AMAP Assessment 2009:
Human Health in the Arctic

Arctic Monitoring and Assessment Programme (AMAP), Oslo, 2009

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Preface

This assessment report details the results of the 2009 AMAP assessment of Human Health in the Arctic. It builds upon the previous AMAP human health assessments that were presented in 1998[1] and 2002[2].

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;*
- *to identify possible causes for the changing conditions;*
- *to 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 the detailed assessment reports that provide the accessible scientific basis and validation for the statements and recommendations made in the AMAP State of the Arctic Environment report, 'Arctic Pollution 2009' that was delivered to Arctic Council Ministers at their meeting in Tromsø, Norway in April 2009. It includes extensive background data and references to the scientific literature, and details the sources for figures reproduced in the 'Arctic Pollution 2009'[3] report. Whereas the 'Arctic Pollution 2009' 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 develops its scientifically-based assessment product in terms of more action-orientated conclusions and recommendations, the 'Executive Summary of the Arctic Pollution 2009 Ministerial Report', which also covers other priority issues (Persistent Organic Pollutants, and Radioactivity), is reproduced in this report on pages xi to xvi.

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 responsibility of the scientific experts involved in the preparation of the assessment. Lead countries for this AMAP Human Health Assessment 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 viii 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 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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[1] AMAP, 1998. AMAP Assessment Report: Arctic Pollution Issues. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xii+859 pp.

[2] AMAP, 2003. AMAP Assessment 2002: Human Health in the Arctic. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xiii+137 pp.

[3] AMAP, 2009. Arctic Pollution 2009. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. xi+83 pp.

Executive Summary to the Arctic Pollution 2009 Ministerial Report

Preamble

The Arctic Monitoring and Assessment Programme (AMAP) was established in 1991 to monitor identified pollution risks and their impacts on Arctic ecosystems. The first AMAP report, Arctic Pollution Issues: A State of the Arctic Environment Report[1] and its update Arctic Pollution 2002[2] were published in 1997 and 2002, respectively. Three further reports have been published on specific topics: the Arctic Climate Impact Assessment[3] (produced by AMAP in cooperation with the Conservation of Arctic Flora and Fauna working group and the International Arctic Science Committee in 2004), and reports on Acidification and Arctic Haze[4] (2006) and Arctic Oil and Gas[5] (2008).

These assessments show that the Arctic is closely connected to the rest of the world. The Arctic receives contaminants from sources far outside the Arctic region; Arctic climate influences the global climate and *vice versa*. The AMAP assessment reports have been welcomed by the Arctic governments, who have 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 and adverse effects of Arctic climate change reported by AMAP.

AMAP information assisted in the establishment, and continues to assist the further evaluation and development of the protocols on persistent organic pollutants (POPs) and heavy metals to the United Nations Economic Commission for Europe's (UN ECE) Convention on Long-range Transboundary Air Pollution (LRTAP Convention) and the Stockholm Convention on Persistent Organic Pollutants. Information from AMAP is useful in documenting trends and in showing whether persistent substances are accumulating in the Arctic, which is relevant with respect to the screening criteria for persistence, long-range transport, and bioaccumulation that are applied to proposals to add substances to the above international agreements.

The Arctic Council's Arctic Contaminants Action Program (ACAP) was established to undertake cooperative actions to reduce pollution of the Arctic as a direct follow-up to address the concerns raised by AMAP. AMAP information is also used in establishing priorities for the Arctic Council/PAME Regional Programme of Action for the Protection of the Arctic Marine Environment from Land-based Activities (RPA). A number of activities have been initiated to follow-up on the Arctic Climate Impact Assessment.

The current assessment report updates the information presented in the AMAP 1997 and 2002 assessment reports with respect to three subject areas: persistent organic pollutants, contaminants and human health, and radioactivity. The POPs update has a particular emphasis on 'emerging' and current use POPs. The human health update addresses health effects of POPs, mercury, and lead exposure.

The information presented in the Arctic Pollution 2009 report is based on scientific information compiled for AMAP by scientists and experts, as listed on page 83. The background documents to this assessment have been subject to peer review and are in the process of being published in AMAP scientific assessment reports or scientific journals. All of these documents are made available on the AMAP website, www.amap.no.

This Executive Summary provides the main conclusions and recommendations of the 2009 AMAP assessments.

Persistent Organic Pollutants (POPs)

Legacy POPs

P1. Levels of many POPs have declined in the Arctic environment. This is a consequence of past bans and restrictions on uses and emissions in Arctic and other countries. 'Legacy' POPs that contaminate the Arctic mainly as a result of past use and emissions include PCBs, DDTs, HCB, chlordane, dieldrin, toxaphene, and dioxins.

P2. National policy efforts to reduce the use and emissions of these POPs have been extended regionally and globally through the UN ECE LRTAP POPs Protocol and Stockholm Convention, respectively. These initiatives made extensive use of the information presented in AMAP assessments. The Stockholm Convention on POPs explicitly acknowledges that "... Arctic ecosystems and indigenous communities are particularly at risk." The occurrence of chemicals in the Arctic can be evidence of their ability for long-range transport and environmental persistence.

[1]AMAP, 1997. Arctic Pollution Issues: A State of the Arctic Environment Report. Arctic Monitoring and Assessment Programme, Oslo. xii+188 pp
[2]AMAP, 2002. Arctic Pollution 2002. Arctic Monitoring and Assessment Programme, Oslo. xii+112 pp
[3]ACIA, 2004. Impacts of a Warming Arctic. Arctic Climate Impact Assessment. Cambridge University Press. 139 pp
[4]AMAP, 2006. Arctic Pollution 2006: Acidification and Arctic haze. Arctic Monitoring and Assessment Programme, Oslo. xii+112 pp
[5]AMAP, 2008. Arctic Oil and Gas 2007. Arctic Monitoring and Assessment Programme, Oslo. xiii+40 pp

P3. Firm conclusions about the impact of policy decisions on environmental levels will require continued monitoring of 'legacy POPs' in both abiotic environments and in key biota. AMAP information on temporal trends in the Arctic has contributed to the evaluation of the 'effectiveness and sufficiency' of the UN ECE LRTAP Convention Protocol on POPs, and the Stockholm Convention.

P4. Additional years of monitoring are needed to increase statistical power of existing time series in order to verify temporal trends. This will allow examination of the response to efforts to reduce global emissions and how this may be affected by climate variability and possible changes in contaminant pathways.

P5. Despite these reductions, concentrations of some legacy POPs, such as PCBs in some top predators in the marine food web, are still high enough to affect the health of wildlife and humans.

Emerging and current-use POPs

P6. Many chemicals in commercial use today have the potential to transport to and accumulate in the Arctic but are not yet regulated by international agreements. Although knowledge about these chemicals in the Arctic remains much more limited than for legacy POPs, new monitoring efforts have extended the information concerning their presence in the Arctic. This information is relevant to ongoing consideration of new chemicals for inclusion under existing national, regional and global agreements to regulate use and emissions of POPs.

P7. Many of these compounds transport over long distances and accumulate in Arctic food webs. New knowledge highlights the potential importance of ocean transport pathways. In contrast to atmospheric pathways ocean currents are slow. This may delay the environmental response to regulations.

P8. Compounds that have some POP characteristics and that are documented in the current AMAP assessment include:

- Brominated flame retardants (BFRs)

  The current AMAP assessment includes new information on three groups of chemicals used as flame retardants: polybrominated diphenyl ethers (PBDEs) (including Penta-, Octa- and Deca-BDEs), Hexabromocyclododecane (HCBD) and tetrabromobisphenol-A (TBBPA). The assessment shows that:

  Penta-BDE transports over long distances and bioaccumulates in biota. Penta-BDE and Octa-BDEs have been banned/restricted in Europe, parts of North America. They are no longer produced in Russia and use there is very limited. Penta-BDE and Octa-BDEs are under consideration for inclusion under the international Conventions regulating POPs; Deca-BDEs are now restricted in the EU.

  HBCD is ubiquitous in the Arctic. It undergoes long-range transport and accumulates in animals. It has also been proposed as a candidate for inclusion under international regulations.

  There is some evidence that environmental levels of Penta-BDE are now starting to level off or decline due to national regulations and reductions in use and production.

  TBPPA is present at low levels in several Arctic animals and plants, but more data are needed to assess its potential to undergo long-range transport.

