, 2001. DDT spraying for malaria control and reproductive function in Mexican men. *Epidemiology*, 12:366–367.

Baaijens, P.A., 1986. Health effect screening and biological monitoring for workers in organotin industries. *In*: Toxicology and analytics of the tributyltins – the present status. Proceedings of a workshop organized by the Organotin Environmental Programme Association, pp. 191–211, Berlin.

Bailey, R.E., 2001. Global hexachlorobenzene emissions. *Chemosphere*, 43:167–182.

Baranowska, I., 1995. Lead and cadmium in human placentas and maternal and neonatal blood (in a heavily polluted area) measured by graphite furnace atomic absorption spectrometry. *Occupational and Environmental Medicine*, 52:229–232.

Barker, D.J., 1990. Fetal and Infant Origins of Adult Disease. *British Medical Journal*, 301(676):1111.

Barnes, G.E., 1979. Solvent abuse: A review. *International Journal of Addictions,* 14:1–26.

Barnett, J.B., L. Barfield, R. Walls, R. Joyner, R. Owens and L.S. Soderberg, 1987. The effect of *in utero* exposure to hexachlorobenzene on the developing immune response of BALB/c mice. *Toxicology Letters*, 39:263–274.

Barrie, L.A., D.J. Gregor, B.T. Hargrave, R. Lake, D.C.G. Muir, R. Shearer, B. Tracey and T.F. Bidleman, 1992. Arctic contaminants: sources, occurrence and pathways. *Science of the Total Environment*, 122:1–74.

Beard, J., S. Marshall, K. Jong, R. Newton, T. Triplett-McBride, B. Humphries and R. Bronks, 2000. 1,1,1-trichloro-2,2-bis (*p*-chlorophenyl)-ethane (DDT) and reduced bone mineral density. *Archives of Environmental Health*, 55:177–180.

Becker, W., 1995. Sociale och regionale faktorer påverkar matvanor och næringsintag. *Vår Føda*, 47:4–12.

Ben-Jonathan, N. and R. Steinmetz, 1998. Xenoestrogens: The emerging story of Bisphenol A. *Trends in Endocrinology and Metabolism*, 9:124–128.

Benedetti, J.L., F. Turcotte, M. Lefebvre, F. Therrien and J.P. Weber, 1992. Blood and urinary cadmium levels in Inuit living in Kuujjuaq, Canada. *Science of the Total Environment*, 127:167–172.

Benedetti, J-L, E. Dewailly, F. Turcotte and M. Lefebvre, 1994. Unusually high blood cadmium associated with cigarette smoking among three subgroups of the general population, Quebec, Canada. *Science of the Total Environment*, 152:161–167.

Bergman, A., E. Klasson-Wehler and H. Kuroki, 1994. Selective retention of hydroxylated PCB metabolites in blood. *Environmental Health Perspectives*, 102:464–469.

Berkowitz, G.S., R.H. Lapinski, S.E. Dolgin, J.G. Gazella, C.A. Bodian and I.R. Holzman, 1993. Prevalence and natural history of cryptorchidism. *Pediatrics*, 92:44–49.

Berman, S., 1991. Epidemiology of acute respiratory infections in children of developing countries. *Review of Infectious Diseases,* 13(6):454–462.

Bertelsen, A., 1943. Grønlandsk medicinsk statistik og nosografi: Undersøgelser og erfaringer fra 30 Aars grønlandsk lægevirksomhed. Bd. IV: Akutte infektionssygdomme i Grønland. *Meddelelser om Grønland*, 117(4).

Berti, P.R., O. Receveur, H.M. Chan and H.V. Kuhnlein, 1998. Dietary exposure to chemical contaminants. *Environmental Research*, Section A, 76:131–142.

Bigsby, R., R.E. Chapin, G.P. Daston, B.J. Davis, J. Gorski, L.E. Gray, K.L. Howdeshell, R.T. Zoeller and F.S. vom Saal, 1999. Evaluating the effects of endocrine disruptors on endocrine function during development. *Environmental Health Perspectives*, 107(4):613–618.

Birnbaum, L.S., 1995. Developmental effects of dioxins and related endocrine disrupting chemicals. *Toxicology Letters*, 82–83: 743–750.

Bitman, J. and H.C. Cecil, 1970. Estrogenic activity of DDT analogs and polychlorinated biphenyls. *Journal of Agricultural and Food Chemistry*, 18:1108–1112.

Bjerregaard, P. and T. Curtis, 2002. Cultural change and mental health in Greenland. *Social Science and Medicine*, 54:33–48.

Bjerregaard, P. and J.C. Hansen, 1996. Effects of smoking and marine diet on birthweight in Greenland. *Arctic Medical Research*, 55:156–164.

Bjerregaard, P. and J.C. Hansen, 2000. Organochlorines and heavy metals in pregnant women from the Disco bay area in Greenland. *Science of the Total Environment*, 245:195–202.

Bjerregaard, P. and T.K. Young, 1998. Health of a population in transition. The Circumpolar Inuit. Munksgaard, Copenhagen. 287 pp.

Bjerregaard, P., G. Mulvad and H.S. Pedersen, 1997. Cardiovascular risk factors in Inuit of Greenland. *International Journal of Epidemiology*, 26:1182–1190.

Bjerregaard, P., H.S. Pedersen and G. Mulvad, 2000. The associations of a marine diet with plasma lipids, blood glucose, blood pressure and obesity among the Inuit in Greenland. *European Journal of Clinical Nutrition*, 54:732–737.

Bjerregaard, P., E. Dewailly, P. Ayotte, T. Pars, L. Ferron and G. Mulvad, 2001. Exposure of Inuit in Greenland to organochlorines through the marine diet. *Journal of Toxicology and Environmental Health*, part A, 62:69–81.

Bjerve, S.K., L. Thoresen, K. Bonaa, T. Vik, H. Johnse and A.M. Brubakk, 1992. Clinical studies with alpha-linolenic acid and long-chain n-3 fatty acids. *Nutrition*, 8(2):130–132.

Blanchet, C., E. Dewailly, P. Ayotte, S. Bruneau, O. Receveur and B.J. Holub, 2000. Contribution of selected traditional and market foods to the diet of Nunavik Inuit women. *Canadian Journal of Dietetic Practice and Research*, 61:50–59.

Bloem, M.W., M. Wedel, R.J. Egger, A J. Speek, J. Schrijver, S. Saowakontha and W.H. Schreurs, 1990. Mild vitamin A deficiency and risk of respiratory tract diseases and diarrhea in preschool and school children in northeastern Thailand. *American Journal of Epidemiology*, 131:332–339.

Blok, W.L., M.B. Katan and J.W. van der Meer, 1996. Modulation of inflammation and cytokine production by dietary (n-3) fatty acids. *Journal of Nutrition*, 126:1515–1533.

Bolger, R., T.E. Wiese, K. Ervin, S. Nestich and W. Checovich, 1998. Rapid screening of environmental chemicals for estrogen receptor binding capacity. *Environmental Health Perspectives*, 106:551–557.

Bonefeld-Jørgensen, E.C., H. Autrup and J.C. Hansen, 1997. Effect of toxaphene on estrogen receptor functions in human breast cancer cells. *Carcinogenesis*, 18:1651–1654.

Bonefeld-Jørgensen, E.C., H.R. Andersen, T.H. Rasmussen and A.M. Vinggaard, 2001a. Effect of highly bioaccumulated polychlorinated biphenyl congeners on estrogen and androgen receptor activity. *Toxicology*, 158:141–153.

Bonefeld-Jørgensen, E.C., S.M. Moller and J.C. Hansen, 2001b. Modulation of atherosclerotic risk factors by seal oil: a preliminary assessment. *International Journal of Circumpolar Health*, 60:25–33.

Boon, J.P., F. Eijgenraam, J.M. Everaarts and J.C. Duinker, 1989. A structure–activity relationship (SAR) approach towards metabolism of PCBs in marine animals from different trophic levels. *Marine Environmental Research*, 27:159–176.

Bosma, H., M.P. van Boxtel, R.W. Ponds, P.J. Houx and J. Jolles, 2000. Pesticide exposure and risk of mild cognitive dysfunction. *Lancet*, 356:912–913.

Boyle, P., P. Maisonneuve and P. Napalkov, 1995. Geographical and temporal patterns of incidence and mortality from prostate cancer. *Urology*, 46:47–55.

Bradlow, H.L., D.L. Davis, G. Lin, D. Sepkovic and R. Tiwari, 1995. Effects of pesticides on the ratio of 16 alpha/2-hydroxyestrone: a biologic marker of breast cancer risk. *Environmental Health Perspectives*, 103(7):147–150.

Brandt, A.M., 1996. Recruiting women smokers: the engineering of consent. *Journal of the American Medical Women's Association*, 51:63–66.

Breivik, K., A. Sweetman, J.M. Pacyna and K.C. Jones, 2002. Towards a global historical emission inventory for selected PCB congeners – a mass balance approach. 1. Global production and consumption. *Science of the Total Environment*, 290: 181–198.

Bromwich, P., J. Cohen, I. Stewart and A. Walker, 1994. Decline in sperm counts: an artefact of changed reference range of 'normal"? *British Medical Journal*, 309:19–22.

Brouwer, A., 1991. Role of biotransformation in PCB-induced alterations in vitamin A and thyroid hormone metabolism in laboratory and wildlife species. *Biochemical Society Transactions*, 19:731–737.

Brouwer, A., D.C. Morse, M.C. Lans, A.G. Schuur, A.J. Murk, E. Klasson-Wehler, A. Bergman and T.J. Visser, 1998. Interactions of persistent environmental organohalogens with the thyroid hormone system: mechanisms and possible consequences for animal and human health. *Toxicology and Industrial Health*, 14:59–84.

Brouwer, A., M.P. Longnecker, L.S. Birnbaum, J. Cogliano, P. Kostyniak, J. Moore, S. Schantz and G. Winneke, 1999. Characterization of potential endocrine-related health effects at low-dose levels of exposure to PCBs. *Environmental Health Perspectives*, 107(4):639–649.

Brown, L.M., L.M. Pottern, R.N. Hoover, S.S. Devesa, P. Aselton and J.T. Flannery, 1986. Testicular cancer in the United States: trends in incidence and mortality. *International Journal of Epidemiology*, 15:164–170.

Brucker-Davis, F., 1998. Effects of environmental synthetic chemicals on thyroid function. *Thyroid*, 8:827–856.

Buck, G.M., L.E. Sever, P. Mendola, M. Zielezny and J.E. Vena, 1997. Consumption of contaminated sport fish from Lake Ontario and time-to-pregnancy. New York State Angler Cohort. *American Journal of Epidemiology*, 146:949–954.

Budtz-Jorgensen, E., N. Keiding, P. Grandjean, R.F. White and P. Weihe, 1999. Methylmercury neurotoxicity independent of PCB exposure. *Environmental Health Perspectives*, 107(5): Correspondence.

Burkow, I.C. and R. Kallenborn, 2000. Sources and transport of persistent pollutants to the Arctic. *Toxicology Letters*, 112–113:87–92.

Calabrese, E.J., M.E. McCarthy and E. Kenyon, 1987. The occurrence of chemical induced hormesis. *Health Physics*, 52: 531–541.

Carlsen, E., A. Giwercman, N. Keiding and N.E. Skakkebaek, 1992. Evidence for decreasing quality of semen during past 50 years. *British Medical Journal*, 305:609–613.

Carpenter, D.O., K.F. Arcaro, B. Bush, W.D. Niemi, S. Pang and D.D. Vakharia, 1998. Human health and chemical mixtures: an overview. *Environmental Health Perspectives*, 106(6):1263–1270.

Cavallo, F., R. Russo, C. Zotti, A. Camerlengo and A.M. Ruggenini, 1995. Moderate alcohol consumption and spontaneous abortion. *Alcohol and Alcoholism*, 30:195–201.

Champ, M.A. and P.F. Seligman, 1996. An introduction to organotin compounds and their use in antifouling coatings. *In*: Champ M.A. and P.F. Seligman (eds.). Organotin Environmental Fate and Effects, pp. 1–25, Chapman and Hall, London.

Chan, H.M., 1998. A database for environmental contaminants in traditional foods in Northern and Arctic Quebeq: development and applications. *Food Additives and Contaminants*, 15: 127–134.

Chang, K.J, K.H. Hsieh, T.P. Lee, S.Y. Tang and T.C. Tung, 1981. Immunologic evaluation of patients with polychlorinated biphenyl poisoning: determination of lymphocyte subpopulations. *Toxicology and Applied Pharmacology*, 61:58–63.

Chanoine, J.P. and L.E. Braverman, 1992. The role of transthyretin in the transport of thyroid hormone to cerebrospinal fluid and brain. *Acta Medica Austriaca*, 19(1):25–28.

Chao, W.Y., C.C. Hsu and Y.L.L. Guo, 1997. Middle-ear disease in children exposed prenatally to polychlorinated biphenyls and polychlorinated dibenzofurans. *Archives of Environmental Health*, 52:257–262.

Chapman, L. and H.M.Chan, 2000. The influence of nutrition on methyl mercury intoxication. *Environmental Health Perspectives*,108:29–51.

Chashschin, V.P., G.P. Artunina and T. Norseth, 1994. Congenital defects, abortion and other health effects in nickel refinery workers. *Science of the Total Environment*, 148:287–291.

Chau, Y.K., R.J. Maguire, M. Brown, F. Yang and S.P. Batchelor, 1997. Occurrence of organotin compounds in the Canadian aquatic environment five years after the regulation of antifouling uses of tributyltin. *Water Quality Research Journal of Canada*, 32:453–521.

Chauhan, K.R., P.R. Kodavanti and J.D. McKinney, 2000. Assessing the role of ortho-substitution on polychlorinated biphenyl binding to transthyretin, a thyroxine transport protein. *Toxicology and Applied Pharmacology*, 162:10–21.

Cheek, A.O., K. Kow, J. Chen and J.A. McLachlan, 1999. Potential mechanisms of thyroid disruption in humans: interaction of organochlorine compounds with thyroid receptor, transthyretin, and thyroid-binding globulin. *Environmental Health Perspectives*, 107:273–278.

Chen, Y.C.J., Y.L. Guo, C.C. Hsu and W.J. Rogan, 1992. Cognitive development of Yu-Cheng ('Oil Disease') children prenatally exposed to heat-degraded PCBs. *Journal of the American Medical Association*, 268:3213–3218.

Choi, B.H., 1989. The effects of methylmercury on the developing brain. *Progress in Neurobiology*, 32:447–470.

Clarkson, T.W., 1993. Mercury: major issues in environmental health. *Environmental Health Perspectives*, 100:31–38.

Clarkson, T.W., 1997. The toxicology of mercury. *Critical Reviews in Clinical Laboratory Sciences*, 34:369–403.

Cnattingius, S., B. Haglund and O. Meirik, 1988. Cigarette smoking as a risk factor for late fetal and early neonatal death. *British Medical Journal*, 297:258–261.

Colorado State University, 2000. The Thyroid and Parathyroid Glands. Hypertextbook for Biomedical Sciences. http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/thyroid/index.html (version updated February 27 2000).

Connor, S.L. and W.E. Connor, 1997. Are fish oils beneficial in the prevention and treatment of coronary heart disease. *American Journal of Clinical Nutrition*, 66(suppl):1020–1031.

Connor, K., K. Ramamoorthy, M. Moore, M. Mustatin, I. Chen, S. Safe, T. Zacharewski, B. Gillesby, A. Joyeux and P. Balaguer, 1997. Hydroxylated polychlorinated biphenyls (PCBs) as estrogens and antiestrogens: Structure–activity relationships. *Toxicology and Applied Pharmacology*, 145:111–123.

Coosen, R. and F.L. van Velsen, 1989. Effects of the beta-isomer of hexachlorocyclohexane on estrogen-sensitive human mammary tumor cells. *Toxicology and Applied Pharmacology*, 101:310–318.

Coughlin, S.S. and M. Piper, 1999. Genetic polymorphisms and risk of breast cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 8:1023–1032.