  Some BFRs that are used as substitutes for phased-out substances have been detected in occasional Arctic samples. Their presence in the Arctic is a warning sign that they may have some POP characteristics.

- Fluorinated compounds

  Fluorinated compounds reach the Arctic both via the atmosphere and via ocean currents. They are extremely persistent and accumulate in animals that are high in the marine food web.

  Production of products containing perfluorooctane sulfonate (PFOS) was substantially reduced in 2001, but PFOS continues to be produced in China. Products that contain PFOS and other fluorinated compounds can still serve as sources to the environment. PFOS and related compounds are currently subject to review for both international and national regulation.

  Perfluorooctanate (PFOA) and other perfluorocarboxylates (PFCAs) continue to be produced. Fluorinated substances can also degrade to PFOA and other PFCAs. Canada is the only Arctic country so far to ban some import and manufacture of several products that are suspected to break down to PFOA and PFCAs.

  Precursors of PFOS and PFCAs have been detected in Arctic air and may be a source of PFOS and PFCAs in Arctic wildlife. Concentrations in Arctic air are one order of magnitude lower than in more southern, urban regions.

  Time trends of PFOS in wildlife show an initial increase starting in the mid-1980s. In recent years, some studies show a continuing increase while others show a sharp decline. The declines follow reduction in PFOS production.

  PFCAs have increased in Arctic wildlife since the 1990s, reflecting continued production of their precursors.

- Polychlorinated naphthalenes

  Polychlorinated naphthalenes (PCNs) are no longer manufactured and levels in the environment peaked almost half a century ago. However, PCNs are still present in the Arctic with indications of further input from a combination of combustion sources and emission from old products. There are no studies to assess their temporal trends in the Arctic. They

contribute to dioxin-like toxicity in Arctic animals but are generally much less important than PCBs.

- Endosulfan

  Endosulfan is a pesticide that is still in use in many parts of the world. Endosulfan and its breakdown products appear to be persistent in the environment. The presence of endosulfan in the Arctic confirms its ability to transport over long distances. There is clear indication of bioaccumulation in fish but there is no evidence for biomagnification by marine mammals.

  Long-term trend analysis of samples taken at Alert (Ellesmere Island, Canada) indicates that endosulfan concentrations have remained unchanged in the remote Arctic atmosphere, unlike most legacy POPs. Calculations based on air and seawater concentrations suggest that endosulfan enters open (i.e. ice-free) waters of the Arctic Ocean.

  The limited information available for wildlife indicates that concentrations of endosulfan and its breakdown product endosulfan sulphate in blubber of marine mammals are an order of magnitude lower than those of major legacy POPs such as DDT and chlordane.

  Endosulfan is currently under discussion for inclusion under the UN-ECE LRTAP POPs Protocol and the Stockholm Convention.

- Other current-use pesticides

  Previous AMAP assessments have highlighted lindane (gamma-hexachlorocyclohexane [HCH]) as a current-use pesticide that is ubiquitously present in the Arctic. Several other current use pesticides (including chlorpyrifos, chlorothalonil, dacthal, diazinon, diclofol, methoxychlor, and trifluralin) have been detected in the Arctic. The levels are often low, but their presence shows that they can transport over long distances and accumulate in the food web.

Biological effects

P9. Recent studies of biological effects of POPs have been able to confirm the causal link between POPs and observations of adverse health effects in Arctic top predators. These controlled experiments on sled-dogs and captive Arctic foxes show effects on hormone, immune and reproductive systems.

P10. The observed effects are mainly due to the breakdown products, indicating that these may be more important than the original POP compounds.

Contaminants and Human Health

Population health and effects of contaminants

H1. In light of current studies, many indigenous populations in the Arctic region have poorer health than national averages. While socioeconomic conditions and lifestyle choices are major determinants of health, contaminants may also have a contributing effect. Toxicological studies show that contaminants, at the levels found in some parts of the Arctic, have the potential for adverse health effects in people. Epidemiological studies, looking at Arctic residents directly, provide evidence for subtle immunological, cardiovascular, and reproductive effects due to contaminants in some Arctic populations. These results indicate that POPs, mercury, and lead can affect health of people and especially children at lower levels of exposure than previously thought. Genetic characteristics of the various Arctic populations also affect their response to contaminants and susceptibility to certain diseases.

H2. A major dietary shift from traditional to store-bought food is underway in most of the Arctic, with important health implications. In addition to environmental concentrations of the contaminants in traditional foods, lifestyle factors and social and cultural practices play a large role in determining human exposure to contaminants in Arctic areas. Despite changes in lifestyle and diet that are resulting in increasing consumption of store-bought foods, traditional foods remain important to Arctic indigenous peoples for social, cultural, nutritional, economic, and spiritual reasons. Store-bought foods are increasingly the main source of dietary energy, but traditional foods provide many nutrients and are still a major contributor to healthy diets in many communities. Some traditional foods can also carry potential risks from contaminants. The combination of high prices for store-bought foods and the work, risks, and costs associated with obtaining traditional foods has made food security a large concern for many Arctic residents.

H3. Recent studies have found a number of mechanisms by which contaminants can affect metabolism. Obesity is associated with an increased risk of cardiovascular disease and of developing diabetes; as in other parts of the world, obesity is increasing in Arctic communities. POPs, even at low concentrations, also increase the risk of diabetes. These new findings emphasize the need to consider the interactions between contaminants and other health conditions.

Trends in exposure and contaminant levels

H4. Human exposure to most legacy POPs and mercury is decreasing in many Arctic populations. This reflects changes in diet, changing levels of environmental contamination, and health advice to critical groups in some areas concerning consumption of certain foods; however, exposure remains high in some populations. The proportion of women of childbearing age who exceed blood level guidelines for PCBs, mercury, and lead is decreasing. For PCBs and lead, in particular, there is evidence that this reflects the declines in environmental levels of these contaminants.

H5. Marine mammals remain a major dietary source of POPs and mercury, so that people who eat large quantities of marine mammals have higher POPs and

mercury levels than those who do not.

H6. Emerging compounds such as brominated flame retardants and fluorinated compounds are a concern for three reasons: they are present in Arctic people and biota, levels globally have increased over the last 15 years, and their toxic effects have not been studied in detail. There is little information on the routes of exposure or trends of these contaminants in Arctic populations.

H7. Reliable interpretation of information on trends and inter-regional differences is critically dependent on an ability to compare data from different studies and different laboratories. Laboratory performance testing procedures initiated by AMAP and others, including the AMAP inter-laboratory comparison programme for analysis of contaminants in human tissue have markedly improved analytical co-operation, data comparability, data reliability and data accuracy in studies using the participating laboratories, and have led to more reliable data on contaminant levels in human tissues. Further improvements can be achieved through continued efforts in this respect.

H8. Increased industrial activity in parts of the Arctic is likely to lead to an increase in local sources of contaminants. Anticipated changes in global and Arctic climate may also result in changes in contaminant transport to the Arctic. Such changes may affect exposure patterns to some contaminants.

Communication

H9. Communicating the results of studies concerning contaminants and people is important in helping Arctic residents make informed food choices. Health advisories issued in response to findings reported in past AMAP assessments have succeeded in reducing exposure to contaminants in some Arctic population groups.

H10. Risk communication must be carried out with great care and respect for culture at a community-level. The involvement of community members and organizations, regional health officials, and indigenous organizations is the key to developing and disseminating messages that are appropriate and relevant.

Radioactivity

R1. Radioactivity in the Arctic is a concern because contamination can persist for long periods in soils and some plants and because pathways in the terrestrial environment can lead to high exposures of people.

Potential sources

R2. In parts of the Arctic, there is a very high density of sources of radionuclides. The risk of accidents combined with the vulnerability of the Arctic environment to radioactive contamination raises a need for continued actions to reduce risks.