Cox, C., T.W. Clarkson, D.O. Marsh, L. Amin-Zaki, S. Tikriti and G. Myers, 1989. Dose-response analysis of infants prenatally exposed to methylmercury: An application of a single compart-

ment model to single-strand hair analysis. *Environmental Research*, 49(2):318–332.
Crawford, M.A., A.G. Hassam, G. Williams and W.E. Whitehouse, 1976. Essential fatty acids and fetal brain. *Lancet*, i:452–453.
Crawford, M.A., W. Doyle, P. Drury, A. Lennon, K. Costeloe and M. Leighfield, 1989. n-6 and n-3 fatty acids during early human development. *Journal of Internal Medicine*, 225(1):159–169.
Crête, M., F. Potvin, P. Walsh, J.-L. Benedetti, M.A. Lefebvre, J.P. Weber, G. Paillard and J. Gagnon, 1987. Pattern of cadmium contamination in the liver and kidneys of moose and white-tailed deer in Quebec. *Science of the Total Environment*, 66: 290–291.
Crisp, T.M., E.D. Clegg, R.L. Cooper, W.P. Wood, D.G. Anderson, K.P. Baetcke, J.L. Hoffmann, M.S. Morrow, D.J. Rodier, J.E. Schaeffer, L.W. Touart, M.G. Zeeman and Y.M. Patel, 1998. Environmental endocrine disruption: an effects assessment and analysis. *Environmental Health Perspectives*, 106(1):11–56.
Cuvin-Aralar, M.L. and R.W. Furness, 1991. Mercury and selenium interaction: a review. *Ecotoxicology and Environmental Safety*, 21:348–364.
Darnerud, P.O., G.S. Eriksen, T. Johannesson, P.B. Larsen and M. Viluksela, 2001. Polybrominated diphenyl ethers: Occurrence, dietary exposure and toxicology. *Environmental Health Perspectives*, 109:49–68.
Darvill, T., E. Lonky, J. Reihman, P. Stewart and J. Pagano, 2000. Prenatal exposure to PCBs and infant performance on the Fagan Test of Infant Intelligence. *Neurotoxicology,* 21(6): 1029–1038.
Daston, G.P., J.W. Gooch, W.J. Breslin, D.L. Shuey, A.I. Nikiforov, T.A. Fico and J.W. Gorsuch, 1997. Environmental estrogens and reproductive health: a discussion of the human and environmental data. *Reproductive Toxicology*, 11:465–481.
Daum, J.R., 1993. Immunotoxicology of cadmium and mercury on B-lymphocytes-1. Effects on lymphocytes function. *International Journal of Immunopharmacoogy*, 15:385–394.
Daum, J.R., D.M. Shepherd and R.J. Noelle, 1993. Immunotoxicology of cadmium and mercury on B-lymphocytes–I. Effects on lymphocyte function. *International Journal of Immunopharmacology*, 15:383–394.
Davidson, P.W., G.J. Myers, C.C. Cox, C. Shamlaye, D.O. Marsh, M.A. Tanner, M. Berlin, J. Sloane-Reeves, E. Cemichiari, O. Choisy, A. Choi and T.W. Clarkson, 1995. Longitudinal neurodevelopmental study of Seychellois children following *in utero* exposure to methylmercury from maternal fish ingestion: Outcomes at 19 and 29 months. *Neurotoxicology*, 16:677–688.
Davidson, P.W., G.J. Myers, C.C. Cox, C. Axtell, C. Shamlaye, J. Sloane-Reeves, E. Cemichiari, L. Needham, A. Choi and Y.N. Wang, 1998. Effects of prenatal and postnatal methylmercury exposure from fish consumption on neurodevelopment. *Journal of the American Medical Association*, 280:701–707.
Davis, D.L. and H.L. Bradlow, 1995. Can environmental estrogens cause breast cancer? *Scientific American*, 273:167–172.
Day, N.L., G.A. Richardson, D. Geva and N. Robles, 1994. Alcohol, marijuana, and tobacco: effects of prenatal exposure on offspring growth and morphology at age six. *Alcoholism: Clinical and Experimental Research*, 18:786–794.
Dearth, M.A. and R.A. Hites, 1991. Complex analysis of technical chlordane using negative ionization mass spectrometry. *Environmental Science & Technology*, 25:245–254.
de Geus, H.-J., H. Besselink, A. Brouwer, J. Klungsøyr, B. McHugh, E. Nixon, G.G. Rimkus, P.G. Wester and J. de Boer, 1999. Environmental occurrence, analysis, and toxicology of toxaphene compounds. *Environmental Health Perspectives*, 107(1):115–144.
Dejin-Karlsson, E., B.S. Hanson and P.-E. Østergren, 1997. Psychosocial resources and persistent alcohol consumption early pregnancy – a population study of women in their first pregnancy in Sweden. *Scandinavian Journal of Social Medicine*, 4:280–288.
Demers, A., P. Ayotte, J. Brisson, S. Dodin, J. Robert and É. Dewailly, 2000. Risk and agressiveness of breast cancer in relation to plasma organochlorine concentrations. *Cancer Epidemiology, Biomarkers & Prevention*, 9:161–166.
de Mouzon, J., P. Thonneau, A. Spira and L. Multigner, 1996. Declining sperm count. Semen quality has declined among men born in France since 1950. *British Medical Journal*, 313:43; discussion 44–45.
Deutch, B., 1999. Lifestyle and contaminants in Greenland 1994–1996. Master of Public Health Thesis; Publication No. 11, Aarhus University.
Deutch, B., in prep. The human health programme in Greenland 1997–2001. *In*: Deutch B. and J.C. Hansen (eds.) AMAP Greenland and The Faroe Islands 1997–2001. Danish Environmental Protection Agency.
Deutch, B. and J.C. Hansen, 1999. High blood levels of persistent organic pollutants are statistically correlated with smoking. *International Journal of Circumpolar Health*, 58:212–217.
Deutch, B. and J.C. Hansen, 2000. High human plasma levels of organochlorine compounds in Greenland: Regional differences and lifestyle effects. *Danish Medical Bulletin*, 47(2):132–137.
Deutch, B., E. Bonefeld-Jørgensen and J.C. Hansen, 2000. N-3 PUFA from fish or seal oil reduce atherogenic risk indicators in Danish women. *Nutrition Research*, 20(8):1065–1077.
Deutch, B., H.S. Pedersen, E.C. Bonefeld-Jørgensen and J.C. Hansen, 2002. Determinants of plasma organochlorine levels among Inuits in Uummanaq. *Archives of Environmental Health*, accepted.
Deutscher, R.L. and K.J. Cathro, 2001. Organochlorine formation in magnesium electrowinning cells. *Chemosphere*, 43:147–155.
DeVito, M., L. Biegel, A. Brouwer, S. Brown, F. Brucker-Davis, A.O. Cheek, R. Christensen, T. Colborn, P. Cooke, J. Crissman, K. Crofton, D. Doerge, E. Gray, P. Hauser, P. Hurley, M. Kohn, J. Lazar, S. McMaster, M. McClain, E. McConnell, C. Meier, R. Miller, J. Tietge and R. Tyl, 1999. Screening methods for thyroid hormone disruptors. *Environmental Health Perspectives*, 107:407–415.
Dewailly, E., A. Nantel, S. Bruneau, C. Laliberté, L. Ferron and S. Gingras, 1992. Breast milk contamination by PCDDs, PCDFs and PCBs in Arctic Québec: A preliminary assessment. *Chemosphere*, 25:1245–1249.
Dewailly, É., S. Bruneau, P. Ayotte, C. Laliberté, S. Gingras, D. Bélanger and L. Ferron, 1993. Health status at birth of Inuit newborn prenatally exposed to organochlorines. *Chemosphere*, 27:359–366.
Dewailly, É., S. Dodin, R. Verreault, P. Ayotte, L. Sauvé, J. Morin and J. Brisson, 1994a. High organochlorine body burden in women with estrogen receptor-positive breast cancer. *Journal of the National Cancer Institute*, 86:232–234.
Dewailly, E., J.J. Ryan, C. Laliberte, S. Bruneau, J.P. Weber, S. Gingras and G. Carrier, 1994b. Exposure of remote maritime populations to coplanar PCBs. *Environmental Health Perspectives*, 102(1):205–209.
Dewailly, E. (program leader), 1998. Integration of 12 years of data in a risk and benefit assessment of traditional food in Nunavik: Final report. Arctic Environmental Strategy (AES) and Northern Contaminants Program (NCP) 1997/98 project report. DIAND Canada.
Dewailly, E., G. Mulvad, H.S. Pedersen, P. Ayotte, A. Demers, J.P. Weber and J.C. Hansen, 1999. Concentration of organochlorines in human brain, liver, and adipose tissue autopsy samples from Greenland. *Environmental Health Perspectives*, 107: 823–828.
Dewailly, E., P. Ayotte, S. Bruneau, S. Gingras, M. Belles-Isles and R. Roy, 2000a. Susceptibility to infections and immune status in Inuit infants exposed to organochlorines. *Environmental Health Perspectives*, 108:205–211.
Dewailly, E., B. Levesque, J.F. Duchesne, P. Dumas, A. Scheuhammer, C. Gariepy, M. Rhainds and J.F. Proulx, 2000b. Lead shot as a source of lead poisoning in the Canadian Arctic. *Epidemiology*, 11(4):S146.
Dewailly, E., P. Ayotte, S. Bruneau, G. Lebel, P. Levallois and J.P. Weber, 2001a. Exposure of the Inuit population of Nunavik (Arctic Quebec) to lead and mercury. *Archives of Environmental Health*, 56:350–357.
Dewailly, E., C. Blanchet, S. Lemieux, L. Sauvé, S. Gringras, P. Ayotte and B.J. Holub, 2001b. N-3 fatty acids and cardiovascular disease risk factors among the Inuit of Nunavik. *American Journal of Clinical Nutrition*, 74(4):464–473.
Dietz, R., F. Riget and P. Johansen, 1996. Lead, cadminum, mercury, and selenium in Greenland marine animals. *Science of the Total Environment*, 186:67–93.
Dorshakova, N.V. and T.A. Karapetian, 2002. Quality of the envi-

ronment and population health in The Republic of Karelia. Abstract from AMAP conference and workshop: Impacts of POPs and mercury on Arctic environments and humans, Tromso, 24 January 2002.

Dunning, A.M., C.S. Healey, P.D. Pharoah, M.D. Teare, B.A. Ponder and D.F. Easton, 1999. A systematic review of genetic polymorphisms and breast cancer risk. *Cancer Epidemiology, Biomarkers & Prevention*, 8:843–854.

Ebbeson, S.O.E., J. Kennish, L. Ebbeson, O. Go and J. Yeh, 1999. Diabetes is related to fatty acid imbalance in Eskimos. *International Journal of Circumpolar Health*, 58:108–119.

Egeland, G.M., L.A. Feyk and J.P. Middaugh, 1998a. The use of traditional foods in a healthy diet in Alaska: Risks in perspective. *Alaska Division of Public Health, Epidemiology Bulletin*, 2(1):1–140.

Egeland, G., K. Perlham-Hester and J. Berner, 1998b. Fetal Alcohol Syndrome in Alaska, 1977–1992. An administrative prevalence derived from multiple data sources. *American Journal of Public Health*, 88(5):781–786.

Eisler, R., 1985. Cadmium hazards to fish, wildlife and invertebrates: A synoptic review. US Department of the Interior, Fish and Wildlife Service. Biological Report No. 85, Washington DC.

Ellermann-Eriksen, S., M.M. Christensen and S.C. Mogensen, 1994. Effect of mercuric chloride on macrophage-mediated resistance mechanisms against infection with herpes simplex virus type 2. *Toxicology*, 93:269–287.

Ellingsen, D., Y. Thomassen, J. Aaseth and J. Alexander, 1997. Cadmium and selenium in blood and urine related to smoking habits and previous exposure to mercury vapor. *Journal of Applied Toxicology*, 17:337–343.

Eriksen, M.P., 1999. Social forces and tobacco in society. *Nicotine & Tobacco Research*, Suppl 1:79–80.

Eriksson, P. and A. Fredriksson, 1998. Neurotoxic effects in adult mice neonatally exposed to 3,3´4,4´5-pentachlorobiphenyl or 2,3,3´4,4´-pentachlorobiphenyl. Changes in brain nicotinic receptors and behaviour. *Environmental Toxicology and Pharmacology*, 5:7–27.

Eriksson, K.M., F.K.Å. Salvesen, K. Haug and S.H. Eik-Nes, 1996. Smoking habits among pregnant women in a Norwegian county 1987–94. *Acta Obstetricia et Gynecologica Scandinavica*, 75:355–359.

Eriksson, K.M., K. Haug, K.Å. Salvesen, B.-I. Nesheim, G. Nylander, S. Rasmussen, K. Andersen, J.O. Nakling and S.H. Eik-Nes, 1998. Smoking habits among pregnant women in Norway 1994–95. *Acta Obstetricia et Gynecologica Scandinavica*, 77: 159–164.

Evans, S.M., 1999. Tributyltin pollution: the catastrophe that never happened. *Marine Pollution Bulletin*, 38:629–636.

Faden, V.B. and B.I. Graubard, 1994. Alcohol consumption during pregnancy and infant birth weight. *Annals of Epidemiology*, 4:279–284.

Fahrig, R., 1993. Genetic effects of dioxins in the spot test with mice. *Environmental Health Perspectives*, 101(3):257–261.

Falandysz, J., 1998. Polychlorinated naphthalenes: an environmental update. *Environmental Pollution*, 101:77–90.

Falck, F.J., A. Ricci, M.S. Wolff, J. Godbold and P. Deckers, 1992. Pesticides and polychlorinated biphenyl residues in human breast lipids and their relation to breast cancer. *Archives of Environmental Health*, 47:143–146.

Fein, G.G., J.L. Jacobson, S.W. Jacobson, P.M. Schwartz and J.K. Dowler, 1984. Prenatal exposure to polychlorinated biphenyls: Effects on birth size and gestational age. *Journal of Pediatrics*, 105:315–320.

Fiedler, H., 1996. Sources of PCDD/PCDF and impact on the environment. *Chemosphere*, 32:55–64.

Finckh, B., A. Kontush, J. Commentz, C. Hubner, M. Burdelski and A. Kohlschutter, 1995. Monitoring of ubiquinol-10, ubiquinone-10, carotenoids, and tocopherols in neonatal plasma microsamples using high-performance liquid chromatography with coulometric electrochemical detection. *Analytical Biochemistry*, 232:210–216.

Fiorentino, D.F., M.W. Bond and T.R. Mosmann, 1989. Two types of mouse T helper cell. IV. Th2 clones secrete a factor that inhibits cytokine production by Th1 clones. *Journal of Experimental Medicine*, 170:2081–2095.

Fisch, H., E.T. Goluboff, J.H. Olson, J. Feldshuh, S.J. Broder and D.H. Barad, 1996. Semen analyses in 1,283 men from the United States over a 25-year period: no decline in quality. *Fertility and Sterility*, 65:1009–1014.

Fisher, B.E., 1999. Most unwanted persistent organic pollutants. *Environmental Health Perspectives,* 107:A18–A23.

Fisher, D.G. and J.M. Booker, 1990. Drug abuse in Alaska: Myths verses reality. *Psychology of Addictive Behaviors*, 4:2–5.

Fisk, A.T., G.T. Tomy, C.D. Cymbalisty and D.C.G. Muir, 2000. Dietary accumulation and quantitative structure–activity relationships for depuration and biotransformation of short (C10), medium (C14) and long (C18) carbon chain polychlorinated alkanes by juvenile rainbow trout (*Oncorhynchus mykiss*). *Environmental Toxicology and Chemistry*, 19:1508–1516.

Forsdahl, A., 1977. Are poor living conditions in childhood and adolescence an important risk factor for arteriosclerotic heart disease? *British Journal of Preventive and Social Medicine*, 31: 91–95.

Fortuine, R., 1975. Health Care and the Alaska Native: Some Historical Perspectives, Polar Notes, Dartmouth College Library, Number XIV.

Fortuine, R., 1989. Chills and Fever. Health and disease in the Early History of Alaska. University of Alaska Press, Anchorage.

Fowles, J.R., A. Fairbrother, L. Baecher-Steppan and N.I. Kerkvliet, 1994. Immunologic and endocrine effects of the flame-retardant pentabromodiphenyl ether (DE-71) in C57BL/6J mice. *Toxicology*, 86:49–61.

Fry, D.M., 1995. Reproductive effects in birds exposed to pesticides and industrial chemicals. *Environmental Health Perspectives*, 103(7):165–171.

Fry, D.M. and C.K. Toone, 1981. DDT-induced feminization of gull embryos. *Science*, 213:922–924.

Fushukima, I., 1978. Environmental pollution and health effects. *In*: K. Tsuchiya (ed.). Cadmium studies in Japan: A review, pp. 170–181, Elsevier Science Publishers, Amsterdam.

Gabble, S.G. and L. Paige Turner, 1997. Reproductive hazards of the American lifestyle: work during pregnancy. *American Journal of Obstetrics and Gynecology*, 176:826–832.

Gad, F., 1974. Fire detailkomplekser i Grønlands historie 1782–1808. Nyt Nordisk Forlag, Copenhagen.

Gaido, K.W., S.C. Maness, L.S. Leonard and W.F. Greenlee, 1992. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin-dependent regulation of transforming growth factors-alpha and -beta 2 expression in a human keratinocyte cell line involves both transcriptional and post-transcriptional control. *Journal of Biological Chemistry*, 267:24591–24595.

Ganther, H.E., C. Goudie, M.L. Sunde, M.J. Kopecky and P. Wagner, 1972. Selenium: relation to decreased toxicity of methylmercury added to diets containing tuna. *Science*, 175(26): 1122–1124.

George, F.W. and J.D. Wilson, 1994. *In*: Knobil E. and J.D. Neill (eds.). The Physiology of Reproduction. Raven Press, New York.

Giesy, J.P. and K. Kannan, 2001. Global distribution of perfluorooctane sulfonate in wildlife. *Environmental Science & Technology*, 35:1339–1342.

Gill, W.B., G.F. Schumacher, M. Bibbo, F.H. Straus, 2nd and H.W. Schoenberg, 1979. Association of diethylstilbestrol exposure *in utero* with cryptorchidism, testicular hypoplasia and semen abnormalities. *Journal of Urology*, 122:36–39.

Giwercman, A., J. Grindsted, B. Hansen, O.M. Jensen and N.E. Skakkebaek, 1987. Testicular cancer risk in boys with maldescended testis: a cohort study. *Journal of Urology*, 138:1214–1216.

Giwercman, A., E. Carlsen, N. Keiding and N.E. Skakkebaek, 1993. Evidence for increasing incidence of abnormalities of the human testis: a review. *Environmental Health Perspectives*, 101(2):65–71.

Gladen, B.C., W.J. Rogan, P. Hardy, J. Thullen, J. Tingelstad and M. Tully, 1988. Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk. *Journal of Pediatrics*, 113:991–995.

Gladen, B.C., N.B. Ragan and W.J. Rogan, 2000. Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. *Journal of Pediatrics*, 136:490–496.