R3. Partly as a result of national and international actions addressing concerns highlighted by AMAP, significant progress has been made with respect to actions to reduce risks of radioactive contamination from several of these potential sources. Previous AMAP assessments recommended actions to address potential sources of radioactive contamination of the Arctic including nuclear powered vessels that were poorly maintained or being decommissioned; dumped and stored radioactive wastes, including wastes stored under inadequate conditions; radioisotope thermoelectric generators (RTGs) used as energy sources in northern regions; and nuclear power plants and reprocessing facilities located close to the Arctic. Many of these potential sources are located in northwest Russia. Other issues remain a source of concern:

- As of 2008, 164 of the 198 obsolete nuclear submarines of the Russian northern fleet had been defueled and dismantled; work to safely decommission these vessels continues. Similar plans exist for dealing with nuclear icebreakers and their associated facilities, including the Lepse storage vessel.
- The facilities at Andreeva Bay and Gremikha are used as temporary storage sites for radioactive wastes, spent fuel, and reactors from decommissioned submarines. Progress has been made in improving the physical infrastructure and the legal arrangements to manage these sites. However, much remains to be done, including transport of spent fuel and waste to safer storage sites.
- About half of the radioisotope thermoelectric generators (RTGs) in northern Russia have been removed or will be in the near future.

R4. Some risk reduction has been achieved through significant joint Russian-international action. This includes a regulatory framework for handling the clean-up actions. Moreover, a long-term strategic master plan has been developed, which could become an important tool for further management of radiation risks.

New potential sources

R5. Russian plans for building floating nuclear power plants raise issues about how waste will be handled and about increased marine transport of spent fuel in the Arctic. These power plants would represent new potential sources and may increase risks of radioactive contamination.

R6. Technologically enhanced naturally occurring radioactive material (TENORM) can become a radiation risk in context of mining of uranium and other minerals, phosphate production, oil- and gas extraction, coal mining and the use of geothermal energy. Several of these activities are likely to increase in the Arctic and more knowledge about waste streams and releases are needed in order to assess human and environmental risks.

Historical contamination

R7. Previous AMAP assessments documented fallout from past nuclear weapons tests, the 1986 Chernobyl

accident, and releases from reprocessing plants close to the Arctic as the three major sources of anthropogenic radioactive contamination in the Arctic. Evidence from long-term monitoring in the European Arctic shows that levels of radioactivity in the environment are declining. However, monitoring and mapping activities have decreased in recent years and documentation is therefore lacking for much of the Arctic. Unless environmental pools are re-mobilized, this historical contamination will continue to decrease as sediments are buried and radionuclides decay.

R8. Application of new technology has reduced routine releases of radionuclides to the marine environment from European reprocessing plants, including releases of technetium-99 from Sellafield that were highlighted in the 2002 AMAP assessment.

Climate change and radioactivity

R9. The current assessment identifies the potential of climate change to mobilize radionuclides in the Arctic terrestrial environment and in glaciers. This may also affect radon emission from the ground, which is a major contributor to human exposure to radiation.

R10. Changes in permafrost, erosion, precipitation and extreme weather events may also affect infrastructure related to nuclear activities.

Protecting the environment

R11. Following recommendations of previous AMAP assessments, a framework for protecting Arctic ecosystems from radiation effects has been developed as a complement to the previous focus on protecting human health. It also opens for assessing combined effects with other environmental stressors. There is a need for more data that are relevant for Arctic conditions and organisms to provide the basis for a comprehensive application of this framework.

Recommendations for actions to reduce contaminant levels and effects through international agreements:

- *Encourage countries that have not yet done so to sign and ratify the Stockholm Convention and LRTAP POPs Protocol (P2, H2, H4, H5).*
- *Support the addition of polybrominated compounds and fluorinated compounds to the Stockholm Convention and the regulation of these compounds under other international and national mechanisms because they undergo long-range transport and bioaccumulation in human tissues similar to other POPs. (P2, P3, H6)*
- *Support the development of a global agreement to limit mercury emissions to complement regional and national efforts that reduce environmental levels and lower human exposure to mercury in the Arctic. (H1)*

Recommendations for actions to promote healthy diets and reduce human exposure to contaminants:

- *Continue to encourage public health officials to recommend breast feeding among Arctic populations as a health practice that optimizes infant growth and development. (H2, H9)*
- *Recommend to health authorities to promote healthy diets through improved access to and consumption of local traditional foods that are high in nutrients but relatively low in contaminants along with improved availability and consumption of store-bought foods with high nutritional value. (H2)*
- *Evaluate past communication efforts in order to improve and refine communication strategies. (H9)*

Recommendations to address potential sources of radioactivity:

- *Continue work to decommission remaining obsolete nuclear vessels, remove remaining RTGs, and to manage spent nuclear fuel and waste at sites in or close to the Arctic. (R3)*
- *Implement additional actions to address continued concerns, especially the storage facilities at Andreeva Bay and Gremikha, and the Lepse storage vessel (R3)*
- *Strengthen plans to ensure safe and secure transport of spent fuel and waste to storage facilities. (R3)*
- *Consider the need to further develop regulatory systems, especially for addressing clean-up operations and improved safety of nuclear facilities. (R4)*
- *Increase attention to technologically enhanced naturally occurring radioactive materials (TENORM) in future assessments, including information from all countries engaged in or planning Arctic oil and gas extraction and uranium and other mining. (R6)*

Recommendations for actions to address gaps in knowledge concerning combined effects:

Monitoring

- *Continue and enhance the geographical coverage of monitoring programs to:*
  - *Document the effectiveness of controls on the use and emissions of POPs (P2, P3, P4)*
  - *Investigate the possible effects of climate change on Arctic contaminants levels, including changes in transport and re-mobilization (P4, H8, R9, R10)*
  - *Detect health threats related to climate change and contaminants (H8)*

- *Identify new sources of contaminants and new contaminants that may pose a threat to Arctic residents and the environment (P6, H6, R7)*

Research

- *Investigate the respective and combined roles of changing contaminant emissions, changing pathways due to climate change, local sources of contamination, and dietary change to determine the causes of changing environmental levels and human exposures. (P4, H8, R9, R10)*
- *Improve predictive models of contaminant transport and behaviour in the Arctic to better understand the likely impacts of climate change with respect to contaminant levels and human exposures. (P4, H8)*
- *Conduct further studies to better understand the combined effects of contaminants and other stressors on Arctic wildlife and humans. (P5, P9, H8, R11)*
- *Include in future assessments the combined effects of POPs, radioactivity, and other stressors on human health and the environment in the Arctic (P5, P9, H8, R11)*

Recommendations to address gaps in knowledge concerning POPs:

Monitoring

- *Continue monitoring of occurrence and trends of brominated flame retardants (including alternatives being introduced to replace phased-out BFRs) and fluorinated compounds. (P8)*
- *Increase monitoring of current- use pesticides and their breakdown products in the Arctic environment. (P7)*

Research

- *Examine the many other chemicals in commerce, such as the cyclic siloxanes for potential Arctic accumulation potential and design programs to search for these chemicals and their breakdown products (to avoid past surprises such as detection of PFOS). (P8)*

Recommendations to address gaps in knowledge concerning human health:

Monitoring

- *Continue and extend the laboratory intercomparison and testing schemes introduced and promoted by AMAP for laboratories engaged in analysis of Arctic human media to cover emerging POPs. The quality assurance group for the human health program should be provided with adequate resources to ensure quality assurance/quality control on an ongoing basis. Only data that have been approved by this group should be used in AMAP human health assessments. (H7)*
- *Continue to monitor for trends in legacy POPs, mercury, and lead in human tissues and traditional food items. Dietary assessments should combine contaminant and nutrient analyses in traditional foods as consumed. (H2, H4)*
- *Conduct further studies combining dietary assessments with contaminant and nutrient analyses in the traditional foods as consumed. (H2)*
- *Continue and expand monitoring for emerging POPs in human tissues and traditional food items, including development of analytical methods (H6)(H7)*
- *Continue gathering basic health statistics on a regular basis by all circumpolar jurisdictions at appropriate regional levels, including ones not currently gathered in all areas (e.g., neonatal vs. post-neonatal death rates in Russia).(H2)*

Research

- *Maintain and expand current human population cohorts in the Arctic in order to provide the information needed to track adverse health outcomes associated with contaminants and changing conditions related to climate change, socio-cultural conditions, and diet. (H1, H2, H3)*
- *Conduct further research on contaminant effects in humans, including interaction between POPs and mercury and other factors such as genetic susceptibility, diet, and lifestyle, and the resulting health impacts on the cardiovascular, reproductive, neurological or metabolic systems. (H1)(H2)(H3)*
- *Conduct further studies to determine causes of regional variations and discrepancies in exposure to contaminants (e.g., low mercury levels in Chukotka in contrast with high POPs levels). (H2)(H8)*
- *Conduct further toxicological studies of POPs mixtures, and emerging compounds where a lack of information is limiting human health risk assessment. (H1)*
- *Conduct further studies on risk perception, dietary patterns, and determinants of food choice to improve risk communication. (H9)*

Recommendations to address gaps in knowledge concerning radioactivity:

Monitoring

- *Improve coverage and implementation of monitoring of radioactivity in the Arctic to meet AMAP objectives and/ or to highlight specific regional needs. (R7)*
- *Improve collection and reporting of data relevant to Arctic species and conditions to allow improved radiation protection of Arctic ecosystems. (R11)*

Chapter 1

Introduction

Constantine Tikhonov and James Berner

Summary

The third AMAP Human Health assessment seeks to update the 2002 AMAP Human Health assessment with the latest data and analysis rather than to provide a new independent assessment. The report synthesizes the latest research results from circumpolar countries, building upon previous assessments of environmental chemicals and the variety of their impacts on the health of Arctic populations. Therefore, to benefit most from this work the reader should be familiar with previous assessments. This introduction provides an overview of the critical components upon which this assessment is based and draws heavily on background information from the two previous AMAP assessments of human health in the Arctic (AMAP, 1998, 2003).