Gould, J.C., L.S. Leonard, S.C. Maness, B.L. Wagner, K. Conner, T.

Zacharewski, S. Safe, D.P. McDonnell and K.W. Gaido, 1998. Bisphenol A interacts with the estrogen receptor alpha in a distinct manner from estradiol. *Molecular and Cellular Endocrinology*, 142:203–214.

Grandjean, P., P. Weihe, P.J. Jørgensen, T. Clarkson, E. Cernichiari and T. Viderø, 1992. Impact of maternal seafood diet on fetal exposure to mercury, selenium, and lead. *Archives of Environmental Health*, 47:185–195.

Grandjean, P., P. Weihe, R.F. White, F. Debes, S. Araki, K. Yokoyama, K. Murata, N. Sørensen, R. Dahl and P.J. Jørgensen, 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicology and Teratology*, 19(6):417–428.

Grandjean, P., E. Budtz-Jorgensen, R.F. White, P.J. Jorgensen, P. Weihe, F. Debes and N. Keiding, 1999a. Methylmercury exposure biomarkers as indicators of neurotoxicity in children aged 7 years. *American Journal of Epidemiology*, 150:301–305.

Grandjean, P., R.F. White, A. Nielsen, D. Cleary and E.C. de Oliveira Santos, 1999b. Methylmercury neurotoxicity in Amazonian children downstream from gold mining. *Environmental Health Perspectives*, 107:587–591.

Grandjean, P., P. Weihe, V.W. Burse, L.L. Needham, E. Storr-Hansen, B. Heinzow, F. Debes, K. Murata, H. Simonsen, P. Ellefsen, E. Budtz-Jorgensen, N. Keiding and R.F. White, 2001. Neurobehavioral deficits associated with PCB in 7-year-old children prenatally exposed to seafood neurotoxicants. *Neurotoxicology and Teratology*, 23:305–317.

Gray, L.E. Jr., J.S. Ostby and W.R. Kelce, 1994. Developmental effects of an environmental antiandrogen: the fungicide vinclozolin alters sex differentiation of the male rat. *Toxicology and Applied Pharmacology*, 129:46–52.

Greiner, R.S., T. Moriguchi, A. Hutton, B.M. Slotnick and N. Jr. Salem, 1999. Rats with low levels of brain doxosahexaenoic acid show impaired performance in olfactory-based and spatial learning tasks. *Lipids*, 34 Suppl:239-243.

Grimstad, H., B. Backe, G. Jacobsen and B. Schei, 1998. Abuse history and health risk behaviors in pregnancy. *Acta Obstetricia et Gynecologica Scandinavica*, 77:893–897.

Guillette, L.J. Jr., T.S. Gross, G.R. Masson, J.M. Matter, H.F. Percival and A.R. Woodward, 1994. Developmental abnormalities of the gonad and abnormal sex hormone concentrations in juvenile alligators from contaminated and control lakes in Florida. *Environmental Health Perspectives*, 102:680–688.

Guillette, L.J. Jr., D.A. Crain, A.A. Rooney and D.B. Pickford, 1995. Organization versus activation: the role of endocrine-disrupting contaminants (EDCs) during embryonic development in wildlife. *Environmental Health Perspectives*, 103(7):157–164.

Gwiazda, R.H. and D.R. Smith, 2000. Lead isotopes as a supplementary tool in the routine evaluation of household lead hazards. *Environmental Health Perspectives*, 108:1091–1097.

Håglin, L., 1988. The food and nutrient intake of a Swedish Saami population. *Arctic Medical Research*, 47(1):139–144.

Håglin, L., 1991. Nutrient intake among Saami people today compared with an old traditional Saami diet. *Arctic Medical Research 1991*. Suppl. 7:41–6.

Hahn, M.E., 1998. The aryl hydrocarbon receptor: a comparative perspective. *Comparative Biochemistry and Physiology C: Pharmacology & Toxicology*, 121:23–53.

Hakulinen, T., A. Andersen, B. Malker, E. Pukkala, G. Schou and H. Tulinius, 1986. Trends in cancer incidence in the Nordic countries. A collaborative study of the five Nordic Cancer Registries. *Acta Pathologica, Microbiologica et Immunologica Scandinavica Supplementum*, 288:1–151.

Hamburgh, M., 1969. The role of thyroid and growth hormons in neurogenesis. *In*: Moscona, A. and A. Monroy (eds.). Current Topics in Developmental Biology, pp. 109–148. Academic Press, New York.

Hanlon, D.P. and V.H. Ferm, 1989. Cadmium effects and biochemical status in hamsters following acute exposure in late gestation. *Experientia*, 45:108–110.

Hansen, J.C., 1990. Human exposure to metals through consumption of marine foods: a case study of exceptionally high intake among Greenlanders. *In*: Furness, R.S. and P.S. Rainbow (eds.). Heavy Metals in the Marine Environment, pp. 227–243. CRP Press. Boca Raton, Florida.

Hansen, J.C., 2000. Dietary selenium intake among Greenlanders. *Bulletin of Selenium–tellurium*, Oct. 1–4.

Hansen, J.C. and G. Danscher, 1997. Organic mercury: an environmental threat to the health of dietary-exposed societies? *Reviews on Environmental Health*, 12:107–116.

Hansen, J.C., T.Y. Toribara and A.G. Huhs, 1989. Trace metals in human and animal samples. *In*: Hart Hansen J.P. and H.C. Guillov (eds.). The Mummies from Qilakitsoq. *Meddl Gronland Man and Society*, 12:161–167.

Hansen, J.R., R. Hansson and S. Norris (eds.), 1996. The State of the European Arctic Environment, EEA Environmental Monograph, No. 3, 136 pp., Oslo.

Hansen, K.G., G. Mulvad and T. Pars, 1997. Kalaalimernit. Inussuk. *Arktisk Forskningsjournal*, 1–168.

Hany, J., H. Lilienthal, A. Roth-Harer, G. Ostendorp, B. Heinzow and G. Winneke, 1999. Behavioral effects following single and combined maternal exposure to PCB 77 (3,4,3',4'-tetrachlorobiphenyl) and PCB 47 (2,4,2',4'- tetrachlorobiphenyl) in rats. *Neurotoxicology and Teratology*, 21:147–156.

Harada, M., 1995. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Critical Reviews in Toxicology*, 25:1–25.

Hardy, R., D. Kuh and M. Wadsworth, 2000. Smoking, body mass index, socioeconomic status and the menopausal transition in a British national cohort. *International Journal of Epidemiology*, 29:845–851.

Harris, C.A., P. Henttu, M.G. Parker and J.P. Sumpter, 1997. The estrogenic activity of phthalate esters *in vitro*. *Environmental Health Perspectives*, 105:802–811.

Hartikainen, A.-L., M. Sorri, H. Anttonen, R. Tuimala and E. Laara, 1994. Effect of occupational noise on the course and outcome of pregnancy. *Scandanavian Journal of Work Environment & Health*, 20:444–450.

Harvey, C.B., E.J. Hollox, M. Poulter, Y. Wang, M. Rossi, S. Auricchio, T.H. Iqbal, B.T. Cooper, R. Barton, M. Sarner, R. Korpela and D.M. Swallow, 1998. Lactase haplotype frequencies in Caucasians: association with the lactase persistence/non-persistence polymorphism. *Annals of Human Genetics*, 62:215–223.

Hauptman, O., D.M. Albert, M.C. Plowman, S.-M. Hopfer and F.W. Sunderman, Jr., 1993. Ocular malformations of *Xenopus laevis* to nickel during embryogenesis. *Annals of Clinical and Laboratory Science*, 23:397–406.

Health Canada, 1991. Towards a Healthy Future: Second report on the Health of Canadians. Health Canada.

Hegele, R.A, T.K. Young and P.W. Connelly, 1997. Are Canadian Inuit at increased genetic risk for coronary heart disease? *Journal of Molecular Medcine*, 74:364–370.

Heo, Y., P.J. Parsons and D.A. Lawrence, 1996. Lead differentially modifies cytokine production *in vitro* and *in vivo*. *Toxicology and Applied Pharmacology*, 138:149–157.

Herbst, A.L., H. Ulfelder and D.C. Poskanzer, 1971. Adenocarcinoma of the vagina. Association of maternal stilbestrol therapy with tumor appearance in young women. *New England Journal of Medicine*, 284:878–881.

HMSO, 1992. The Annual Report of the Chief Medical Officer of the Department of Health. On the States of The Public Health, HMSO, London.

Hoffmann, D. and I. Hoffmann, 1997. The changing cigarette, 1950–1995. *Journal of Toxicology and Environmental Health*, 50:307–364.

Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson and K.K. Steinberg, 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *Journal of the American Medical association*, 255:2031–2038.

Holder, T., 1998. Education on health risks of smoking in Magadan, Russia. *International Journal of Circumpolar Health*, 57:493–494.

Holladay, S.D. and M.I. Luster, 1996. Alterations in fetal thymic and liver hematopoietic cells as indicators of exposure to developmental immunotoxicants. *Environmental Health Perspectives*, 104(4):809–813.

Höök, O., K.-D. Lundgren and Åswensson, 1954. On alkyl mercury poisoning, with description of two cases. *Acta Medica Scandinavica*, 150:131–137.

Hooper, K. and T.A. McDonald, 2000. The PBDEs: An emerging environmental challenge and another reason for breast-milk monitoring programs. *Environmental Health Perspectives*, 108:387–392.

Hovander, L., T. Malmberg, M. Athanasiadou, L. Athanassiadis, S. Rahm, A. Bergman and E.K. Wehler, 2002. Identification of hydroxylated PCB metabolites and other phenolic halogenated pollutants in human blood plasma. *Archives of Environmental Contamination and Toxicology*, 42:105–117.

Høyer, A.P., P. Grandjean, T. Jørgensen, J.W. Brock and H.B. Hartvig, 1998. Organochlorine exposure and risk of breast cancer. *Lancet*, 352:1816–1820.

Huisman, M., C. Koopman-Esseboom, V. Fidler, M. Hadders-Algra, C.G. Van der Paauw, L.G.M.Th. Tuinstra, N. Weisglas-Kuperus, P.J.J. Sauer, B.C.L. Touwen and E.R. Boersma, 1995a. Perinatal exposure to polychlorinated biphenyls and dioxins and its effect on neonatal neurological development. *Early Human Development*, 41:111–127.

Huisman, M., C. Koopman-Esseboom, C.I. Lanting, C.G. Van der Paauw, L.G.M.Th. Tuinstra, V. Fidler, N. Weisglas-Kuperus, P.J.J. Sauer, E.R. Boersma and B.C.L. Touwen, 1995b. Neurological condition in 18-month-old children perinatally exposed to polychlorinated biphenyls and dioxins. *Early Human Development*, 43:165–176.

Hunter, D.J., S.E. Hankinson, F. Laden, G.A. Colditz, J.E. Manson, W.C. Willett, F.E. Speizer and M.S. Wolff, 1997. Plasma organochlorine levels and the risk of breast cancer. *New England Journal of Medicine*, 337:1253–1258.

Hussain, R.J., J. Gyori, A.P. DeCaprio and D.O. Carpenter, 2000. *In vivo* and *in vitro* exposure to PCB 153 reduces long-term potentiation. *Environmental Health Perspectives*, 108:827–831.

IARC, 1983. Polynuclear aromatic compounds. Part 1: Chemical, environmental and experimental data. International Agency for Research on Cancer, Lyon, 477 pp.

Ilback, N.G., L. Wesslen, J. Fohlman and G. Friman, 1996. Effects of methyl mercury on cytokines, inflammation and virus clearance in a common infection (coxsackie B3 myocarditis). *Toxicology Letters*, 89:19–28.

Innis, S.A., 2000. The role of dietary n-6 and n-3 fatty acids in the developing brain. *Developmental Neuroscience*, 22:474–480.

IPCS, 1992. IPCS Environmental Health Criteria 135, Cadmium Environmental Aspects. UNEP/World Health Organization, Geneva, International Programme on Chemical Safety. 156 pp.

Irvine, S., E. Cawood, D. Richardson, E. MacDonald and J. Aitken, 1996. Evidence of deteriorating semen quality in the United Kingdom: birth cohort study in 577 men in Scotland over 11 years. *British Medical Journal*, 312:467–471.

ISO, 1999. General requirements for the competence of testing and calibration laboratories. International Organisation for Standardisation, Geneva, 26 pp.

Jaakkola, N., R. Ruotsalainen and J.K. Jaakkola, 1994. What are the determinants of children's exposure to environmental tobacco smoke at home? *Scandinavian Journal of Social Medicine*, 2:107–112.

Jacobson, J.L. and S.W. Jacobson, 1996. Intellectual impairment in children exposed to polychlorinated biphenyls *in utero*. *New England Journal of Medicine*, 335:783–789.

Jacobson, S.W., G.G. Fein, J.L. Jacobson, P.M. Schwartz and J.K. Dowler, 1985. The effects of intrauterine PCB exposure in visual recognition memory. *Child Development*, 56:853–860.

Jacobson, J.L., S.W. Jacobson and H.E.B. Humphrey, 1990a. Effects of *in utero* exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children. *Journal of Pediatrics*, 116:38–45.

Jacobson, J.L., S.W. Jacobson and H.E.B. Humphrey, 1990b. Effects of exposure to PCBs and related compounds on growth and activity in children. *Neurotoxicology and Teratology*, 12:319–326.

Jacobson, J.L., S.W. Jacobson, R.J. Padgett, G.A. Brumitt and R.L.Billings, 1992. Effects of prenatal PCB exposure on cognitive processing efficiency and sustained attention. *Developmental Psychology*, 28:297–306.

Jacobson, J.L., S.W. Jacobson, R.J. Sokol, S.S. Martier, J.W. Ager and M.G. Kaplan-Estrin, 1993. Teratogenic effects of alcohol on infant development. *Alcoholism: Clinical and Experimental Research*, 17:174–83.

Jarvis, M.J., E. Goddard, V. Higgins, C. Feyerabend, A. Bryant and D.G. Cook, 2000. Children's exposure to passive smoking in England since the 1980s: cotinine evidence from population surveys. *British Medical Journal*, 321:343–345.

Jensen, G.E. and J. Clausen, 1979. Organochlorine compounds in adipose tissue of Greenlanders and southern Danes. *Journal of Toxicology and Environmental Health*, 5:617–629.

Jensen, J., K. Adare and R. Shearer (eds.), 1997. Canadian Arctic Contaminants Assessment Report, Northern Contaminants Program, Minister of Indian Affairs and Northern Development, Ottawa, 460 pp.

Jensen, B.L., J. Skouv, B.K. Lundholt and A.E. Lykkesfeldt, 1999. Differential regulation of specific genes in MCF-7 and the ICI 182780-resistant cell line MCF-7/182R-6. *British Journal of Cancer*, 79:386–392.

Jenssen, B.M., J.U. Skaare, M. Ekker, D. Vongraven and S.H. Lorentsen, 1996. Organochlorine compounds in blubber, liver and brain in neonatal grey seal pups. *Chemosphere*, 32:2115–2125.

Jobling, S., T. Reynolds, R. White, M.G. Parker and J.P. Sumpter, 1995. A variety of environmentally persistent chemicals, including some phthalate plasticizers, are weakly estrogenic. *Environmental Health Perspectives*, 103:582–587.

Johansen, P., T. Pars and P. Bjerregaard, 2000. Lead, cadmium, mercury, and selenium intake by Greenlanders from local marine food. *Science of the Total Environment*, 200:187–194.

Johansen, P., G. Asmund and F. Riget, 2001. Lead contamination of seabirds harvested with lead shot – implications to human diet in Greenland. *Environmental Pollution*, 112(3):501–504.

Johansen, P., in prep. Manuscript in preparation for the 2002 Danish National AMAP Report (preliminary title). *In*: Deutch B. and J.C. Hansen (eds.) AMAP Greenland and The Faroe Islands 1997–2001. Danish Environmental Protection Agency.

Jokiel, M., 1996. Changes in tobacco smoking patterns in Poland in the years 1876, 1986 and 1990. *Przeglad Epidemiologiczny*, 50:299–307.

Jury, H.H., T.R. Zacharewski and G.L. Hammond, 2000. Interaction between human plasma sex hormone-binding globulin and xenobiotic ligands. *Journal of Steroid Biochemistry & Molecular Biology*, 75:167–176.

Kaikkonen, J., K. Nyyssonen, T.P. Tuomainen, U. Ristonmaa and J.T. Salonen, 1999. Determinants of plasma coenzyme Q10 in humans. *FEBS Letters*, 443:163–166.

Kallen, B., R. Bertollini, E. Castilla, A. Czeizel, L.B. Knudsen, M.L. Martinez-Frias, P. Mastroiacovo and O. Mutchinick, 1986. A joint international study on the epidemiology of hypospadias. *Acta Paediatrica Scandinavica Supplementum*, 324:1–52.

Kallenborn, R. and H. Hühnerfuss, 2001. Chiral Environmental Pollutants. Trace Analysis and Ecotoxicology. Springer-Verlag, Berlin, 209 pp.

Kannan, K., K. Senthilkumar and J.P. Giesy, 1999. Occurrence of butyltin compounds in human blood. *Environmental Science & Technology*, 33(10):1776–1779.

Kannan, K., J. Koistinen, K. Beckmen, T. Evans, J.F. Gorzelany, K.J. Hansen, P.D. Jones, E. Helle, M. Nyman and J.P. Giesy, 2001. Accumulation of perfluorooctane sulfonate in marine mammals. *Environmental Science & Technology*, 35:1593–1598.