1.1. Arctic Monitoring and Assessment Programme

The Arctic Monitoring and Assessment Programme (AMAP) was established in 1991 to fulfill several key goals of the Arctic Environmental Protection Strategy (AEPS). Since 1996, it is one of the cornerstone programs of the Arctic Council focused on providing reliable and sufficient information on the status of, and threats to, the Arctic environment.

The scope of the Arctic Monitoring and Assessment Program addresses levels of environmental chemicals in abiotic and biotic components of the Arctic ecosystem, temporal and spatial trends, the fate of pollutants in the environment, and their effects on the food chain and humans. AMAP aims to provide timely scientific advice on actions to be taken in order to support Arctic governments in their efforts to take remedial and preventive measures relating to environmental contamination. AMAP also seeks to promote the communication of information on the state of the Arctic environment to the public.

One of the principal tasks of AMAP continues to be the assessment of implications and impacts of pollution on the health of Arctic residents, residents both indigenous and non-indigenous to the region. Since its inception, AMAP has been designed to have roots in the national programs of participating countries; soon after its establishment therefore, a Human Health Assessment Group (HHAG) was created bringing together leading researchers and research coordinators from circumpolar countries. The AMAP HHAG is dedicated to circumpolar research and monitoring, assessment and synthesis of trends and human health effects of environmental pollutants in the Arctic.

The AMAP HHAG aims at the continuous assessment of the concentrations and possible effects of anthropogenic pollutants on human health. It seeks to document trends in concentrations of these pollutants and to assess the possibility of human health effects at present and future levels, while striving to consider the combined effects of all contaminants. In the present assessment, the possible implications of climate change on these issues have also been considered.

AMAP has presented a series of key new findings in the areas of human health, persistent organic pollutants (POPs), radioactivity, and mercury, as well as recommendations for actions based on those findings. To date, AMAP has completed two human health assessments (in 1997/1998 and 2003). The AMAP human health program is focused mainly on the potential health effects arising from exposure to POPs and heavy metals and, to a lesser degree, ultraviolet-B (UV-B) radiation. Radionuclide issues have been addressed in cooperation with the AMAP Radioactivity Expert Group (AMAP, 2004c). Acidification and petroleum hydrocarbons were regarded during AMAP Phase I (1991 – 1996) as having no immediate impact on human health and so were not addressed in the health assessment prepared under AMAP Phase II (AMAP, 2003).

The AMAP HHAG participated in two major assessments completed recently by the Arctic Council: the Arctic Climate Impact Assessment (ACIA, 2005) and the Future of Children and Youth of the Arctic Initiative, and was also involved in the AMAP Oil and Gas Assessment (AMAP, 2009).

1.2. The Arctic

The Arctic region remained, until the second half of the twentieth century, a final frontier of human habitation. The Arctic is characterized by a harsh climate, strikingly unique ecosystems, and an array of highly resilient and adaptable plants, animals, and people. The Arctic region derives its name from the Greek αρκτικός (Arktikos) referring to the stellar constellation of *Ursa major*, the Great Bear, surrounding the North Star which is located almost directly above the North Pole (AMAP, 1997).

The Arctic Circle is a vast circumpolar area consisting for the most part of seasonally ice-covered ocean, surrounded by continental land masses and islands, and which conventionally ends at 66° 32′ N. This latitude constitutes the southern limit to a region for which there is at least one 24-hour period a year during which the sun does not set and one 24-hour period during which it does not rise. Other definitions of the Arctic region (NSIDC, 2006) include:

- the area north of the treeline (the northern limit of upright tree growth); and
- locations at high latitude where the average daily summer temperature does not rise above 10 °C.

However, none of these definitions is particularly satisfactory, especially from the perspective of monitoring and assessing the human health impacts of pollution. Consequently, and considering that it is most likely that climatic gradients, rather than simple latitude, determine the effective boundaries of the circumpolar region (Ingold, 1988), AMAP has defined a specific area of Arctic and sub-Arctic regions within which it is considered essential to continue monitoring.

AMAP has not attempted to define the Arctic *per se* but rather to provide guidance relevant for all areas of science about the core area to be covered by AMAP assessments (Figure 1.1). The boundary lies between 60° N and the Arctic Circle, with the following modifications:

- In the North-East Atlantic, the southern boundary follows 62° N, and includes the Faroe Islands. To the west, the Labrador Sea and Greenland Sea are included in the AMAP area.
- In the Bering Sea area, the southern boundary is the Aleutian chain.
- Hudson Bay and the White Sea are considered part of the Arctic for the purposes of this assessment.
- In the terrestrial environment, the southern boundary in each country is determined by that country, but lies between the Arctic Circle and 60° N. Eight countries have land within the area of AMAP's responsibility: Canada, the Kingdom of Denmark, including Greenland and the Faroe Islands, Finland, Iceland, Norway, Russia, Sweden, and the United States of America (Alaska).

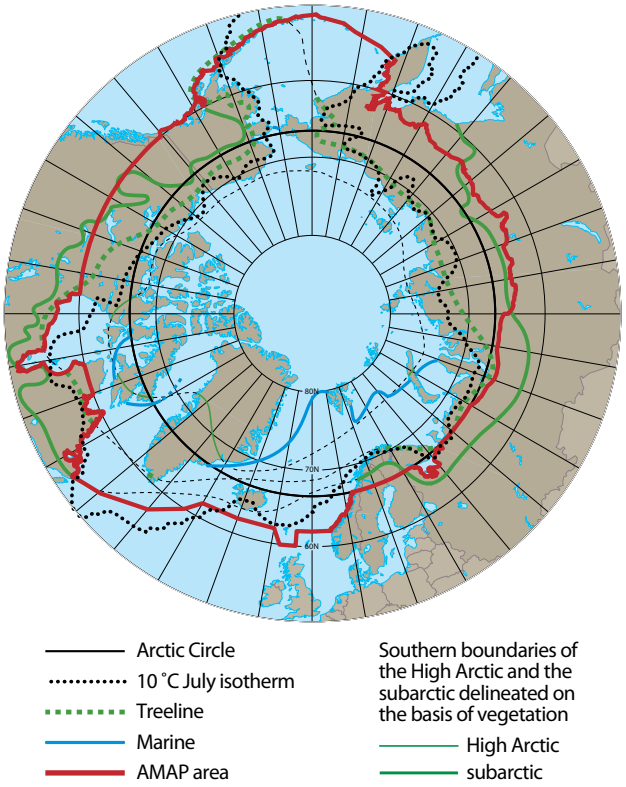

Figure 1.1. Definitions of the Arctic region. Source: AMAP (1998).

Figure 1.2. Administrative areas of the northern Russian Federation.

This definition was reaffirmed in the Arctic Human Development Report (AHDR, 2004), but expanded to advance the southern boundaries in Labrador, Canada, and the Russian Federation.

The present assessment continues to consider the previously (1997 – 2002) defined observation area as well as the following administrative areas of the Russian Federation: Murmansk Oblast, Kareliya Republic, Arkhangelsk Oblast, Nenets Autonomous Okrug, Komi Republic, Yamalo-Nenets Autonomous Okrug, Khanty-Mansiysk Autonomous Okrug, Taymir Autonomous Okrug, Evenky Autonomous Okrug, Sakha Republic, Magadan Oblast, Koryak Autonomous Okrug, and Chukotka Autonomous Okrug (see Figure 1.2).