Karlsson, H., M. Oehme, S. Skopp and I.C. Burkow, 2000. Enantiomer ratios of chlordane congeners are gender specific in cod (*Gadus morhua*) from the Barents Sea. *Environmental Science & Technology*, 34:2126–2130.

Karron, R.A., R.J. Singleton, L. Bulkow, A. Parkins, D. Druse, I. Desmet, C. Indorf, K.M. Petersen, D. Leombruno, D. Hurlburt, M. Santosham and L.H. Harrison, 1999. Severe Respiratory Syncytial Virus Disease in Alaska Native Children. RSV Alaska Study Group. *Journal of Infectious Disease*, 180(1):41–49.

Kelce, W.R. and E.M. Wilson, 1997. Environmental antiandrogens: developmental effects, molecular mechanisms, and clinical implications. *Journal of Molecular Medicine*, 75:198–207.

Kelce, W.R., E. Monosson, M.P. Gamcsik, S.C. Laws and L.E. Gray Jr, 1994. Environmental hormone disruptors: evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metabolites. *Toxicology and Applied Pharmacology*, 126:276–285.

Kelce, W.R., C.R. Stone, S.C. Laws, L.E. Gray, J.A. Kemppainen and E.M. Wilson, 1995. Persistent DDT metabolite *p,p'*-DDE is

a potent androgen receptor antagonist. *Nature*, 375:581–585.
Kelce, W.R., C.R. Lambright, L.E. Gray Jr. and K.P. Roberts, 1997. Vinclozolin and *p,p'*-DDE alter androgen-dependent gene expression: *in vivo* confirmation of an androgen receptor-mediated mechanism. *Toxicology and Applied Pharmacology*, 142: 192– 200.
Kendall, M.D., B. Safieh, J. Harwood and P.P. Pomeroy, 1992. Plasma thymulin concentrations, the thymus and organochlorine contaminant levels in seals infected with phocine distemper virus. *Science of the Total Environment*, 115:133–144.
Kershaw, T.G., T.W. Clarkson and P.H. Dhahir, 1980. The relationship between blood–brain levels and dose of methylmercury in man. *Archives of Environmental Health*, 35(1):28–36.
Kester, M.H.A., S. Bulduk, D. Tibboel, W. Meinl, H. Glatt, C.N. Falany, M.W.H. Coughtrie, A. Bergman, S.H. Safe, G.G.J.M. Kuiper, A.G. Schuur, A. Brouwer and T.J. Visser, 2000. Potent inhibition of estrogen sulfotransferase by hydroxylated PCB metabolites: A novel pathway explaining the estrogenic activity of PCBs. *Endocrinology*, 141:1897–1900.
Key, B.D., R.D. Howell and C.S. Criddle, 1997. Fluorinated organics in the biosphere. *Environmental Science & Technology*, 31: 2445–2454.
Kharat, I. and F. Saatcioglu, 1996. Antiestrogenic effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin are mediated by direct transcriptional interference with the liganded estrogen receptor. Cross-talk between aryl hydrocarbon- and estrogen-mediated signaling. *Journal of Biological Chemistry*, 271:10533–10537.
Kim, C., H.M. Chan and O. Receveur, 1998. Risk assessment of cadmium exposure in Fort Resolution, NWT, Canada. *Food Additives and Contaminants*, 15(3):307–317.
Kjellstrom, T., P. Kennedy, S. Wallis and C. Mantell, 1986. Physical and mental development of children with prenatal exposure to mercury from fish. Stage 1: Preliminary test at age 4. National Swedish Environmental Protection Board, Sweden.
Klopov, V., 1998. Levels of heavy metals in women residing in the Russian Arctic. *International Journal of Circumpolar Health*, 57(1):582–585.
Klopov, V.P., 2000. Hygienic Assessment of Environmental Pollution in the North of Russia and its Effect on Population Health. Doctoral thesis. St. Petersburg, 46 pp. (In Russian).
Klopov, V.P. and V.N. Shepovalnikov, 2000. The levels of exposure to key POPs among adult and children populations in Yamal Peninsula, Arctic Russia. Proceedings of the Workshop on Persistent Organic Pollutants (POPs) in the Arctic: Human Health and Environmental Concerns. Rovaniemi, 18–20 January 2000. Univ of Arctic: Rovaniemi. Abstract 19; 4 pp.
Klopov, V.P. and V.P. Tchachchine, 2001. Environmental Pollution and Risk Assessment for Population in the Russian North. St. Petersburg, 225 pp. (In Russian).
Klopov, V., J.Ø. Odland and I.C. Burkow, 1998. Persistent organic pollutants in maternal blood plasma and breast milk from Russian Arctic populations. *International Journal of Circumpolar Health*, 57(4)(suppl. 1):239–248.
Koch, A., T. Krause, K. Krogfelt, O.R. Olsen and M. Melbye, 2000. Forekomsten af Helicobacter pylori infektion blandt grønlændere. Nuna Med conference 2000 (Abstract).
Kociba, R.J., D.G. Keyes, J.E. Beyer, R.M. Carreon, C.E. Wade, D.A. Dittenber, R.P. Kalnins, L.E. Frauson, C.N. Park, S.D. Barnard, R.A. Hummel and C.G. Humiston, 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in rats. *Toxicology and Applied Pharmacology*, 46:279–303.
Koopman-Esseboom, C., M. Huisman, N. Weisglas-Kuperus, E.R. Boersma, M.A.J. de Ridder, C.G. Van der Paauw, L.G.M.Th. Tuinstra and P.J.J. Sauer, 1994a. Dioxin and PCB levels in blood and human milk in relation to living areas in the Netherlands. *Chemosphere*, 29:2327–2338.
Koopman-Esseboom, C., D.C. Morse, N. Weisglas-Kuperus, I.J. Lutkeschipholt, C.G. Van der Paauw, L.G. Tuinstra, A. Brouwer and P.J. Sauer, 1994b. Effects of dioxins and polychlorinated biphenyls on thyroid hormone status of pregnant women and their infants. *Pediatric Research*, 36:468–473.
Koren, G., T. Koren and J. Gladstone, 1996. Mild maternal drinking and pregnancy outcome: perceived versus true risks. *Clinica Chimica Acta*, 15:155–162.
Kosatsky, T. and C. Dumont, 1991. Human exposure as a monitor of environmental contamination: its possibilities and limitations as illustrated by the case of methylmercury in northern Quebec. *Arctic Medical Research*, 50(5):712–714.
Krieger, N., M.S. Wolff, R.A., Hiatt, M. Rivera, J. Vogelman and N. Orentreich, 1994. Breast cancer and serum organochlorines: a prospective study among white, black, and Asian women. *Journal of the National Cancer Institute*, 86:589–599.
Kuhnlein, H.V., 1995. Benefits and risks of traditional food for indigenous peoples: focus on dietary intakes of Arctic men. *Canadian Journal of Physiology and Pharmacology*, 73:765–771.
Kuhnlein, H.V., 1997. Benefits and Risks of traditional food for indigenous peoples: Focus on dietary intakes of Arctic men. *In*: Thorling, E.B. and J.C. Hansen (eds.). Foodtables for Greenland, pp. 51–58, Inussuk.
Kuhnlein, H.V. and O. Receveur, 1996. Dietary change and traditional food systems of indigenous peoples. *Annual Review of Nutrition*, 16:417–442.
Kuhnlein, H.V., S. Kubow and R. Soueida, 1991. Lipid components of traditional Inuit foods and diets of Baffin Island. *Journal of Food Composition and Analysis*, 4:227–236.
Kuhnlein, H.V., O. Receveur, D.C.G. Muir and H.M. Chan, 1995a. Arctic indigenous women consume greater than acceptable levels of organochlorines. *Community and International Nutrition*, 125:2501–2510.
Kuhnlein, H.V., O. Receveur, N.E. Morrison, D.M. Appavoo, R. Soueida and P. Pierrot, 1995b. Dietary nutrients of Sahtu Dene/Metis vary by food source, season and age. *Ecology of Food and Nutrition*, 34(3):183–195.
Kuhnlein, H.V., R. Soueida and O. Receveur, 1996. Dietary nutrient profiles of Canadian Baffin Island Inuit differ by food source, season and age. *Journal of the American Dietetic Association*, 2:155–162.
Kuiper, G.G., J.G. Lemmen, B. Carlsson, J.C. Corton, S.H. Safe, P.T. van der Saag, B. van der Burg and J.A. Gustafsson, 1998. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. *Endocrinology*, 139:4252–4263.
Laden, F. and D.J. Hunter, 1998. Environmental risk factors and female breast cancer. *Annual Review of Public Health*, 19:101–123.
Lagendijk, J., J.B. Ubbink and W.J. Vermaak, 1996. Measurement of the ratio between the reduced and oxidized forms of coenzyme Q10 in human plasma as a possible marker of oxidative stress. *Journal of Lipid Research*, 37:67–75.
Lagueux, J., D. Pereg, P. Ayotte, E. Dewailly and G.G. Poirier, 1999. Cytochrome P-450 CYP1A1 enzyme activity and DNA adducts in placenta of women environmentally exposed to organochlorines. *Environmental Research, Section A*, 80:369–382.
Landen, M.G., J. Middaugh and A.L. Dannenberg, 1999. Injuries associated with snowmobiles, Alaska, 1993–94. *Public Health Reports,* 114:48–52.
Landon, M. and B. Saylor, 1997. Community solutions to alcohol-related problems: Alaskan examples. Presented at the Health Problems of the North Lecture Series; Anchorage, Alaska.
Langworth, S., C.G. Elinder and K.G. Sundqvist, 1993. Minor effects of low exposure to inorganic mercury on the human immune system. *Scandanavian Journal of Work Environment & Health*, 19:405–413.
Lanier, A., J. Kelly, P. Holck, B. Smith, T. McEvoys and T. Sandige, 2001. Chapter 3, *In*: Cancer Incidence in Alaska Natives Thirty year report, 1969–1998. Report Alaska Native Tribal Health Consortium (ANTHC), Anchorage. Alaska Med 2001, 43(4): 87–115.
Lans, M.C., C. Spiertz, A. Brouwer and J.H. Koeman, 1994. Different competition of thyroxine binding to transthyretin and thyroxine-binding globulin by hydroxy-PCBs, PCDDs and PCDFs. *European Journal of Pharmacology*, 270:129–136.
Larsen, C., S. Lokke and L.I. Andersen, 1999. Brominated flame retardants, substance flow analysis and assessment of alternatives. Danish Environmental Protection Agency, Copenhagen.
Larsson, S. and B.S. Hanson, 2000. To prevent alcohol problems in Europe by community actions – various national and regional contexts. *Substance Use and Misuse*, 35:11–30.
Lauwerys, R., J.P. Buchet, H. Roels and G. Hubermont, 1978. Placental transfer of lead, mercury, cadmium and carbon monoxide in women. *Environmental Research*, 15:278–289.
Lejon, J., 1996. Polychlorinated Biphenyls, Dioxins and Furans in

Breast Milk from the Kiruna Area. Examination project in environmental chemistry, MK D96:3. Umea University, Sweden.

Lemmens, P.H.H.M. and R.A. Knibbe, 1993. Seasonal variation in survey and sales estimates of alcohol consumption. *Journal of Studies on Alcohol*, 54:157–163.

Lerchl, A. and E. Nieschlag, 1996. Decreasing sperm counts? A critical (re)view. *Experimental and Clinical Endocrinology & Diabetes*, 104:301–307.

Letcher, R.J., R.J. Norstrom and D.C.G. Muir, 1998. Biotransformation versus bioaccumulation: Sources of methyl sulfone PCB and 4,4'-DDE metabolites in the polar bear food chain. *Environmental Science & Technology*, 32:1656–1661.

Leversha, A.M. and R.E. Marks, 1995. Alcohol and pregnancy: doctor's attitudes, knowledge and clinical practice. *New Zealand Medical Journal*, 27:428–430.

Levine, M.E., L.K. Duffy and R.T. Bowyer, 1994. Fatigue, sleep and seasonal hormone levels: Implications for drinking behavior in northern climates. *Drugs and Society*, 8:61–70.

Li, Y.-F., 1999. Global technical hexachlorocyclohexane usage and its contamination consequences in environment from 1948 to 1997. *Science of the Total Environment,* 232:121–158.

Li, H., R.I. Kieger and Q.X. Li, 2000. Improved HPLC method for analysis of 1-hydroxypyrene in human urine specimens of cigarette smokers. *Science of the Total Environment*, 10:147–153.

Lippman, M.E. and R.B. Dickson, 1989. Mechanisms of normal and malignant breast epithelial growth regulation. *Journal of Steroid Biochemistry*, 34:107–121.

Longnecker, M.P., B.C. Gladen, D.G. Patterson and W.J. Rogan, 2000. Polychlorinated biphenyl (PCB) exposure in relation to thyroid hormone levels in neonates. *Epidemiology*, 11:249–254.

Lønne, O.J., R. Sætre, S. Tikhonov, G.W. Gabrielsen, H. Loeng, S. Dahle and K. Sjevljagin (eds.), 1997. Status Report on the Marine Environment of the Barents Region. The Joint Norwegian-Russian Commission on Environmental Co-operation, The Working Group on the Marine Environment of the Bartents Region, Oslo, 97 pp.

López-Carrillo, L., A. Blair, M. López Cervantes, M. Cebrián, C. Rueda, R. Reyes, A. Mohar and J. Bravo, 1997. Dichlorodiphenyltrichloroethane serum levels and breast cancer risk: a case-control study from Mexico. *Cancer Research*, 57:3728–3732.

Lucier, G.W., K.G. Nelson, R.B. Everson, T.K. Wong, R.M. Philpot, T. Tiernan, M. Taylor, and G.I. Sunahara, 1987. Placental markers of human exposure to polychlorinated biphenyls and polychlorinated dibenzofurans. *Environmental Health Perspectives*, 76:79–87.

Luke, B., M. Avni, L. Min and R. Misiunas, 1999. Work and pregnancy: The role of fatigue and the "second shift" on antenatal morbidity. *American Journal of Obstetrics and Gynecology*, 181:1172–1179.

Lund, B.O., D.M. Miller and J.S. Woods, 1993. Studies on Hg(II)-induced H_2O_2 formation and oxidative stress *in vivo* and *in vitro* in rat kidney mitochondria. *Biochemical Pharmacology*, 45:2017–2024.

Luo, S.Q., M.C. Plowman, S.M. Hopfer and F.W. Sunderman, Jr., 1993. Mg^{2+} deprivation enhances and Mg^{2+} supplementation diminishes the embryotoxic and teratogenic effects of Ni^{2+}, Co^{2+}, Zn^{2+}, and Cd^{2+} for frog embryos in the FETAX assay. *Annals of Clinical Laboratory Science*, 23:121–129.

Luopa, P., S. Orre, M. Hyry-Andersson, J. Jokela and M. Rimpela, 2002. Kouluterveys 2001. Stakes, Helsinki.

Luzina, I.G., L.A. Suplotova and G.A. Osadchenko, 1998. Endemic goiter in the extreme North of West Siberia. *Klinicheskaia Meditsina*, 78(1):38–39.

Mably, T.A., D.L. Bjerke, R.W. Moore, A. Gendron-Fitzpatrick and R.E. Peterson, 1992. *In utero* and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. 3. Effects on spermatogenesis and reproductive capability. *Toxicology and Applied Pharmacology*, 114:118–126.

Madeley, R.J., P.A. Gillies, F.L. Power and E.M. Symonds, 1989. Nottingham mothers stop smoking project – baseline survey of smoking in pregnancy. *Community Medicine*, 11:124–130.

Magnúsdottir, E.V, K. Òlafsdottir, T. Thorsteinsson, S. Thorsteinsdottir and U. Egilsdottir, 2002. AMAP conference and workshop, Tromsø 20–22 January. Poster abstract.

Marchetti, B., M.C. Morale, F. Gallo, N. Baiticane, Z. Farinella and M. Cioni, 1995. Neuroendocrinimmunology at the turn of the century: towards a molecular understanding of basic mechanisms and clinical implications for reproductive physiology. *Endocrine*, 3: 845-871.

Marckman, P., A. Lassen, J. Haraldsdottir and B. Sandstrøm, 1995. Biomarkers of habitual fish intake in adipose tissue. *American Journal of Clinical Nutrition*, 62:956–959.

Marsh, J.A. and C.G. Scanes, 1994. Neuroendocrine-immune interactions. *Poultry Science*, 73:1049–1061.

Marsh, D.O., T.W. Clarkson, C. Cox, G. Myers, J. Amin-Zaki and S.L.Tikriti, 1987. Fetal methylmercury poisoning: relationship between concentration in single strands of maternal hair and child effects. *Archives of Neurology*, 44:1017–1022.

Marsh, D.O., M.D. Turner, J.C. Smith, P. Allen and N. Richdale, 1995. Fetal methylmercury in a Peruvian fish-eating population. *Neurotoxicology*, 16(4):717–726.

Maynard, J.E. and L.M. Harmmes, 1970. A study of growth, morbidity and mortality among Eskimo infants of Western Alaska. *Bulletin of the World Health Organization*, 42:613–622.

McDougal, A. and S. Safe, 1998. Induction of 16alpha-/2-hydroxyestrone metabolite ratios in MCF-7 cells by pesticides, carcinogens, and antiestrogens does not predict mammary carcinogens. *Environmental Health Perspectives*, 106:203–206.

McIntyre, B.S., N.J. Barlow, D.G. Wallace, S.C. Maness, K.W. Gaido and P.M. Foster, 2000. Effects of *in utero* exposure to linuron on androgen-dependent reproductive development in the male Crl:CD(SD)BR rat. *Toxicology and Applied Pharmacology*, 167:87–99.

McKeown-Eyssen, G.E., J. Ruedy and A. Neims, 1983. Methyl mercury exposure in northern Quebec. II. Neurologic findings in children. *American Journal of Epidemiology*, 118(4):470–479.

McLachlan, J.A., 1981. *In*: Herbst, A.L. and H.A. Bern (eds.). Developmental Effects of Diethylstilboestrol (DES) in Pregnancy, New York, 148 pp.

McLean, M.R., L.W. Robertson and R.C. Gupta, 1996. Detection of PCB adducts by the 32P-postlabeling technique. *Chemical Research in Toxicology*, 9:165–171.

Meerts, I.A., J.J. van Zanden, E.A. Luijks, I. van Leeuwen-Bol, G. Marsh, E. Jakobsson, A. Bergman and A. Brouwer, 2000. Potent competitive interactions of some brominated flame retardants and related compounds with human transthyretin *in vitro*. *Toxicological Sciences*, 56:95–104.

Mehendale, H.M., 1994. Amplified Interactive Toxicity of Chemicals of Non-toxic Levels: Mechanistic considerations to Public Health. *Environmental Health Perspectives*, 102(9):139–149.

Mellanby, K., 1992. The DDT story. British Crop Protection Council, Farnham, 113 pp.

Merrill, R.M. and O.W. Brawley, 1997. Prostate cancer incidence and mortality rates among white and black men. *Epidemiology*, 8:126–131.

Michalke, B., H. Witte and P. Schramel, 2001. Development of a rugged method for selenium speciation, *Journal of Analytical Atomic Spectrometry*, 16:593–597.

Milman, N., J. Laursen, H.S. Pedersen, G. Mulvad, E. Jul, H. Saaby and J.C. Hansen, 2000. Elements in autopsy liver tissue samples from Greenlandic Inuit and Danes. II Iron measured by X-ray fluorescence spectrometry. *Journal of Trace Elements in Medicine and Biology*, 14(2):100–107.

Milnerowicz, H., 1997. Concentration of metals, ceruloplasmin, metallothionein and activity of N-Acetyl-beta-D-glucosaminidase and gamma-glutamyltransferase in pregnant women who smoke and in those environmentally exposed to tobacco and in their infants. II. Influence of environmental exposure in the Copper Basin. *International Journal of Occupational Medical Environmental Health*, 10:273–282.

Mocarelli, P., P. Brambilla, P.M. Gerthoux, D.G. Patterson, Jr. and L.L. Needham, 1996. Change in sex ratio with exposure to dioxin. *Lancet*, 348:409.

Moller, H., A. Prener and N.E. Skakkebaek, 1996. Testicular cancer, cryptorchidism, inguinal hernia, testicular atrophy, and genital malformations: case-control studies in Denmark. *Cancer Causes Control*, 7:264–274.

Monsees, T.K., M. Franz, S. Gebhardt, U. Winterstein, W.B. Schill and J. Hayatpour, 2000. Sertoli cells as a target for reproductive

hazards. *Andrologia*, 32:239–246.
Moody, C.A. and J.A. Field, 2000. Perfluorinated surfactants and the environmental implications of their use in fire-fighting foams. *Environmental Science & Technology*, 34:3864–3870.
Moore, M., M. Mustain, K. Daniel, I. Chen, S. Safe, T. Zacharewski, B. Gillesby, A. Joyeux, and P. Balaguer, 1997. Antiestrogenic activity of hydroxylated polychlorinated biphenyl congeners identified in human serum. *Toxicology and Applied Pharmacology*, 142:160–168.
Morabia, A., M.S. Bernstein, I. Bouchardy, J. Kurtz and M.A. Morris, 2000. Breast cancer and active and passive smoking: the role of the N-acetyltransferase 2 genotype. *American Journal of Epidemiology*, 152:226–232.
Morabia, A., M.S. Bernstein, F. Curtin and M. Berode, 2001. Validation of self-reported smoking status by simultaneous measurement of carbon monoxide and salivary thiocyanate. *Preventive Medicine*, 32:82–88.
Moskalewicz, J., 1993. Lessions to be learnt from Poland's attempt at moderating its consumption of alcohol. *Addiction*, 88:135S–142S.
Moysich, K.B., C.B. Ambrosone, J.E. Vena, P.G. Shields, P. Mendola, P. Kostyniak, H. Greizerstein, S. Graham, J.R. Marshall, E.F. Schisterman and J.L. Freudenheim, 1998. Environmental organochlorine exposure and postmenopausal breast cancer risk. *Cancer Epidemiology, Biomarkers & Prevention*, 7:181–188.
Moysich, K.B., P.G. Shields, J.L. Freudenheim, E.F. Schisterman, J.E. Vena, P. Kostyniak, H. Greizerstein, J.R. Marshall, S. Graham and C.B. Ambrosone, 1999. Polychlorinated biphenyls, cytochrome P4501A1 polymorphism, and postmenopausal breast cancer risk. *Cancer Epidemiology, Biomarkers & Prevention*, 8:41–44.
Mozurkewich, E.L., B. Luke, M. Avni and F.M. Wolf, 2000. Working conditions and adverse pregnancy outcome: a meta-analysis. *Obstetrics amd Gynecology*, 95:623–635.
Muckle, G., P. Ayotte, E. Dewailly, S.W. Jacobson and J.L. Jacobson, 2001a. Determinants of polychlorinated biphenyls and methylmercury exposure in inuit women of childbearing age. *Environmental Health Perspectives*, 109:957–963.
Muckle, G., P. Ayotte, E. Dewailly, S.W. Jacobson and J.L. Jacobson, 2001b. Prenatal exposure of Inuit infants from Northern Quebec to elevated levels of environmental contaminants. *Environmental Health Perspectives,* 109(12):1291–1299.
Muir, D.C.G. and J. de Boer, 1995. Recent developments in the analysis and environmental chemistry of toxaphene with emphasis on the marine environment. *Trends in Analytical Chemistry*, 14:56–66.
Muir, D., D. Bennie, C. Teixeira, A. Fisk, G. Tomy, G. Stern and M. Whittle, 2001. Short chain chlorinated paraffins: Are they persistent and bioaccumulative? *In*: Lipnick, R.L., B. Jansson, D. Mackay and M. Petreas (eds.). Persistent, Bioaccumulative, and Toxic Chemicals II. Assessment and New Chemicals, ACS Symposium Series 773, pp. 184–202. American Chemical Society, Washington DC.
Murk, A.J., P.E.G. Leonards, B. van Hattum, R. Luit, M.E.J. van der Weiden and M. Smit, 1998. Application of biomarkers for exposure and effect of polyhalogenated aromatic hydrocarbons in naturally exposed European otters (*Lutra lutra*). *Environmental Toxicology and Pharmacology*, 6:91–102.
Murkies, A.L., G. Wilcox and S.R. Davis, 1998. Clinical review 92: Phytoestrogens. *Journal of Clinical Endocrinology and Metabolism*, 83:297–303.
Mussalo-Rauhamaa, H., E. Häsänen, H. Pyysalo, K. Antervo, P. Kauppila and P. Pantzar, 1990. Occurrence of beta-hexachlorocyclohexane in breast cancer patients. *Cancer*, 66:2124–2128.
Myers, G.J., D.O. Marsh, C. Cox, P.W. Davidson, C.F. Shamlaye, M.A. Tanner, A. Choi, E. Cernichiari, E. Choisy and T.W. Clarkson, 1995a. A pilot neurodevelopmental study of Seychellois children following *in utero* exposure to methylmercury from a maternal fish diet. *Neurotoxicology*, 16:629–638.
Myers, G.J., D.O. Marsh, P.W. Davidson, C. Cox, C.F. Shamlaye. M.A. Tanner, A. Choi, E. Cernichiari, E. Choisy and T.W. Clarkson, 1995b. Main neurodevelopmental study of Seychellois children following *in utero* exposure to methylmercury from a maternal fish diet: Outcome at six months. *Neurotoxicology*, 16:653–664.
Mylchreest, E., M. Sar, R.C. Cattley and P.M. Foster, 1999. Disruption of androgen-regulated male reproductive development by di(n-butyl) phthalate during late gestation in rats is different from flutamide. *Toxicology and Applied Pharmacology*, 156:81–95.
Myles, T.D., R. Espinoza, W. Meyer, A. Bieniarz and T. Ngyen, 1998. Effects of smoking, alcohol, and drugs of abuse on the outcome of "expectantly" managed cases of preterm premature rupture of membranes. *Journal of Maternal-Fetal Medicine*, 7:157–161.
Nagayama, J., K. Okamura, T. Iida, H. Hirakawa, T. Matsueda, H. Tsuji, M. Hasegawa, K. Sato, H.Y. Ma, T. Yanagawa, H. Igarashi, J. Fukushige and T. Watanabe, 1998. Postnatal exposure to chlorinated dioxins and related chemicals on thyroid hormone status in Japanese breast-fed infants. *Chemosphere*, 37:1789–1793.
Nakamura, P., 1996. Prevention that works. *Alaska Medicine*, 38:18–20.
Näyha, S. and J Hassi, 1993. Lifestyle, work and health of Finnish reindeer herders. *Publications of Social Insurance Institution*, ML:127.
Ndayibagira, A. and P.A. Spear, 1999. Esterification and hydrolysis of vitamin A in the liver of brook trout (*Salvelinus fontinalis*) and the influence of a coplanar polychlorinated biphenyl. *Comparative Biochemistry and Physiology C: Pharmacology & Toxicology*, 122:317–325.
Nei, M. and N. Saitou, 1986. Genetic relationship of human populations and ethnic differences in reaction to drugs and food. *Progress in Clinical and Biological Research*, 214:21–37.
Nieboer, E., V.P. Tchachtchine, J.O. Odland and Y. Thomassen, 1997. Reproductive and Developmental Health in Relation to Occupational Exposure to Nickel in the Kola Peninsula of Russia: A Feasibility Study. Hamilton, Canada: McMaster University (unpublished).
Nieboer, E., V.P. Chaschchin, S. Ignatikova, J.O. Odland, Y. Thomassen and D. Ellingsen, 2000. A critical evaluation of the evidence of cardiomyopathy among Russian cobalt workers. Hamilton, Ontario, Canada: McMaster University (unpublished).
Nilsen, H., E. Utsi and K.H. Bønaa, 1999. Dietary and nutrient intake of a Sami population living in traditional reindeer herding areas of North Norway: comparisons with a group of Norwegians. *International Journal of Circumpolar Health*, 58:120–133.
Nielsen, J., 2000. Health Statistics in the Nordic Countries 1998. Nordisk Medicinalstatistisk Komite, Copenhagen.
Nielsen, N.H., H.H. Storm, L.A. Gaudette and A. Lanier, 1996. Cancer in Circumpolar Inuit. *Acta Oncologica*, 35:621–628.
Nobman, E.D., S.O.E. Ebbeson, R.G. White, R. Bulkow and C.D. Schraer, 1999. Associations between dietary factors and plasma lipids related to cardiovascular disease among Siberian Yupiks of Alaska. *International Journal of Circumpolar Health*, 58:254–271.
NOMESCO, 2001. Health statistics in the Nordic countries. Nordic Medico-Statistical Committee. International Council of Ministers. Denmark.
Nonneman, D.J., V.K. Ganjam, W.V. Welshons and F.S. Vom Saal, 1992. Intrauterine position effects on steroid metabolism and steroid receptors of reproductive organs in male mice. *Biology of Reproduction*, 47:723–729.
Nordiska Närings Rekommendationer, 1996. (In Swedish).
Nordstrøm, M.-L. and S. Cnattingius, 1996. Effects on birthweights of maternal education, socio-economic status, and work-related characteristics. *Scandinavian Journal of Social Medicine*, 24: 55–61.
Norén, K. and D. Meironyté, 2000. Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20–30 years. *Chemosphere*, 40:1111–1123.
NRC, 1992. Biological markers in immunotoxicology. US National Research Council, National Academic Press, Washington DC.
NRC, 2000. Toxicological Effects of Methylmercury. US National Research Council, National Academy Press, Washington, DC.
Nriagu, J., 1989. A global assessment of natural sources of atmospheric trace metals. *Nature*, 338:47–49.
Nummela, O., S. Helekorpi, T. Laatikainen, A. Uutela and P. Puska, 2000. Health behavior and Health status in provinces in Fin-

land 1978–1999. Publications of the National Health Institute, B 10.

NWT, 1999. The NWT Health Status Report. Government of the North West Territories, Health and Social Services. 21 pp.

Oakley, G.G., L.W. Robertson and R.C. Gupta, 1996. Analysis of polychlorinated biphenyl-DNA adducts by 32P-postlabeling. *Carcinogenesis*, 17:109–114.

Odland J.Ø., 2000. Environmental and occupational exposure, lifestyle factors and pregnancy outcome in Arctic and sub-Arctic populations of Norway and Russia. Doctoral thesis: ISM Skriftserie No. 50. Institute of Community Medicine, University of Tromsø, Norway.

Odland, J.Ø., N. Romanova, G. Sand, Y. Thomassen, E. Khotova, A. Duriagin, E. Lund and E. Nieboer, 1996. Preliminary report of the trace elements in mothers and newborn living in the Kola peninsula and Arkhangelsk region of Russia compared to Norwegian population. *Arctic Medical Research*, 55(1):38–46.

Odland, J.Ø., E. Nieboer, N. Romanova, Y. Thomassen, T. Norseth and E. Lund, 1999a. Urinary nickel concentrations and selected pregnancy outcomes in delivering women and their newborns among Arctic populations of Norway and Russia. *Journal of Environmental Monitoring*, 1(2):153–161.

Odland, J.Ø., E. Nieboer, N. Romanova, Y. Thomassen, J. Brox and E. Lund, 1999b. Essential elements, birth weight and newborn body mass index in Arctic populations of Norway and Russia. *Acta Obstetricia et Gynecologica Scandinavica*, 78: 605– 614.

Odland, J.Ø., E. Nieboer, N. Romanova, Y. Thomassen and E. Lund, 1999c. Blood lead and cadmium and birth weight among sub-Arctic and Arctic populations of Norway and Russia. *Acta Obstetricia et Gynecologica Scandinavica*, 78(10):852–860.

Odland, J.Ø., E. Nieboer, N. Romanova, Y. Thomassen, J. Brox and E. Lund, 1999d. Selfreported ethnic status of delivering women, newborn body mass index, and blood, serum and urine concentrations of toxic and essential elements in Norwegian and Russian Arctic populations. *International Journal of Circumpolar Health*, 58:4–13.

Odland, J.Ø., E. Nieboer, N. Romanova, Y. Thomassen, D. Hofoss and E. Lund, 2001. Factor analysis of essential and toxic elements in human placentas from deliveries in arctic and subarctic areas of Russia and Norway. *Journal of Environmental Monitoring*, 3(2):177–184.

Olafsdottir, H., 1998. The dynamics of shifts in alcoholic beverage preference: effects of the legalization of beer in Iceland. *Journal of Studies on Alcohol*, 59:107–114.

Olsen, J., F. Bolumar, J. Boldsen and L. Bisanti, 1997. Does moderate alcohol intake reduce fecundability? A European multicenter study on infertility and subfecundity. European Group on Infertility and Subfecundity. *Alcoholism, Clinical and Experimental Research*, 21:206–212.

Olson, J.A., 1994. Hypovitaminosis A: contemporary scientific issues. *Journal of Nutrition*, 124:1461S–1466S.

Oppenheimer, J.H., H.L. Schwartz and K.A. Strait, 1995. An Integrated View of Thyroid Hormone Actions *In Vivo*. *In*: B.D. Weintraub (ed.). Molecular Endocrinonology: Basic Concepts and Clinical Correlations, pp. 249–268. Raven Press Ltd, New York.

Ornaghi, F., S. Ferrini, M. Prati and E. Giavini, 1993. The protective effects of N-acetyl-L-cysteine against methyl mercury embryotoxicity in mice. *Fundamental and Applied Toxicology*, 20:437–445.

Ortayli, N., M. Ozugurlu and G. Gokeay, 1996. Female health workers: an obstetric risk group. *International Journal of Gynaecology and Obstetrics*, 54:263–270.

Osterhaus, A.D., R.L. de Swart, H.W. Vos, P.S. Ross, M.J. Kenter and T. Barrett, 1995. Morbillivirus infections of aquatic mammals: newly identified members of the genus. *Vetinary Microbiology*, 44:219–227.

Paigen, B., 1999. Dioxins and Dioxin-Like Chemicals. *Pesticides, People and Nature*, 1:33–52.

Pajarinen, J., P. Laippala, A. Penttila and P.J. Karhunen, 1997. Incidence of disorders of spermatogenesis in middle aged finnish men, 1981–91: two necropsy series. *British Medical Journal*, 314:13–18.

Panin, L.E. and S.I. Kiseleva, 1997. Assessment of current diet of children in boarding schools in Taymir. *Problems of Nutrition* N3, 26–30. (In Russian).

Park, S.T., K.T. Lim, Y.T. Chung and S.U. Kim, 1996. Methylmercury-induced neurotoxicity in cerebral neuron culture is blocked by antioxidants and NMDA receptor antagonists. *Neurotoxicology*, 17:37–45.

Parkinson, A.J., B.D. Gold, L. Bulkow, R.B. Wainwright, B. Swaminathan, B. Khanna, K.M. Petersen and M.A. Fitzgerald, 2000. High prevalence of *Helicobacter pylori* in the Alaska Native population and association with low serum ferritin levels in young adults. *Clinical and Diagnostic Laboratory Immunology*, 7(6):885–888.