1.3. Uniqueness of the Arctic as a human environment

People have been living in and adapting to changing conditions in the Arctic for thousands of years. Initial knowledge about the Arctic environment was accumulated through the oral traditions of indigenous peoples, and through written records of the Viking era, and accounts of hunters, whalers and trappers (AMAP, 1997). In modern times, international scientific expeditions and monitoring stations have continued this exploration and have led to the evolution of the major, internationally coordinated campaigns of the International Polar Year initiatives, which began with the first International Polar Year in 1882–83.

The Arctic is home to around four million residents of which about 10% are indigenous peoples, spread over many communities around the Arctic (UNEP/GRID-Arendal, 2005). The relative size of the indigenous population varies widely for different areas, ranging from the Inuit comprising about 91% of the population of the Nunavik region of the Province of Quebec, Canada, to the Saami accounting for 2.5% of the population in northern Scandinavia and the Kola Peninsula (UNEP/GRID-Arendal, 2005; Statistics Canada, 2008a).

The indigenous peoples of the Arctic (Figure 1.3) include the Inuit and Iñupiat, who live in 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

Figure 1·3. Location of Arctic indigenous peoples. Source: AMAP (1998).

with some 26 to 40 groups of 'numerically small peoples of the North' (Kozlov et al., 2007), ranging from Saami and Nenets in the west to Chukchi and Eskimo (Yupik) in the east; the Aleuts, Yup'ik, Athabaskans and other indigenous peoples of Alaska; and in Canada the Dene and Yukon First Nations, who inhabit the western Canadian Arctic and subarctic regions along with the Métis (AMAP, 2003). The peoples of the Arctic were described in detail in previous AMAP assessments (AMAP, 1997, 1998, 2003).

The population of most Arctic regions has increased considerably over the last sixty years. This increase is attributed not only to increased in-migration to the Arctic, but also to the notable increase in life expectancy and the decrease in infant mortality of Arctic peoples since the mid-twentieth century. There has also been a significant reduction in mortality from infectious diseases (AMAP, 2003). At the same time, there are indications that the prevalence of chronic 'western' diseases such as cardiovascular disease, stroke, hypertension and diabetes, is increasing. These conditions tend to increase in traditional societies (such as circumpolar indigenous peoples) undergoing rapid social change, dietary transition, decreased physical activity, and exposure to new environmental hazards (Trowell and Burkitt, 1981, cited in Bjerregaard et al., 2004b).

The intense industrial development in circumpolar regions characterizing the end of the second half of the twentieth century has had a significant impact on the Arctic. Energy and mineral extraction developments, although localized and widely scattered, tend to be of large scale, for example the *Prudhoe Bay* oil field complex in Alaska, the mining and associated metallurgical developments in the Taymir and Kola regions of Russia, and the hydroelectric development in northern Quebec (ACIA, 2005). These contribute to the pollution of the Arctic waters, atmosphere, and lands and result in local loss of wildlife through habitat destruction, excessive hunting, and other cumulative impacts (ACIA, 2005). Throughout most of the Arctic region, ecosystems have until recently remained essentially as they have evolved in response to natural conditions. However, regional ecosystem changes in the Arctic are becoming evident in response to climate change and variability. Therefore, under present trends of global industrialization the Arctic ecosystem that we have known in the past may not continue into the future, or will be much more restricted in geographic range (ACIA, 2005).

1.4. The concept of combined effects and determinants of health

Human health is potentially affected by many environmental factors. Income, education, social status, genetic endowment, as well as access to social safety networks are all powerful factors that influence health outcomes in a given population and disparities among population groups. When these are combined with personal lifestyle choices, coping capacity, and the availability and quality of primary health care at the community level, particularly in early life stages, the impact of exposures to environmental contaminants may seem less significant. However, focusing on low-level chronic environmental exposures, a study based in the Faroe Islands which examined children's performance in neurobehavioral tests in relation to maternal exposures (primarily due to consumption of pilot whale) to methylmercury (Grandjean et al., 1997, 1999b; AMAP, 2003) found key neurodevelopmental endpoints. Further, there are a number of possible links between polychlorinated biphenyl (PCB) and organochlorine mixture exposures and pregnancy outcome (Jacobson et al., 1990b; Patandin et al., 1998), immune system function (Dewailly et al., 2000a), and modulation of cancer growth (Demers et al., 2000).

While contaminants may play a relatively modest role, in comparison to lifestyle choices and genetic endowment in the often multi-factorial causes of disease, exposure to many persistent organic contaminants is preventable and their presence in the remote Arctic is, from a public health perspective, of great concern (AMAP, 2003).

The human health assessment must consider risks to the Arctic population from exposure to the major contaminants in the context of combined effects risk assessment. Environmental exposure is almost always an exposure to a mixture of chemicals in the environment, rather than to a single substance. Evaluation of the combined effect of pollutants in the Arctic must be based on cellular models of effect, examination of genetic susceptibility, identification of relevant and validated biomarkers of exposure, extensive environmental and biological monitoring, and on nutritional, epidemiological and socio-economic data (AMAP, 2003).

1.5. Major health-related issues and recommendations identified in AMAP Phase I

The first AMAP human health assessment concluded that there were Arctic communities that were highly exposed to environmental contaminants (AMAP, 1997, 1998). The assessment identified the food pathway as a primary source of human exposure to persistent contaminants, due to their accumulation in wildlife species used as traditional foods, and concluded that variation in human exposure depended 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.

The assessment confirmed that exposure to POPs was the primary concern. The biomagnification of PCBs and certain pesticides in marine food webs, resulted in high concentrations in some marine mammals, birds, and, to a lesser extent, fish. Some indigenous peoples were found to be exposed to concentrations that exceeded established tolerable daily/weekly intake levels. These exposure concentrations were of particular concern in the context of early human development. The potential for the transfer of these contaminants to the fetus *in utero*, or to infants through breast milk was the key concern, because this could lead to contaminant levels in newborns, that were two- to ten-fold higher than in regions further south (AMAP, 1997, 2003).

Arctic peoples were generally found to be exposed to higher concentrations of radionuclides than people in temperate zones. Atmospheric transfer and deposition of radionuclides to terrestrial ecosystems, coupled with the capacity of certain plants to bioconcentrate some radionuclides enabled the development of high concentrations in caribou/reindeer and wild game.

Methylmercury is taken up following human consumption of fish, fish-eating marine mammals and birds. Methylmercury in the maternal bloodstream can be transferred to the fetus and, in certain areas and within certain populations, concentrations were found to be high enough to indicate a need for public health intervention. Although mercury concentrations can be high, it was proposed that 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 is related to possible ocular damage and additional immunosuppressive effects and dermatological disorders.

The assessment stressed that while controls on emissions had resulted in measurable reductions in inputs of some contaminants (e.g., lead, radionuclides, atmospheric sulfur, and possibly PCBs, and DDT), there was considerable variation across the Arctic. It concluded that recycling of accumulated pools of long-lived contaminants in ocean and lake water and in sediments, could result in continued exposure long after controls had been enforced.

Weighing the well-known benefits of breast milk and traditional foods against not yet completely understood effects of contaminants, the recommendations, arising from AMAP Phase I, reaffirmed the benefits of consuming traditional/country food. At the same time, the assessment recognized the need to develop public health focused dietary advice such that Arctic residents could make informed choices concerning the food they eat. The assessment clearly stressed that breast feeding could continue to be promoted, despite, in some instances, high concentrations of persistent pollutants having been found in breast milk. Increasingly strong

evidence was found in the Arctic, as elsewhere in the world, about the positive benefits of breast feeding for infant development, especially the psycho-social development of children and the development of their immune system (AMAP 1997, 2003).

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 participatory community-based approaches in research and policy development.

The assessment recommended the establishment of a long-term communication program to provide public information for population groups with different educational levels about environmental contaminants studied by AMAP. This was intended 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 HHAG 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:

- It was recommended to support further research and evaluation of the sources and levels of exposure to hexachlorocyclohexane (HCH) and DDT/DDE, in market foods, water supplies, air, and industrial/ agricultural workplaces in Arctic Russia to identify causes 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 were requested to undertake an evaluation of their data on dioxins, furans and co-planar PCBs and to determine the relative contribution of these chemicals to the total TCDD toxic equivalencies;
- It was suggested that data showing levels of brominated flame retardants (e.g., polybrominated diphenylethers) 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 Interim Report concluded by recommending that the Arctic Council implement the Phase II AMAP Human Health program, with its emphasis on human health effects and monitoring of spatial distributions and temporal trends according to a specified program of activities, in order to improve the scientific background for local advice to Arctic peoples.