Parlar, H., G. Reil, D. Angerhöfer and M. Coelham, 2001. Structure–activity relationship model for toxaphene congeners. *Fresenius Environmental Bulletin*, 10:122–130.

Pars, T., 2000. Forbruget af traditionelle grønlandske fødevarer i Vestgrønland. Ph.D. Thesis, University of Copenhagen.

Paschane, D., 1998. Variability of substance abuse. Global variability of substance abuse: Is latitude a unique etiological factor? *International Journal of Circumpolar Health*, 57:228–238.

Patandin, S., C.I. Lanting, E.R. Boersma, P.J.J. Sauer and N. Weisglas-Kuperus, 1997. Pre- and Posnatal exposure to PCBs and dioxins and cognitive development of Dutch children at 31/2 years of age. *Organohalogen Compounds*, 34:451–454.

Patandin, S., C. Koopman-Esseboom, M.A.J. De Ridder, N. Weisglas-Kuperus and P.J.J. Sauer, 1998. Effects of environmental exposure to polychlorinated biphenyls and dioxins on birth size and growth in Dutch children. *Pediatric Research*, 44:538–545.

Patandin, S., C.I. Lanting, P.G. Mulder, E.R. Boersma, P.J. Sauer and N. Weisglas-Kuperus, 1999. Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age. *Journal of Pediatrics*, 134:33–41.

Patrono, C. and G.A. FitzGerald, 1997. Isoprostanes: potential markers of oxidant stress in atherothrombotic disease. *Arteriosclerosis, Thrombosis and Vascular Biology*, 17:2309–2315.

Pedersen, H.S., 2000. Det grønlandske obduktionsprojekt Athero sclerose og intracerebral hæmoragi i relation til fedtsyre sammensætningen i fedtvæv og validering af dødsårsagsmønstret. Ph.D. Thesis, Aarhus University. (In Danish and English).

Pedersen, H.S., G. Mulvad, K.N. Seidelin, G.T. Malcolm and D.A. Boudreau, 1999. N-3 fatty acids as a risk factor for hemoragic stroke. *Lancet*, 353(9155):812–813.

Peen, A., P. Bergsjø, B.-I. Nesheim, Å.M. Ullern, B.W. Heggelund and I. Matheson, 1991. Characterization of birth populations in two Norwegian counties (Akershus and Hordaland). *Tidsskrft for den Norske Lægeforening*, 111:1613–1616.

Pekkanen, J., T. Husman, J. Sivonen, M. Kajosaari, A. Koivikko, M. Korppi and L. Soininen, 1996. Data book of the Finnish ISAAC study. National Public Health Institute, Helsinki, Finland.

Pelkonen, O., N. Karki, M. Koivisto, R. Tuimala and A. Kauppila, 1979. Maternal cigarette smoking, placental aryl hydrocarbon hydroxylase and neonatal size. *Toxicology Letters*, 3:331–335.

Pereg, D., J. Lagueux, E. Dewailly, G.G. Poirier and P. Ayotte, 2001. Cigarette smoking during pregnancy: comparison of biomarkers for inclusion in epidemiological studies. *Biomarkers*, 6:161–173.

Pereg, D., E. Dewailly, G.G. Poirier and P. Ayotte, 2002. Environmental exposure to polychlorinated biphenyls and placental CYP1A1 activity in Inuit women from Northern Quebec. *Environmental Health Perspectives*, 110(6):607–612.

Petersen, P.M., N.E. Skakkebaek and A. Giwercman, 1998. Gonadal function in men with testicular cancer: biological and clinical aspects. *Apmis,* 106:24–34; discussion 34–36.

Peterson, R.E., H.M. Theobald and G.L. Kimmel, 1993. Developmental and reproductive toxicity of dioxins and related compounds: cross-species comparisons. *Critical Reviews in Toxicology*, 23:283–335.

Pichini, S., X.B. Na, R. Pacifici, O. Garcia, C. Puig, O. Oriol, J. Harris, P. Zucarro, J. Segura and J. Sunyer, 2000. Cord serum cotinine as a biomarker of fetal exposure to cigarette smoke at the end of pregnancy. *Environmental Health Perspectives*, 108: 1079–1082.

Pirkle, J.L., D.J. Brody and E.W. Gunter, 1994. The decline in blood lead levels in the United States: the National Health and Nutrition Examination Surveys. *Journal of the American Medical Association*, 272:284–291.

Polder, A., J.O. Odland, A. Tkachev, S. Foreid, T.N. Savinova and J.U. Skaare, 2002a. Chlorinated pesticides, toxaphenes and PCBs in human milk from northern Russia, and possible effects on birth weight. Abstract from AMAP conference and workshop: Impacts of POPs and mercury on Arctic environments and humans, Tromsø, 20–24 January 2002

Polder, A., A. Tkachev, J.O. Odland and J.U. Skaare, 2002b. Residue pattern of chlorinated pesticides and PCBs in foodstuffs from northern Russia and human dietary exposure. Abstract from AMAP conference and workshop: Impacts of POPs and mercury on Arctic environments and humans, Tromsø 20–24 January 2002.

Polygenis, D., S. Wharton, C. Malmberg, N. Sherman, D. Kennedy, G. Koren and T.R. Einarson, 1998. Moderate alcohol consumption during pregnancy and the incidence of fetal malformations: a meta-analysis. *Neurotoxicology and Teratology*, 20:61–67.

Porta, M., N. Malats, M. Jariod, J.O. Grimalt, J. Rifa, A. Carrato, L. Guarner, A. Salas, M. Santiago-Silva, J.M. Corominas, M. Andreu and F. X. Real, 1999. Serum concentrations of organochlorine compounds and K-ras mutations in exocrine pancreatic cancer. PANKRAS II Study Group. *Lancet*, 354:2125–2129.

Porterfield, S.P., 2000. Thyroidal dysfunction and environmental chemicals – potential impact on brain development. *Environmental Health Perspectives*, 108(3):433–438.

Porterfield, S.P. and L.B. Hendry, 1998. Impact of PCBs on thyroid hormone directed brain development. *Toxicology and Industrial Health*, 14:103–120.

Pratico, D., 1999. F(2)-isoprostanes: sensitive and specific non-invasive indices of lipid peroxidation *in vivo*. *Atherosclerosis*, 147: 1–10.

Prener, A., G. Engholm and O.M. Jensen, 1996. Genital anomalies and risk for testicular cancer in Danish men. *Epidemiology*, 7: 14–19.

Quinn, M. and E. Allen, 1995. Changes in incidence of and mortality from breast cancer in England and Wales since introduction of screening. United Kingdom Association of Cancer Registries. *British Medical Journal*, 311:1391–1395.

Raby, R., M. Blaiss, S. Gross and H.G. Herrod, 1996. Antibody response to unconjugated Haemophilus influenzae b and pneumococcal polysaccharide vaccines in children with recurrent infections. *Journal of Allergy and Clinical Immunology*, 98:451–459.

Rahman, F., K.H. Langford, M.D. Scrimshaw and J.N. Lester, 2001. Polybrominated diphenyl ether (PBDE) flame retardants. *Science of the Total Environment*, 275:1–17.

Ramamoorthy, K., F. Wang, I.-C. Chen, J.D. Norris, D.P. McDonnell, L.S. Leonard, K.W. Gaido, W.P. Bocchinfuso, K.S. Korach and S. Safe, 1997. Estrogenic activity of a dieldrin/toxaphene mixture in the mouse uterus, MCF-7 human breast cancer cells, and yeast-based estrogen receptor assays: no apparent synergism. *Endocrinology*, 138:1520–1527.

Rayman, M.P., 1997. Dietary selenium: time to act. *British Medical Journal*, 314:387–388.

Receveur, O., M. Boulay and H.V. Kuhnlein, 1997. Decreasing traditional food use affects diet quality for adult Déne/Métis in 16 communities in Canadian NWT. *Journal of Nutrition*, 127(11): 2179–2186.

Reijnders, P.J., 1986. Reproductive failure in common seals feeding on fish from polluted coastal waters. *Nature*, 324:456–457.

Remington, G. and B.F. Hoffman, 1984. Gas sniffing as a form of substance abuse. *Canadian Journal of Psychiatry*, 29:31–35.

Renner, R., 2000. What fate for brominated fire retardants? *Environmental Science & Technology*, 34(9):222A–226A.

Rhainds, M., P. Levallois, E. Dewailly and P. Ayotte, 1999. Lead, mercury and organochlorine compound levels in cord blood in Quebec, Canada. *Archives of Environmental Health*, 54:40–47.

Ribas-Fito, N., M. Sala, M. Kogevinas and J. Sunyer, 2001. Polychlorinated biphenyls (PCBs) and neurological development in children: a systematic review. *Journal of Epidemiology and Community Health*, 55:537–546.

Rissanen, T., 2000. Fish Oil-Derived Fatty Acids, Docosahexaenoic Acid and Docosapentaenoic Acid, and the Risk of Acute Coronary Events. *Circulation*, 28: 2677–2679.

Robinson, J., 1981. Lead in Greenland snow. *Ecotoxicology and Environmental Safety*, 5:24–37.

Rodier, P.M., 1994. Vulnerable Periods and Processes during Central Nervous System Development. *Environmental Health Perspectives*, 102(2):121–124.

Roels, H., G. Hubermont, J.P. Buchet and R. Lauwerys, 1978. Placental transfer of lead, mercury, cadmium and carbon monoxide in women, Part III. *Environmental Research*, 16:236–247.

Rogan, W. and B.C. Gladen, 1991. PCBs, DDE, and child development at 18 and 24 months. *Annals of Epidemiology*, 1:409–413.

Rogan, W., B.C. Gladen, J.D. McKinney, N. Carreras, P. Hardy, J. Thullen, J. Tinglestad and M. Tully, 1986a. Neonatal effects of transplacental exposure to PCBs and DDE. *Journal of Pediatrics*, 109:335–341.

Rogan, W., B.C. Gladen, J.D. McKinney, N. Carreras, P. Hardy, J. Thullen, J. Tinglestad and M. Tully, 1986b, Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human milk: Effects of maternal factors and previous lactation. *American Journal of Public Health*, 76:172–177.

Rogan, W., B.C. Gladen, K. Hung, S. Koong and L. Shih, 1988. Congenital poisoning by polychlorinated biphenyls and their contaminants in Taiwan. *Science*, 241:334–336.

Romberg, R.W., S.B. Needleman and M. Past, 1992. Factors influencing confirmed drug positives for Navy and Marine Corps recruits. *Military Medicine*, 157:33–37.

Romieu, I., M. Hernandez-Avila, E. Lazcano-Ponce, J.P. Weber and E. Dewailly, 2000. Breast cancer, lactation history, and serum organochlorines. *American Journal of Epidemiology*, 152:363–370.

Romkes, M., J. Piskorska Pliszczynska and S. Safe, 1987. Effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin on hepatic and uterine estrogen receptor levels in rats. *Toxicology and Applied Pharmacology*, 87:306–314.

Routledge, E.J., J. Parker, J. Odum, J. Ashby and J.P. Sumpter, 1998. Some alkyl hydroxy benzoate preservatives (parabens) are estrogenic. *Toxicology and Applied Pharmacology*, 153:12–19.

Rubin, C.H., A. Lanier, M. Socha, J.W. Brock, S. Kieszak and S. Zahm, 2001. Exposure to persistent organochlorines among Alaska Native women. *Internationl Journal of Circumpolar Health*, 60(2):157–169.

Ruiz, J.M., G. Bachelet, P. Caumette and O.F.X. Donard, 1996. Three decades of tributyltin in the coastal environment with emphasis on Arcachon Bay, France. *Environmental Pollution*, 93:195–203.

RFCSES, 1998. Annual Report. Russian Federal Center for Sanitary and Epidemiological Surveillance. (in Russian).

Rylander, L., U. Stromberg and L. Hagmar, 1995. Decreased birthweight among infants born to women with a high dietary intake of fish contaminated with persistent organochlorine compounds. *Scandanavian Journal of Work Environment & Health*, 21:368–375.

Rylander, L., U. Stromberg, E. Dyremark, C. Ostman, P. Nilsson-Ehle and L. Hagmar, 1998. Polychlorinated biphenyls in blood plasma among Swedish female fish consumers in relation to low birth weight. *American Journal of Epidemiology*, 147:493–502.

Rylander, L, U. Strömberg and L. Hagmar, 2000. Lowered birth weight among infants born to women with a high intake of fish contaminated with persistent organochlorine compounds. *Chemosphere*, 40:1255–1262.

Sadiki, A. and D. Williams, 1996. Speciation of organotin and organolead compounds in drinking water by gas chromatography-atomic emission spectrometry. *Chemosphere*, 32:1983–1992.

Safe, S.H., 1994. Polychlorinated biphenyls (PCBs): Environmental impact, biochemical and toxic responses, and implications for risk assessment. *Critical Reviews in Toxicology*, 24:87–149.

Safe, S.H., 1997. Is there an association between exposure to environmental estrogens and breast cancer? *Environmental Health Perspectives*, 105(3):675–678.

Safe, S.H., 2000. Endocrine disruptors and human health – is there a problem? An update. *Environmental Health Perspectives*, 108:487–493.

Safe, S. and V. Krishnan, 1995. Cellular and molecular biology of aryl hydrocarbon (Ah) receptor-mediated gene expression. *Archives of Toxicology. Supplement*, 17:99–115.

Sager, D.B., W. Shih-Schroeder and D. Girard, 1987. Effect of early postnatal exposure to polychlorinated biphenyls (PCBs) on fertility in male rats. *Bulletin of Environmental Contamination and Toxicology*, 38:946–953.

Saillard, J., P. Forster, N. Lynnerup, H.J. Bandelt and S. Norby, 2000. mtDna variation among Greenland Eskimos: the edge of the Beringian expansion. *American Journal of Human Genetics*, 67:718–726.

Sallsten, G., S. Kreku and H. Unosson, 2000. A small dose of ethanol increases the exhalation of mercury in low-level-exposed humans. *Journal of Toxicology and Environmental Health*, 60:89–100.

Salonen, J.T., G. Alfthan, J.K. Huttunen, J. Pikkarainen and P. Puska, 1982. Association between cardiovascular death and myocardial infarction and serum selenium in a matched-pair longitudinal study. *Lancet*, ii:175–179.

Salonen, J.T., K. Seppanen, K. Nyyssnen, H. Korpela, J. Kauhanen, M. Kantola, J. Tuomilehto, H. Esterbauer, F. Tatzber and R. Salonen, 1995. Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular and any death in Eastern Finnish men. *Circulation*, 91: 645–655.

Sandau, C.D., P. Ayotte, E. Dewailly, J. Duffe and R.J. Norstrom, 2000a. Analysis of hydroxylated metabolites of PCBs (OH-PCBs) and other chlorinated phenolic compounds in whole blood from Canadian Inuit. *Environmental Health Perspectives*, 108:611–616.

Sandau, C.D., I.A.T.M. Meerts, R.J. Letcher, A.J. Mcalees, B. Chittim, A. Brouwer and R.J. Norstrom, 2000b. Identification of 4-hydroxyheptachlorostyrene in polar bear plasma and its binding affinity to transthyretin: A metabolite of octachlorostyrene? *Environmental Science & Technology*, 34:3871–3877.

Sandau, C.D., P. Ayotte, É. Dewailly, J. Duffe and R.J. Norstrom, 2002. Pentachlorophenol and hydroxylated polychlorinated biphenyl metabolites in umbilical cord plasma of neonates from coastal populations in Quebec. *Environmental Health Perspectives*, 110(4):411–417.

Sandyk, R. and J.D. Kanofsky, 1992. Cocaine addiction: Relationship to seasonal affective disorder. *International Journal of Neuroscience*, 64:195–201.

Sarafian, T. and M.A. Verity, 1991. Oxidative mechanisms underlying methyl mercury neurotoxicity. *International Journal of Developmental Neuroscience*, 9:147–153.

Sarkola, T., C.J. Eriksson, O. Niemela, P. Sillanaukee and E. Halmesmaki, 2000. Mean cell volume and gamma-glutamyl transferase are superior to carbohydrate-deficient transferrin and hemoglobin-acetaldehyde adducts in the follow-up of pregnant women with alcohol abuse. *Acta Obstetricia et Gynecologica Scandinavica*, 79:359–366.

Satel, S.L. and F.H. Gawin, 1989. Seasonal cocaine abuse. *American Journal of Psychiatry*, 146:534–535.

Satoh, K., F. Nagai and N. Aoki, 2001. Several environmental pollutions have binding affinities for both androgen receptor and estrogen receptor alpha. *Journal of Health Science*, 47:495–501.

Sauer, P.J.J., M. Huisman, C. Koopman-Esseboom, D.C. Morse, A.E. Smits-van Prooije, A.E. van der Berg, L.G.M.T. Tuinstra, C.G. van der Paauw, E.R. Boersma, N. Weisglas-Kuperus, J.H.C.M. Lammers, B.M. Kulig and A. Bouwer, 1994. Effects of polychlorinated biphenyls (PCBs) and dioxins on growth and development. *Human and Experimental Toxicology*, 13:900–906.

Saurel-Cubizolles, M.-J., M. Kaminski, C. Du Mazaubrun and G. Breart, 1991a. Working conditions of women with arterial hypertension during pregnancy. *Revue d'Epidemiologie et de Sante Publique*, 39:37–43.

Saurel-Cubizolles, M.-J., M. Kaminski, C. Du Mazaubrun, J. llado and M. Estryn-Behar, 1991b. High blood pressure during pregnancy and working conditions among hospital personnel. *European Journal of Obstetrics, Gynecology and Reproductive Biology*, 40:29–34.