1.6. Major conclusions of the human health assessment in AMAP Phase II

The 2002 Human Health Assessment (AMAP, 2003) concentrated on the concept of the combined effects of environmental contaminants, as requested in the AMAP Ministerial mandate. It addressed 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. The 2002 assessment re-evaluated the relationship between environmental contaminants and health status for Arctic residents by integrating what was known about multiple stressors. The assessment was built on data generated and experience gained during AMAP Phase I, but was mainly based on new data from studies conducted during AMAP Phase II, and other relevant research. It was the hope of the AMAP HHAG that this assessment was a further step toward a better understanding of the relationship and linkages between health and environment in the Arctic.

The Phase II assessment concluded 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*. The assessment encouraged the expansion of the human health effects program initiated through Phases I and II to allow a more holistic assessment of the health of Arctic peoples. The Phase II assessment stated that in some areas of the Arctic the indigenous peoples enjoy the same level of health as the non-indigenous populations, but in most areas their health is significantly poorer. The assessment validated most of the Phase I conclusions, highlighting the availability of strengthened evidence to support several of them, such as the influence of contaminants on fetal and neonatal development supported by further evidence from the Faroe Islands. The assessment stressed, however, the paucity of population health effects data (reproductive health outcomes, neurobehavioral development, immune system response, hypertension and cardiovascular diseases, etc.) for the Arctic. Further, although continued monitoring provided new data on POPs body burdens at the time of the 2002 assessment, significant temporal trends could not yet be observed due to the short period of observation and the scarcity of available archived Arctic population samples for retrospective studies.

With regard to heavy metals, the Phase II assessment emphasized concerns for *in utero* exposure to methylmercury, due to observation of dose-related, subtle neurotoxic effects in children in some regions of the Arctic. This underscored the importance of local public health strategies in some regions to reduce the exposure of women of child-bearing age and especially those that are pregnant.

At the same time, the nutritional importance of food of marine origin has been reaffirmed, because the data continued to show that populations' 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. This further illuminated the importance of developing a methodology for consistent, careful and accurate risk-benefit analyses of traditional diets, leading to balanced dietary advice taking both risks and benefits into account.

The assessment reflected on the availability of new information showing that uptake, metabolism and excretion of xenobiotic substances are influenced by both genetic and lifestyle (e.g., smoking, body mass) factors and that these factors must be considered in future research.

The future target of the AMAP human health program was focused on new methodologies that could integrate epidemiological and mechanistic biomarker effects 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.

A set of recommendations from the Phase II assessment included the following key components:

- To continue monitoring contaminants in human blood and tissues in order to reveal temporal and spatial trends.
- To continue towards the adoption of more uniform methodologies for the objective assessment of diets and estimation of exposure. In addition, to promote studies on the nutrient content of traditional foods.
- To continue to support human population studies of contaminant-related effects on reproduction and fetal and child development, immune and hormone status, and cancer.
- To influence the development of tolerable daily intake guidelines that are based on regional and local needs and aim to strike a balance between benefits from traditional foods and potential negative effects from exposure to contaminants.
- To advise Arctic peoples to continue to eat traditional foods and to breastfeed their children, taking dietary recommendations into account.
- To strengthen international efforts to control production, use and emissions to the environment of persistent organic pollutants and mercury.

1.7. Scope of the 2009 AMAP human health assessment

The AMAP human health program continues to focus on contaminant exposure and the health effects of such exposure, both for individual substances and combinations of substances. Human exposures to POPs and methylmercury continue to be of primary concern. The relevance of human exposure to new xenobiotic compounds (such as polybrominated and perfluorinated compounds) being identified in the Arctic environment is of further concern.

The third AMAP human health assessment differs in format from the first two assessments. The main difference is in the frequent use of references to past assessments (which are readily available via the AMAP website). The report is shorter, and emphasizes new data, new research findings, emerging trends, new hypotheses to be tested, new Arctic policy initiatives that have been influenced by the research community, and new recommendations for future research and risk-benefit analysis.

Human health in the Arctic is linked inextricably to the climate and the Arctic ecosystem. Some of these links include overlap between contaminant cycling and climate (increased transport to and from the Arctic), and contaminant exposure and risk of infectious disease in Arctic animals, and the associated increased risk of transmission to subsistence users. The latter is particularly relevant for indigenous Arctic residents. Topics new to the AMAP health assessment process, such as the health impact of climate change in the Arctic, are presented in a condensed form in Chapter 2.

The epidemic of obesity (Snodgrass et al., 2006) and the increase in rates of diabetes (Young, 1993; Bjerregaard et al, 2004b) among Arctic indigenous populations can be traced to lifestyle and a dietary transition away from traditional life practices (Receveur et al., 1998; Berti et al., 1999; Fediuk et al., 2002; Kuhnlein et al., 2004; Snodgrass et al., 2006). There is a sound scientifically-based hypothesis that contaminants exert an additive effect on an otherwise obesitogenic lifestyle. In this way, contaminants may exert a negative health effect at much lower concentrations than previously anticipated (Hansen et al., 2008).

Chapter 3 presents recent research findings concerning food sources and diets of Arctic populations, and how food choices, availability and consumption patterns influence their nutritional status and exposure to contaminants. Specific aspects of contaminant–nutrient interactions are examined in detail in Chapter 7.

Topics discussed at length in the previous assessments, such as descriptive discussions of Arctic indigenous residents, basic toxicology of well-known organic compounds and metals, and details of analytical procedures and quality control and quality assurance procedures are not repeated. However, new data on these topics is integrated into Chapters 4 and 7.

The indigenous populations of the Arctic often live in remote, small communities with little economic opportunity. The result is that these residents are more likely to harvest and consume subsistence wildlife, and are more likely to be exposed to contaminants that bioaccumulate in living organisms and biomagnify in the food chain. Chapter 5 examines the extent of

human exposure based on current biomonitoring data across the circumpolar region and provides new data on temporal and spatial trends, which includes Russian data, not available in previous assessments.

Assessment of human health impacts in Arctic populations exposed to contaminants is complex: small populations; exposures to mixtures of contaminants; mitigating effects of micronutrients which co-exist with contaminants; confounding effects of lifestyle choices (i.e., alcohol consumption and use of tobacco), increasing prevalence of obesity and diabetes mellitus; and the influence of genetic and epigenetic factors. Chapter 6 undertakes a detailed review of cardinal genetic and epigenetic factors associated with exposures and effects of exposures in some Arctic populations.

The health status of Arctic populations is presented in an abbreviated form at the start of Chapter 8, as an update to the 1998 and 2002 assessments, and focuses on key indicators of health outcomes. A large part of Chapter 8 concerns the public health significance of environmental contaminants exposures, with a specific focus on prenatal exposure and adverse developmental effects resulting in altered immune and nervous system function early in life. New data on cardiovascular outcomes related to mercury exposure, and potential POPs effects on the hormonal system are also discussed.

The importance of sensitive risk communication in preventing risk transfer and facilitating the overall reduction of health risk is clear. The perceptions of risk associated with various exposures to environmental chemicals and the sense of fear, anxiety, and loss of control that these perceptions fuel, may have an additional effect on human health, and thus on well-being, by having a lasting impression on personal choices in diet and lifestyle (Donaldson et al., 2007). Chapter 9 describes and evaluates how results from research and related advisories are communicated back to communities, the types of methodologies used, the types of impact that they have, and suggestions for the development of a more effective circumpolar communication strategy.

Indigenous peoples in the Arctic are living through a period of dramatic cultural and social change. Stresses imposed by the discrepancy between modern and traditional values may be so strong and unfamiliar that they affect the health of both individuals and communities (Bjerregaard et al., 2004b). Understanding and addressing the greater health disparities, the greater contaminant exposure of some remote indigenous communities, and the complexity of the interactions between contaminants and other health factors inevitably requires more research. This assessment concludes by identifying areas where further research is needed.

The 2008 human health assessment seeks to share the latest information on trends in exposure, to discuss new perspectives on genetic susceptibility, to assess the latest toxicological advances, and to highlight the most up-to-date results from various cohort studies, thereby adding to the body of knowledge on environmental contaminant impacts on human health in the Arctic. AMAP, aided by many academic and public health experts in the circumpolar countries, hopes that better understanding of environmental contaminant impacts in the public health context will help Arctic peoples in better maintaining and improving their health and well-being.

Chapter 2

Factors Influencing Human Exposure to Contaminants and Population Vulnerability

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Summary

Contaminants in the Arctic are either produced and released locally (e.g., waste sites, old military sites, mining) or more often, are transported to the Arctic from distant sites by a variety of mechanisms, especially air and water currents. Once in the Arctic, contaminants can either remain unchanged or can undergo some chemical or physical state change. They can move between compartments, enter the lower trophic levels, move between regions, undergo 'burial' in sediment, or be removed from the Arctic by a variety of mechanisms. These processes can be accelerated or slowed by changes in one or more components of climate and local weather. The characteristics of the contaminant compound are equally important, in that transport, uptake and metabolic degradation are all influenced by volatility, solubility characteristics, and attraction to particles. How climate change will affect the distribution of contaminants is still not well understood and affects the precision of population health predictions. Social and psychological impacts of contamination, changes in cultural dynamics and employment and the availability and quality of traditional food and water can also influence health outcomes. Industrialization of the Arctic (exploration and extraction of resources) can have benefits and costs. Awareness of how other determinants of health influence exposure to contaminants and how contaminants exacerbate changing health conditions are important considerations of a holistic assessment. National, regional and international management of chemicals and waste clean-up efforts are likely to reduce the losses of deleterious substances to the environment and, in the long term, reduce exposure of Arctic populations to chemicals and metals of concern.

2.1. Introduction

This chapter addresses briefly how global climate change and climate variability, global and regional control initiatives, local industrial activities and social and cultural activities may be influencing environmental contamination and/or human exposure and vulnerability in the Arctic. The chapter provides some background and scope for the chapters which follow; however, it does not provide detailed information in each area because complete and more extensive reference documents are available and these are cited in the sections that follow. The chapter ends with a series of conclusions and recommendations.

2.2. Global influences

2.2.1. Climate change

This section is a new addition relative to the previous AMAP assessment of human health in the Arctic (AMAP, 2003). The topic of climate change impact on contaminants has been discussed in some detail in other publications, including the Canadian Arctic Contaminants Assessment Report II (NCP, 2003), the AMAP assessment of the influence of global change on contaminant pathways to, within and from the Arctic (Macdonald et al., 2003), and a special edition of the International Journal of Circumpolar Health (Kraemer et al., 2005). The reader is referred to these reports for an in-depth discussion of the topic, from both the climate and transport pathway perspective and the human health perspective.

The perspective of the present discussion is that of the potential effect of the recent climate trends, and those that climate models predict, on the contaminant exposure of Arctic human residents. Topics discussed include basic Arctic climate processes, observed trends in Arctic climate, model predictions for Arctic climate, potential impacts of predicted changes on levels of contaminants in the Arctic, and vulnerability of biological species (including human populations and the species upon which they depend for food).

2.2.1.1. Arctic climate

As is the case globally, the Arctic has experienced a warming trend over the past century. In general, the amount of warming in the Arctic is greater than the global mean average, with most of the warming experienced in winter, where certain parts of the Arctic have averaged a 5 °C to 7 °C increase over the past four decades. This is particularly true in northwestern Canada, central Alaska, and eastern Siberia. Some regions have not warmed, or have even undergone slight cooling over the same period, such as eastern Arctic Canada and southern Greenland. Large sections of the central Arctic have no temperature time series for that period, so nothing can be said for those regions (ACIA, 2005).

Additional changes include warming of the Atlantic Ocean water entering the Arctic Ocean at a depth of 200 m to 900 m over the last four decades and warming of the Bering Sea water entering the Arctic through the Bering Strait over the last two decades. In terrestrial ecosystems there has been warming of permafrost temperatures in Alaska and Arctic Russia, decreased snow and ice cover, decreased sea-ice cover, increased plant growth in the Arctic, increased primary

production of terrestrial algae in freshwater lakes, and northward movement of the tree line in those most-warmed Arctic regions (ACIA, 2005).

2.2.1.1.1. *Arctic climate processes*

The record of climate change in the Arctic and sub-Arctic over the last 40 years is not homogeneous. Global climate models predict that future changes will not be homogeneous and will produce different climates between and within regions. These changes may lead to an altered definition of what is currently considered 'Arctic' by AMAP and could then affect how resources are assigned for adaptation strategies and Arctic observation and monitoring.

Climate and weather in the Arctic are greatly influenced by the land masses surrounding the Arctic Ocean, as well as by the Arctic Ocean, itself. The same climate-forcing elements that act globally, are operant in the Arctic, including greenhouse gases, solar variability, and volcanoes. Other forcing elements include weather patterns at lower latitudes. These give rise to Arctic and sub-Arctic circulation regimes that result in great natural variability in Arctic climate, over long and short time scales and among regions in the Arctic. Feedback mechanisms resulting from clouds, surface reflectivity (albedo), exposed tundra and seawater, all have significant effects on surface temperature, sometimes over multi-year time scales (Richter-Menge et al., 2006).

Permanent cyclonic wind patterns exist over the North and South Poles. Over the North Pole, this tropospheric wind pattern, influenced by the presence of continental land masses and oceans, creates a set of semi-permanent atmospheric pressure fields in the Arctic and sub-Arctic circumpolar regions. The Arctic Polar Vortex is strongest in winter and weakest in summer, in contrast to the Antarctic Polar Vortex, which is much stronger and more constant.

The semi-permanent circumpolar pressure fields consist of two areas of generally low pressure over northern ocean areas and three generally high-pressure fields over land masses. These fields are all much stronger in winter, reflecting the stronger Polar Vortex at this time. The most persistent low-pressure fields are centered in the North Pacific over the Aleutian Islands (the 'Aleutian Low') and over Iceland (the 'Icelandic Low') extending to the Barents Sea. A stable high-pressure field, the 'Siberian High', exists over the eastern Siberian region in winter and disappears in summer. A second high-pressure field exists over the Chukchi Sea–Beaufort Sea area extending to the Yukon region of western Canada. A third high-pressure field, the 'Arctic High', usually occurs over Baffin Island (ACIA, 2005).

The significance of the semi-permanent pressure fields for the transport of contaminants is the formation of relatively predictable wind patterns from the northern mid-latitudes into the Arctic. The Siberian High forces northward air circulation on its western edge transporting contaminants from Eastern Europe and Russia to the Arctic, whereas the ridge of high pressure over western Canada transports Arctic air south to the mid-latitudes of North America. The Icelandic Low creates strong westerly winds from eastern North America to the southern Norwegian Sea, where southerly winds transport the airborne contaminants from southern Europe and Scandinavia and the eastern part of North America into the Arctic. The Aleutian Low circulates air from Asia westward and northward into Alaska and the Bering Sea and then into the Arctic.

Along the course of the wind circulation patterns, precipitation can scavenge airborne contaminants into seawater, where the surface currents generally reflect the surface winds, and transport is slowed considerably for this fraction of the contaminant load. In this atmospheric circulation pattern, very significant amounts of air (and contaminants) are transported into the Arctic. It is estimated that the Siberian High contributes about 15%, the Aleutian Low about 25%, and the Icelandic Low about 40% of the air movement into the Arctic (Iversen, 1996).

2.2.1.1.2. *The Arctic Oscillation Index*

The Arctic Oscillation (AO) Index is an expression of the relative strength of the atmospheric pressure field at sea level in the high Arctic, compared with the field strength in the northern hemisphere mid-latitudes. The index is expressed as a unitless number, relative to a 50-year norm. When the atmospheric pressure in the Arctic is lower and the pressure in the mid-latitudes is higher, the AO Index is positive; when the reverse is the case, the AO Index is negative. These two variations represent the dominant circulation regimes in the Arctic. Between the 1950s and the late 1980s the AO Index was low and fluctuating. Following this period the AO Index became strongly positive, until around 2000 when the trend changed to follow more the pre-1990s pattern. There is a big difference in climate between a strong AO negative regime and a strong AO positive regime (Richter-Menge et al., 2006).