Schwartz, P.M., S.W. Jacobson, G. Fein, J.L. Jacobson and H.A. Price, 1983. Lake Michigan fish consumption as a source of polychlorinated biphenyls in human cord serum, maternal serum, and milk. *American Journal of Public Health*, 73: 293–296.

SCTEE, 1999. Human and wildlife health effects of endocrine disrupting chemicals with emphasis on wildlife and on ecotoxicology test methods. Committee for Toxicity and the environment (SCTEE). http://europa.eu.int/comm/food/fs/sc/sct/out37.

Selden, A.I., Y. Nygren, H.B. Westberg and L.S. Bodin, 1997. Hexachlorobenzene and octachlorostyrene in plasma of aluminium foundry workers using hexachloroethane for degassing. *Occupational and Environmental Medicine*, 54:613–618.

Selevan, S.G., C.A. Kimmel and P. Mendola, 2000. Identifying critical windows of exposure for children's health. *Environmental Health Perspectives*, 108(3):451–455.

Semba, R.D., 1994. Vitamin A, immunity, and infection. *Clinical Infectious Diseases*, 19:489–499.

Semba, R.D., Muhilal, B.J. Ward, D.E. Griffin, A.L. Scott, G. Natadisastra, K.P. West, Jr., and A. Sommer, 1993. Abnormal T-cell subset proportions in vitamin-A-deficient children. *Lancet*, 341:5–8.

Shaham, J., A. Meltzer, R. Ashkenazi and J. Ribak, 1996. Biological monitoring of exposure to cadmium, a human carcinogen, as a result of active and passive smoking. *Journal of Occupational and Environmental Medicine*, 38:1220–1228.

Sharma, M. and P. Bhatnagar, 1996. Organochlorine pesticides and preterm labour in human beings. *Current Science*, 71(8): 628–631.

Sharpe, R.M., 1993. Declining sperm counts in men – is there an endocrine cause? *Journal of Endocrinology*, 136:357–360.

Sharpe, R.M., 1994. *In*: E. Knobil and J.D. Neill (eds.), The Physiology of Reproduction, pp. 1363–1434. Raven Press, New York.

Sharpe, R.M. and N.E. Skakkebaek, 1993. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? *Lancet*, 341:1392–1395.

Sherlock, J., J. Hislop, D. Newton, G. Topping and K. Whittle, 1984. Elevation of mercury in human blood from controlled chronic ingestion of methylmercury in fish. *Human Toxicology*, 3(2):117–131.

Shu, X.O., M.C. Hatch, J. Mills, J. Clemens and M. Susser, 1995. Maternal smoking, alcohol drinking, caffeine consumption, and fetal growth: results from a prospective study. *Epidemiology*, 6:115–120.

Shultz, J.M., D.P. Rice, D.L. Parker, R.A. Goodman, G. Stroh and N. Chalmers, 1991. Quantifying the disease impact of alcohol with ARDI software. *Public Health Reports*, 106:443–450.

Schuur, A.G., F.F. Legger, M.E. van Meeteren, M.J. Moonen, I. van Leeuwen-Bol, A. Bergman, T.J. Visser and A. Brouwer, 1998. In vitro inhibition of thyroid hormone sulfation by hydroxylated metabolites of halogenated aromatic hydrocarbons. *Chemical Research in Toxicology*, 11:1075–1081.

Simopolous, A.P., 1991. Omega fatty acids in health and disease and in growth and development. *American Journal of Clinical Nutrition*, 54:438.

Simopolous, A.P., 1999. Human Rrequirement for n-3 polyunsaturated fatty acids. *Poultry Science*, 79(7):961–970.

Simpura, J., C. Tigerstedt, S. Hanhinen, M. Lagerspetz, H. Leifman, J. Moskalewicz and J. Torronen, 1999. Alcohol misuse as a health and social issue in the Baltic Sea region. A summary of findings from the Baltica Study. *Alcohol and Alcoholism*, 34: 805–823.

Singleton, R.J., N.M. Davidson, I.J. Desmet, J.E. Berner, R.B. Wainwright, L.R. Bulkow, C.M. Lilly and G.R. Siber, 1994. Decline of Hemophilus influenza type B disease in a region of high risk: impact of active and passive immunization. *Pediatric Infectious Disease Journal*, 13:362–367.

Sjodin, A., L. Hagmar, E. Klasson-Wehler, J. Bjork and A. Bergman, 2000. Influence of the consumption of fatty Baltic Sea fish on plasma levels of halogenated environmental contaminants in Latvian and Swedish men. *Environmental Health Perspectives*, 108:1035–1041.

Skaare, J.U., A. Bernhoft, A. Derocher, G.W. Gabrielsen, A. Goksoyr, E. Henriksen, H.J. Larsen, E. Lie and Ø. Wiig, 2000. Organochlorines in top predators at Svalbard – occurrence, levels and effects. *Toxicology Letters*, 112:103–109.

Smith, S.M. and J.P. Middaugh, 1986. Injuries associated with three-wheeled, all-terrain vehicles, Alaska, 1983 and 1984. *Journal of the American Medical Association*, 255:2454–2458.

Smith, A.H., C. Hopenhayn-Rich, M.N. Bates, H.M. Goeden, I. Hertz-Picciotto, H.M. Duggan, R. Wood, M.J. Kosnett and

M.T. Smith, 1992. Cancer risks from arsenic in drinking water. *Environmental Health Perspectives*, 97:259–267.

Smith, A.H., E.O. Lingas and M. Rahman, 2000. Contamination of drinking-water by arsenic in Bangladesh: a public health emergency. *Bulletin of the World Health Organization*, 78:1093–1103.

SOA, 2001. Mercury and National Fish Advisories. Statement from Alaska Division of Public Health. Recommendations for Fish Consumption in Alaska. Bulletin No. 6 June 15 2001. State of Alaska.

Sohlenius, A.K., A.M. Eriksson, C. Hogstrom, M. Kimland and J.W. De Pierre, 1993. Perfluorooctane sulfonic acid is a potent inducer of peroxisomal fatty acid beta-oxidation and other activities known to be affected by peroxisome proliferators in mouse liver. *Pharmacology and Toxicology*, 72:90–93.

Sohoni, P. and J.P. Sumpter, 1998. Several environmental oestrogens are also anti-androgens. *Journal of Endocrinology*, 158:327–339.

Soininen, L., H. Mussalo-Rauhamaa and R. Vitikka, 2000. Abstracts of presentations at the workshop on Persistent Organic Pollutants (POPs) in the Arctic: Human Health and Environmental Concerns. Rovaniemi, Finland, January 18–20, 2000.

Sommer, A. and K.P. West, 1996. Vitamin A Deficiency: Health, Survival and Vision. Oxford University Press, New York.

Sonnenschein, C., A.M. Soto, M.F. Fernandez, N. Olea, M.F. Olea Serrano and M.D. Ruiz Lopez, 1995. Development of a marker of estrogenic exposure in human serum. *Clinical Chemistry*, 41:1888–1895.

Sorensen, T.I., 2000. The changing lifestyle in the world. Body weight and what else? *Diabetes Care*, 23(2):B1–B4.

Sorensen, N., K. Murata, E. Budtz-Jorgensen, P. Weihe and P. Grandjean, 1999. Prenatal methylmercury exposure as a cardiovascular risk factor at seven years of age. *Epidemiology*, 10(4):370–375.

Soto, A.M., K.L. Chung and C. Sonnenschein, 1994. The pesticides endosulfan, toxaphene, and dieldrin have estrogenic effects on human estrogen-sensitive cells. *Environmental Health Perspectives*, 102:380–383.

Spink, D.C., H.P. Eugster, D.W. Lincoln, 2nd, J.D. Schuetz, E.G. Schuetz, J.A. Johnson, L.S. Kaminsky and J.F. Gierthy, 1992a. 17 beta-estradiol hydroxylation catalyzed by human cytochrome P450 1A1: a comparison of the activities induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin in MCF-7 cells with those from heterologous expression of the cDNA. *Archives of Biochemistry and Biophysics*, 293:342–348.

Spink, D.C., D.W. Lincoln II, J.A. Johnson, H.W. Dickerman and J.F. Gierthy, 1992b. Stimulation of 17 -beta- etradiol metabolism in MCF-7 breast cancer cells by 2,3,7,8-tetrachlorodibenzo-P-dioxin. *Chemosphere*, 25:87–90.

Spink, D.C., C.L. Hayes, N.R. Young, M. Christou, T.R. Sutter, C.R. Jefcoate and J.F. Gierthy, 1994. The effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on estrogen metabolism in MCF-7 breast cancer cells: evidence for induction of a novel 17 beta-estradiol 4-hydroxylase. *Journal of Steroid Biochemistry & Molecular Biology*, 51:251–258.

Spink, D.C., B.C. Spink, J.Q. Cao, J.A. DePasquale, B.T. Pentecost, M.J. Fasco, Y. Li and T.R. Sutter, 1998. Differential expression of CYP1A1 and CYP1B1 in human breast epithelial cells and breast tumor cells. *Carcinogenesis*, 19:291–298.

Stark, K., G. Mulvad, H.S. Pedersen, E. Park, E. Dewailly and B. Holub, 1999. The fatty acid composition of serum phospholipids of postmenopausal women from Greenland and Canada. The 91th meeting of American Oil Chemists.

Stenback, F. and P. Saukko, 1996. Alcohol-associated deaths and their geographical locations. *Arctic Medical Research*, 44: 42–47.

Stengel, B., M.J. Saurel-Cubizolles and M. Kaminski, 1986. Pregnant Immigrant Women: Occupational Activity, Antenatal Care and Outcome. *International Journal of Epidemiology*, 15:533–539.

Steuerwald, U., P. Weihe, P.J. Jorgensen, K. Bjerve, J. Brock, B. Heinzow, E. Budtz-Jorgensen and P. Grandjean, 2000. Maternal seafood diet, methylmercury exposure, and neonatal neurologic function. *Journal of Pediatrics*, 136:599–605.

Stewart, P., T. Darvill, E. Lonky, J. Reihman, J. Pagano and B. Bush, 1999. Assessment of prenatal exposure to PCBs from maternal consumption of Great Lakes fish: An analysis of PCB pattern and concentration. *Environmental Research Section A,* 80:S87–S96.

Stewart, P., J. Reihman, E. Lonky, T. Darvill and J. Pagano, 2000. Prenatal PCB exposure and neonatal behavioral assessment scale (NBAS) performance. *Neurotoxicology and Teratology*, 22:21–29.

Strand, K., E. Wergeland and T. Bjerkedal, 1996. Fertility patterns according to occupational grouping in Norway, 1989. *Scandinavian Journal of Social Medicine*, 1:50–54.

Strand, K., E. Wergeland and T. Bjerkedal, 1997a. Job adjustment as a means to reduce sickness absence during pregnancy. *Scandanavian Journal of Work Environment & Health*, 23:378–384.

Strand, K., E. Wergeland and T. Bjerkedal, 1997b. Work load, job control and risk of leaving work by sickness certification before delivery, Norway 1989. *Scandinavian Journal of Social Medicine*, 25:193–201.

Stratton, K., C. Howe and F. Battaglia (eds.), 1996. Fetal Alcohol Syndrome. Diagnosis, Epidemiology, Prevention, and Treatment. National Academy Press, Washington, D.C.

Thomassen, Y., E. Nieboer, D. Ellingsen, S. Hetland, T. Norseth, J.O. Odland, N. Romanova, S. Chernova and V.P. Tchachtchine, 1999. Characterization of worker's exposure in a Russian nickel refinery. *Journal of Environmental Monitoring*, 1: 15–25.

Thrasher, J.D., 2000. Are chlorinated pesticides a causation in maternal mitochondrial DNA (mtDNA) mutations? *Archives of Environmental Health*, 55:292–294.

Tilson, H.A., J.L. Jacobson and W.J. Rogan,1990. Polychlorinated biphenyls and the developing nervous system: cross-species comparisons. *Neurotoxicology and Teratology*, 12:239–248.

To-Figueras, J., C. Barrot, M. Sala, R. Otero, M. Silva, M.D. Ozalla, C. Herrero, J. Corbella, J. Grimalt and J. Sunyer, 2000. Excretion of hexachlorobenzene and metabolites in feces in a highly exposed human population. *Environmental Health Perspectives*, 108:595–598.

Tomy, G.T., A.T. Fisk, J.B. Westmore and D.C.G. Muir, 1998. Environmental chemistry and toxicology of polychlorinated n-alkanes. *Reviews of Environmental Contamination and Toxicology*, 158:53–128.

Tremblay, N.W. and A.P. Gilman, 1995. Human health, the Great Lakes, and environmental pollution: a 1994 perspective. *Environmental Health Perspectives*, 103(9):3–5.

Tseng, W-P., 1977. Effects and dose-response relationships of skin cancer and Blackfoot disease with arsenic. *Environmental Health Perspectives,* 19:109–119.

Tsuchiya, H., S. Shima, H. Kurita, T. Ito, Y. Kato, Y. Kato and S. Tachikawa, 1987. Effects of maternal exposure to six heavy metals on fetal development. *Bulletin of Environmental Contamination and Toxicology*, 38:580–587.

Uauy, R., D.G. Birch, E.E. Birch, J.E. Tyson and D.R. Hoffman, 1990. Effects of dietary omega-3 fatty acids on retinal function of very-low-birth-weight neonates. *Pediatric Research*, 28(5):485–492.

Ubelaker, D.H, 1992. North American Indian population size: changing perspectives. *In*: J.W. Verano and D.H. Ubelaker (eds.). Disease and Demography in the Americas, pp. 169–76. Smithsonian Institution Press.

Upham, B.L., N.D. Deocampo, B. Wurl and J.E. Trosko, 1998. Inhibition of gap junctional intercellular communication by perfluorinated fatty acids is dependent on the chain length of the fluorinated tail. *International Journal of Cancer*, 78:491–495.

Ursin, G., S. London, F.Z. Stanczyk, E. Gentzschein, A. Paganini Hill, R.K. Ross and M.C. Pike, 1997. A pilot study of urinary estrogen metabolites (16alpha-OHE1 and 2-OHE1) in postmenopausal women with and without breast cancer. *Environmental Health Perspectives*, 105(3):601–605.

US EPA, 1991. National air quality and emission trends report. Research Triangle Park, North Carolina, U.S. Environmental Protection Agency (EPA-450/4-91-023).

USGS, 1996. U.S. Geological Survey and U.S. Bureau of Mines, Mineral Commodities Summaries: Lead Statistics, Washington DC.

USGS, 2001a. U.S. Geological Survey Open-File Report 01-006, Historical Statistics for Mineral Commodities in the United States.

USGS, 2001b. U.S. Geological Survey Open-File Report 01-006, Historical Statistics for Mineral Commodities in the United States.

USGS, 2001c. U.S. Geological Survey Open-File Report 01-006, Historical Statistics for Mineral Commodities in the United States.

US IHS, 2000. Regional differences in Indian health 1998–99. Department of Health and Human Services. US Indian Health Service. 113 pp.

Vacchio, M.S., J.D. Ashwell and L.B. King, 1998. A positive role for thymus-derived steroids in formation of the T-cell repertoire. *Annals of the New York Academy of Sciences*, 840:317–327.

van den Berg, K.J., 1990. Interaction of chlorinated phenols with thyroxine binding sites of human transthyretin, albumin and thyroid binding globulin. *Chemico-Biological Interactions*, 76: 63–75.

van den Berg, K.J., J.A. van Raaij, P.C. Bragt and W.R. Notten, 1991. Interactions of halogenated industrial chemicals with transthyretin and effects on thyroid hormone levels *in vivo*. *Archives of Toxicology*, 65:15–19.

Van Loveren, H., D. Germolec and H.S. Koren, 1999. Report of the Bilthoven Symposium: Advancement of Epidemiological Studies in Assessing the Human Effects of Immunotoxic Agent in the Environment and the Workplace. *Biomarkers*, 4:135–157.

Van Oostdam, J., A. Gilman, E. Dewailly, P. Usher, B. Wheatly, H.V. Kuhnlein, S. Neve, J. Walker, B. Tracy, M. Feely, V. Jerome and B. Kwavnick, 1999. Human health implications of environmental contaminants in Arctic Canada: A review. *Science of the Total Environment*, 230:1–82.

Van Oostdam, J.C., E. Dewailly, A. Gilman, J.C. Hansen, J.P. Weber, J.O. Odland, V. Tchaatchchine, J. Berner, J. Walker, B.J. Lagerkvist, K. Olafsdottir, L. Soininen, P. Bjerregard and V. Klopov, in prep. Circumpolar Blood Contaminant Survey 1994–1997.

van't Veer, P., I.E. Lobbezoo, J.M. Martín-Moreno, E. Guallar, J. Gómez Aracena, A.F.M. Kardinaal, L. Kohlmeier, B.C. Martin, J.J. Strain, M. Thamm, M.P. van Zoonen, B.A. Baumann, J.K. Huttunen and F.J. Kok, 1997. DDT (dicophane) and postmenopausal breast cancer in Europe: case-control study. *British Medical Journal*, 315:81–85.

Van Waeleghem, K., N. De Clercq, L. Vermeulen, F. Schoonjans and F. Comhaire, 1996. Deterioration of sperm quality in young healthy Belgian men. *Human Reproduction*, 11:325–329.

Vercauteren, J., C. Peres, C. Devos, P. Sandra, F. Vanhaecke and L. Moens, 2001. Stir bar sorptive extraction for the determination of ppq-level traces of organotin compounds in environmental samples with thermal desorption-capillary gas chromatography-ICP mass spectrometry. *Analytical Chemistry*, 73:1509–1514.

Verkerk, P.H., S.E. Buitendijk and S.P. Verloove-Vanhorick, 1994. Differential misclassifiaction of alcohol and cigarette consumption by pregnancy outcome. *International Journal of Epidemiology*, 23:1218–1225.

Villeneuve, D.L., K. Kannan, J.S. Khim, J. Falandysz, V.A. Nikiforov, A.L. Blakenship and J.P. Giesy, 2000. Relative potencies of individual polychlorinated naphthalenes to induce dioxin-like responses in fish and mammalian *in vitro* bioassays. *Archives of Environmental Contamination and Toxicology*, 39:273–281.

Vinggaard, A.M., C. Hnida and J.C. Larsen, 2000. Environmental polycyclic aromatic hydrocarbons affect androgen receptor activation *in vitro*. *Toxicology*, 145:173–183.

Voldner, E.C. and Y.F. Li, 1993. Global usage of toxaphene. *Chemosphere*, 27:2073–2078.

Voldner, E.C. and Y.F. Li, 1995. Global usage of selected persistent organochlorines. *Science of the Total Environment*, 160/161: 201–210.

Vos, J.G. and M.I. Luste, 1989. Immune alterations. *In*: Kimbrough and Jensen (eds.), Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxin and related products. pp. 295–322. Elsevier Science Publishers, New York.

Wakita, Y., 1987. Hypertension induced by methyl mercury in rats. *Toxicology and Applied Pharmacology*, l89:144–147.

Waldram, J.B., D.A. Herring and T.K. Young, 1995. Aboriginal health in Canada: Historical cultural, and epidemiological perspectives. Toronto, Canada: University of Toronto Press.

Walker, J., J. Van Oostdam and E. McMullen, 2001. Human Contaminant Trends in Arctic Canada: Northwest Territories and Nunavut Environmental Contaminants Exposure Baseline. Final Technical Report. Department of Health and Social Services, Government of the Northwest Territories. Produced under contract to J. Walker.

Walkowiak, J., J.A. Wiener, A. Fastabend, B. Heinzow, U. Kramer, E. Schmidt, H.J. Steingruber, S. Wundram and G. Winneke, 2001. Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. *Lancet*, 358:1602–1607.

Ward, J.I., M.K. Lum, D.B. Hall, D.R. Silimperi and T.R. Bender, 1986. Invasive Haemophilus influenzae type b disease in Alaska: background epidemiology for a vaccine efficacy trial. *Journal of Infectious Diseases*, 153:17–26.

Ward, J.I., J.M. Liebman and S.L. Cochi, 1994. Haemophilus influenza vaccine. *In*: S.A. Plotkin (ed.), In vaccines, pp. 337–387. WB Saunders.

Warkany, J. and D.M. Hubbard, 1953. Acrodynia and mercury. *Journal of Pediatrics*, 19:365–386.

Weber, J.P., 1996. Quality in environmental toxicology measurements. *Therapeutic Drug Monitoring*, 18:477–483.

Weihe, P., P. Grandjean and U. Steurwald, 2000. Pregnancy outcome in relation to contaminated maternal diet in the Faroe Islands. Proceedings of the Workshop on persistent organic pollutants in the Arctic: Human Health and environmental concerns, AMAP report 2000:1, Rovaniemi, 18–20 January.

Weihe, P., J.C. Hansen, K. Murata, F. Debes, P. Jorgensen, U. Steuerwald, R.F. White and P. Grandjean, 2002. Neurobehavioral performance of inuit children with increased prenatal exposure to methylmercury. *International Journal of Circumpolar Health*, 61(1):41–49.

Weisglas-Kuperus, N., T.C. Sas, C. Koopman-Esseboom, C.W. van der Zwan, M.A. De Ridder, A. Beishuizen, H. Hooijkaas and P.J. Sauer, 1995. Immunologic effects of background prenatal and postnatal exposure to dioxins and polychlorinated biphenyls in Dutch infants. *Pediatric Research*, 38:404–410.

Weisglas-Kuperus, N., S. Patandin, G.A. Berbers, T.C. Sas, P.G. Mulder, P.J. Sauer and H. Hooijkaas, 2000. Immunologic effects of background exposure to polychlorinated biphenyls and dioxins in Dutch preschool children. *Environmental Health Perspectives*, 108:1203–1207.

Weistrand, C. and K. Norén, 1998. Polychlorinated naphthalenes and other organochlorine contaminants in human adipose and liver tissue. *Journal of Toxicology and Environmental Health*, Part A, 53:293–311.

Wergeland, E. and K. Strand, 1997. Working conditions and prevalence of pre-eclampsia, Norway 1989. *International Journal of Gynaecology and Obstetrics*, 58:1989–1996.

Wergeland, E. and K. Strand, 1998a. Need for job adjustment in pregnancy. Early prediction based on work history. *Scandinavian Journal of Primary Health Care*, 16:90–94.

Wergeland, E. and K. Strand, 1998b. Work pace control and pregnancy health in a population-based sample of employed women in Norway. *Scandanavian Journal of Work Environment & Health*, 24:206–212.

Wergeland, E., K. Strand and T. Bjerkedal, 1996. Smoking in pregnancy: a way to cope with excessive workload? *Scandinavian Journal of Primary Health Care*, 14:21–28.

Wergeland, E., K. Strand and P.E. Børdahl, 1998. Strenous working conditions and birthweight, Norway 1989. *Acta Obstetricia et Gynecologica Scandinavica*, 77:263–271.

Whalen, M.M., B.G. Loganathan and K. Kannan, 1999. Immunotoxicity of environmentally relevant concentrations of butyltins on human natural killer cells *in vitro*. *Environmental Research*, 81(2):108–116.

Whanger, P.D., 1992. Selenium in the treatment of heavy metal poisoning and chemical carcinogenesis. *Journal of Trace Elements and Electrolytes in Health and Disease*, 6:209–221.

Wheatley, B. and S. Paradis, 1998. Northern exposure: further analysis of the results of the Canadian aboriginal methylmercury program. *International Journal of Circumpolar Health*, 57(1): 586–590.

White, K.L., Jr., H.H. Lysy, J.A. McCay and A.C. Anderson, 1986. Modulation of serum complement levels following exposure to polychlorinated dibenzo-p-dioxins. *Toxicology and Applied*

Pharmacology, 84:209–219.
WHO, 1990. Evaluation of certain food additives and the contaminants mercury, lead and cadmium. Sixteenth report of the Joint FAO/WHO Committee of Food Additives. WHO Technical Report Series no 505. World Health Organization, Geneva.
WHO, 1992. Environmental Health Criteria 134. Cadmium. World Health Organization, Geneva.
WHO, 1995. Publication of the largest global study on cocaine use ever undertaken. World Health Organization, Geneva.
WHO, 2000. Joint FAO/WHO Expert Committee on Food Additives. Evaluation of certain food additives and contaminants. Fifty-third report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series. Geneva.
Whysner, J. and G.M. Williams, 1996. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin mechanistic data and risk assessment: gene regulation, cytotoxicity, enhanced cell proliferation, and tumor promotion. *Pharmacology and Therapeutics*, 71:193–223.
Wiberg, K., R.J. Letcher, C.D. Sandau, R.J. Norstrom, M. Tysklind and T.F. Bidleman, 2000. The enantioselective bioaccumulation of chiral chlordane and a-HCH contaminants in the polar bear food chain. *Environmental Science & Technology*, 34:2668–2674.
Wiig, O., A.E. Derocher, M.M. Cronin and J.U. Skaare, 1998. Female pseudohermaphrodite polar bears at Svalbard. *Journal of Wildlife Diseases*, 34:792–796.
Wilcox, A.J., D.D. Baird, C.R. Weinberg, P.P. Hornsby and A.L. Herbst, 1995. Fertility in men exposed prenatally to diethylstilbestrol. *New England Journal of Medicine*, 332:1411–1416.
Wilkinson, T.J., B.M. Colls and P.J. Schluter, 1992. Increased incidence of germ cell testicular cancer in New Zealand Maoris. *British Journal of Cancer*, 65:769–771.
Willers, S., A. Axmon, C. Feyerabend, J. Nielsen, G. Skarping and S. Skerfving, 2000. Assessment of environmental tobacco smoke exposure in children with asthmatic symptoms by questionnaire and cotinine concentrations in plasma, saliva, and urine. *Journal of Clinical Epidemiology*, 53:715–721.
Willet, W., 1998. Nutritional Epidemiology. Oxford University press. New York Oxford.
Winneke, G., A. Bucholski, B. Heinzow, U. Kramer, E. Schmidt, J. Walkowiak, J.A. Wiener, and H.J. Steingruber, 1998. Developmental neurotoxicity of polychlorinated biphenyls (PCBS): cognitive and psychomotor functions in 7-month old children. *Toxicology Letters*, 28;102–103:423–428.
Wolff, M.S. and P.G. Toniolo, 1995. Environmental organochlorine exposure as a potential etiologic factor in breast cancer. *Environmental Health Perspectives*, 103(7):141–145.
Wolff, M.S., P.G. Toniolo, E.W. Lee, M. Rivera and N. Dubin, 1993. Blood levels of organochlorine residues and risk of breast cancer. *Journal of the National Cancer Institute*, 85:648–653.
Wong, T.K., R.B. Everson and S.T. Hsu, 1985. Potent induction of human placental mono-oxygenase activity by previous dietary exposure to polychlorinated biphenyls and their thermal degradation products. *Lancet*, 1:721–724.
Yamabe, Y., A. Hoshino, N. Imura, T. Suzuki and S. Himeno, 2000. Enhancement of androgen-dependent transcription and cell proliferation by tributyltin and triphenyltin in human prostate cancer cells. *Toxicology and Applied Pharmacology*, 169:177–184.
Yamashita, S. and Y. Yamamoto, 1997. Simultaneous detection of ubiquinol and ubiquinone in human plasma as a marker of oxidative stress. *Analytical Biochemistry*, 250:66–73.
Yang, G.Q., R.H. Gu, S.A. Zhou, L. Yin, B. Gu, Y.Q. Yan and Y.Q. Lin, 1989. Studies of safe maximal dietary Se-intake in a Seliniferous Area in China. Part 1. Selenium intake and tissue selenium levels of the inhabitants. *Journal of Trace Elements and Electrolytes in Health and Disease*, 3:77–87.
Yee, S. and B.H. Choi, 1996. Oxidative stress in neurotoxic effects of methylmercury poisoning. *Neurotoxicology*, 17:17–26.
Yip, R., P.J. Limburg, D.A. Ahlquist and H.A. Carpenter, 1997. Pervasive occult gastrointestinal bleeding in Alaska native population with prevalent iron deficiency. Role of *Helicobacter pylori* gastritis. *Journal of the American Medical Association*, 277(14): 1135–1139.
Young, T.K., 1994. The health of Native Americans: Toward a biocultural epidemiology. New York, Oxford University Press.
Young, T.K., C.D. Schraer, E.V. Shubnikoff , E.J.E. Szathmary and Y. Nikitin, 1992. Prevalence of diagnosed diabetes in circumpolar Indigenous populations. *International Journal of Epidemiology*, 21(4):730–736.
Young, T.K., J.M. Gerrard and J.D. O'Neill, 1999. Plasma phospholipid fatty acids in the central Canadian Arctic: Biocultural explanations for ethnic differences. *American Journal of Physical Anthropology*, 109:9–18.
Yu, M.L., C.C. Hsu, B.C. Gladen and W.J. Rogan, 1991. *In utero* PCB-PCDF exposure: relation of developmental delay to dysmorphology and dose. *Neurotoxicology and Teratology*, 13: 195–202.
Zdolsek, J.M., O. Soder and P. Hultman, 1994. Mercury induces *in vivo* and *in vitro* secretion of interleukin-1 in mice. *Immunopharmacology*, 28:201–208.
Zenzes, M.T., S. Krishnan, B. Krishnan, H. Zg and R.F. Casper, 1995. Cadmium accumulation in follicular fluid of women in *in vitro* fertilization-embryo transfer is higher in smokers. *Fertility and Sterility*, 64:599–603.
Zile, M.H., 1992. Vitamin A homeostasis endangered by environmental pollutants. *Proceedings of the Society for Experimental Biology and Medicine*, 201:141–153.
Zinkernagel, R.M., 1993. Immunity to viruses. *In*: W.E. Paul (ed.), Fundamental immunology, pp. 1211–1250. Raven press, New York.

Abbreviations

AA	Arachidonic acid (n-3 fatty acid)
AAS	Atomic absorption spectrophotometry
AEPS	Arctic Environmental Protection Strategy
AHH	Aryl hydrocarbon hydroxylase
AhR	Aryl hydrocarbon receptor
ALWI	Allowable lifetime weekly intake
AMAP	Arctic Monitoring and Assessment Programme
anti-PRB	Anti polyribosylribitol phosphate
BFRs	Brominated flame retardants
BMD	Benchmark dose
BMDL	Benchmark dose lower confidence limit
BMI	Body mass index
C'-system	Complement system
Cd	Cadmium
CFCs	Chlorofluorocarbons
CHBs	Chorinated bornanes
CI	Confidence interval
CINE	Centre for Indigenous Peoples' Nutrition and Environment (Canada)
CYP	Cytochrome P450
CYP1A1	Cytochrome P450 1A1
CYP1A2	Cytochrome P450 1A2
DBCP	Dibromochloropropane
DDD	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane
DDE	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethene
DDT	1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane
DES	Diethylstilbestrol
DHA	Docosahexaenoic acid (an n-3 fatty acid)
DHEA	Dehydroepiandrosterone
DHT	Dihydrotestosterone
DMA	Dimethylarsinic acid
DMF	Decayed, missing, or filled teeth
ECD	Electon capture detection
EDSTAC	Endocrine Disrupter Screening and Testing Advisory Committee (U.S. EPA)
EPA	Eicosapentaenoic acid (an n-3 fatty acid)
ER	Estrogen receptor
EROD	Ethoxyresorufin-*O*-deethylase
FAS	Fetal Alcohol Syndrome
FFQ	Food frequency questionnaire
FSH	Follicle stimulating hormone
GC	Gas chromatography
GF	Graphite furnace
GGT	g-glutamyl transferase
GSHPx	Glutathione peroxidase
GSHRd	Glutathione reductase
HCB	Hexachlorobenzene
HCH	Hexachlorocyclohexane
HDL	High-density lipoprotein
Hg	Mercury
Hib	Hemophilus Influenza type b
HIV	Human Immunodeficiency Virus
HPLC	High-performance liquid chromatography
HSV-2	Herpes Simplex Virus 2
ICI 182,780	Manufactured trivial name for a pure antiestrogen
ICP–MS	Inductively-coupled plasma-mass spectrometry
IQ	Intelligence quotient
ITK	Inuit Tapiriit Kanatami (ITK), previously the Inuit Tapirisat of Canada (ITC)
LDL	Low-density lipoprotein
LH	Luteinizing hormone
lw	Lipid weight
MCV	Mean cell volume
MeHg	Methylmercury
MMA	Methylarsonic acid
mRNA	Messenger RNA (ribonucleic acid)
mtDNA	Mitochondrial DNA (deoxyribonucleic acid)
NAAEC	North American Agreement on Environmental Cooperation
NK cells	Natural killer cells
NOAEL	No observed adverse effect level
NWT	Northwest Territories (Canada)
OCs	Organochlorines
OCS	Octachlorostyrene
OH-PCBs	Hydroxylated metabolites of PCBs
Ox-LDL	Oxidized low-density lipoprotein
PAHs	Polycyclic aromatic hydrocarbons
Pb	Lead
PBBs	Polybrominated biphenyls
PBDE 209	Decabromo diphenylether
PBDEs	Polybrominated diphenylethers
PCAs	Polychlorinated-*n*-alkanes
PCB	Polychlorinated biphenyl
PCCs	Polychlorinated camphenes
PCDDs	Polychlorinated dibenzo-*p*-dioxins
PCDFs	Polychlorinated dibenzofurans
PCNs	Polychlorinated naphthalenes
PCP	Pentachlorophenol
PeCP	Pentachlorophenol
PFOS	Perfluorooctane sulfonate
POP	Persistent organic pollutant
PTS	Persistent toxic substance
PTWI	Provisional tolerable weekly intake
QA	Quality assurance
QC	Quality control
RDI	Recommended daily intake
RfD	Reference dose
RR	Relative risk
RSV	Respiratory Syncytial Virus
SAD	Seasonal Affective Disorder
SCCPs	Short-chained chlorinated paraffins
Se	Selenium
SHBG	Sex hormone-binding globulin
SIDS	Sudden Infant Death Syndrome
SIR	Standardized incidence ratio
SQFFQ	Semi-quantitative food frequency questionnaire
STD	Sexually transmitted disease
TBBPA	Tetrabromobisphenol A
TBG	Thyroxin binding globulin
TBT	Tributyltin
TBTO	Tributyltin oxide
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
TDI	Tolerable daily intake
TEF	Toxic Equivalency Factor
TEQ	TCDD equivalents
TSH	Thyroid stimulating hormone
UN ECE	United Nations Economic Commission for Europe
UNEP	United Nations Environment Programme
US EPA	U.S. Environmental Protection Agency
US FDA	U.S. Food and Drug Administration
US NRC	U.S. National Research Council
UV-B	Ultraviolet-B radiation
VLDL	Very low density lipoprotein
WHO	World Health Organization
$\sum PCB_{10}$	Sum of specified number of chlorobiphenyl congeners