With a strong positive AO index, there is strong cyclonic wind circulation in the Icelandic Low and warm, wet air is moved into the Arctic with resultant cyclonic movement in Arctic Ocean ice and surface air. Freshwater input from contaminant-laden Arctic Russian rivers is diverted to the east, as much as 1000 cubic kilometers of water per year, into the Canada Basin, with a high probability of flow through the Canadian Archipelago into the Labrador Sea. Under these conditions, the residence time of this water in the Arctic Ocean is significantly increased (from 2 to 10 years), resulting in increased length and concentration of exposure of species living in the ocean. Under these circumstances, exposures of residents of eastern Arctic Canada who depend on food species living in the marine environment increase.

Under strong AO negative conditions, the Arctic air is colder, sea-ice extent is greater and cold air flows into the northern and mid-latitudes of North America and Eurasia. Russian river discharge and sea ice tend to flow into the central Arctic Ocean and out through the Fram Strait with exposure of the residents of eastern Greenland to discharged Arctic Russian river contaminants. Surface air in the Arctic tends to circulate in an anti-cyclonic

pattern, as does surface ice, as the transpolar ice drift shifts toward the North Pole and away from the Canada Basin (Macdonald et al., 2003).

2.2.1.2. **Ocean processes affecting Arctic climate and contaminant transport**

Oceans tend to moderate extremes of temperature, and increase precipitation in the regions adjacent to them. In addition, the major currents into the Arctic deliver heat energy from warmer lower latitudes. The Arctic serves as a major heat sink for the northern hemisphere. The recent trend in reduction of sea-ice cover increases the energy absorption of the Arctic Ocean and increases atmospheric moisture exchange. This change has the potential to affect the strength and size of existing high- and low-pressure fields in ways that are difficult to predict.

In the Atlantic, the global thermohaline circulation delivers warm salty water to the Fram Strait and Barents Sea and moderates the Arctic-like climate of the northern coastal region of Scandinavia. In the Pacific Ocean, where seawater temperatures have warmed over the last three decades, water from the north-flowing currents off the Asian coast and the currents from the eastern North Pacific flow into the Bering Sea and through the Bering Strait at an average of about 800 000 cubic meters per second (Melling et al., 2005).

2.2.1.3. **Lower latitude ocean processes that affect Arctic contaminant transport**

While the Arctic Oscillation is a climate regime that is a response to tropospheric winds, the Southern Oscillation (in the equatorial Pacific Ocean) is not. Instead, the Southern Oscillation refers to the change in gradient of the difference in sea level barometric pressure between the southeastern tropical Pacific and the Australian-Indonesian regions, this causes changes in the wind fields that result in periods of anomolously warm surface waters in the eastern Pacific Ocean ('El Niño' events) and periods of cold-water upwelling along the South American coast (El Niña conditions). El Niño events have now been combined with the Southern Oscillation to become El Niño–Southern Oscillation, or ENSO, events. For the most part, these weather responses take place in the mid-latitudes of both the northern and southern hemispheres. It has been discovered, however, that ENSO events result in significant wind transport to Baffin Island, thus exposing that region to contaminants produced in distant southern regions (Macdonald et al., 2003).

2.2.1.4. **Arctic climate model predictions**

In general, depending on the carbon dioxide production scenario chosen for a given model run, the mean air temperature in the Arctic is predicted by climate models to increase slowly over the next eight to ten decades by between 3 °C and 7 °C, with an increase in precipitation, mostly as rain. The predicted warming will not be uniform, nor will the precipitation. The model predictions include a reduction in sea ice, with perhaps a complete disappearance of sea ice in summer, along with a rise in sea level of perhaps 20 – 50 cm (ACIA, 2005). However, because the observed loss of permanent sea ice has been greater than the most pessimistic model predictions (Stroeve et al., 2007), Hansen et al. (2007) have suggested that sea level rise could be as much as one meter.

Associated with the rising air temperatures predicted are decreases in permafrost in some regions, decreases in the extent of major ice fields, northward movement of the tree line, an increase in levels of ultraviolet (UV) radiation and possibly an increased river discharge from certain Arctic Rivers, notably the Mackenzie River in Canada and the Ob River in Russia (ACIA, 2005).

2.2.1.5. **Possible impact of future climate change on contaminants in the Arctic**

While climate models cannot predict future trends in the AO Index, the basic scenarios describe many of the characteristics of a strongly positive AO Index. A brief summary of some of the major impacts possible in this climate regime on the transport and fate of contaminants in the Arctic are presented below. It is important to remember that the contaminant concentrations in Arctic environmental matrices and biota (including humans) are a product of transport and removal mechanisms, flux between environmental compartments and residence time within environmental compartments, and international efforts to manage chemical and metal releases to the environment. In addition, geochemical cycling, biological uptake and metabolic degradation, movements of wildlife species and availability of species for human consumption as well as human food choice, are all contributors to measured contaminant levels in Arctic matrices. Any discussion of current or possible future trends can only take place with a full knowledge of all the variables involved, many of which are yet to be discovered. All known factors that affect human exposure to contaminants are impacted by climate.

Warming air temperature at lower latitudes will increase volatilization of most organic contaminants and mercury. Under strong AO positive conditions, air transport will be increased into the Arctic, particularly into the Canada Basin and perhaps into the Canadian Archipelago. In the presence of increased precipitation, there could be increased scavenging by rain and snow which will increase delivery of airborne contaminants to seawater, fresh water systems and terrestrial environments. Toxaphene and hexachlorocyclohexane (HCH) are both subject to this behavior (Ma et al., 2003). Increased precipitation will scavenge organic contaminants with differing efficiency, reflecting the solubility of the compound. For example, polychlorinated biphenyls (PCBs) are most effectively scavenged by snow; HCH isomers are most effectively scavenged by rain (Lei and Wania, 2004).

An extended ice-free area in the Arctic Ocean will favor partitioning into seawater, as well as scavenging by precipitation. The quantity of PCBs transferred from the atmosphere into the Arctic Ocean is estimated to be

about 20 tonnes per year and increases in the ice-free area of the Arctic Ocean would increase that amount proportionately. Other contaminants such as HCH may be removed faster than they accumulate by means of gaseous evasion from surface seawater (Macdonald et al., 2005). In addition, warming water favors microbial activity, which has been shown to reduce the half-life of HCH (Harner et al., 2000). Using DDT and PCBs as examples, it appears that melting sea ice will add little to the contaminant load of the Arctic Ocean (NCP, 2003).

Increasing areas of ice-free margins in the Arctic Ocean and Bering Sea are also associated with northward movement of marine species such as Pacific salmon (*Oncorhynchus* spp.) (Welch et al., 1998) that spawn in streams and die, adding their contaminant load to local ecosystems (Ewald et al., 1998). Ice-free Arctic model projections and actual reductions in summer sea ice, for longer periods of time, are likely to lead to greater vessel traffic with increasing likelihood of contaminant spills, and the appearance of invasive species originating from vessel ballast water (Occhipinti-Ambrogi et al., 2007).

Warming winter air temperatures will increase the vapor concentration of many volatile organic compounds in the atmosphere during winter, which could increase air transport movement toward the Canada Basin in AO positive conditions, and to lower latitudes in AO negative conditions. Contaminants such as polybrominated diphenylethers (PBDEs) and polybrominated dibenzodioxins (PBDDs) are highly particle-bound, which may reduce the chance for photo-degradation during air transport. The concentrations of these compounds, which are still rising, closely follow production and release data and may well do so into the future (Macdonald et al., 2005).

Mercury transport by atmospheric means appears to reflect its production and release, such as releases from the increasing use of coal-fired power plants (Munthe et al., 2001). Mercury is effectively scavenged by any form of precipitation (Macdonald et al., 2005). The mercury can then enter the trophic web at the same time that rising temperatures and incident solar radiation are increasing productivity. Here, mercury can undergo methylation and be delivered to higher trophic levels directly or be transported by runoff to local and distant marine ecosystems. Methylmercury is extremely toxic and the process of methylation is known to increase as temperature increases. It may well be the case that the effect of climate change on methylation is the most important effect from the perspective of human and wildlife health (Outridge et al., 2008).

Precipitation is predicted to be most increased in northern Scandinavia and eastern Greenland. The increase in precipitation over continental areas is predicted to increase the flow of the Ob River and the Mackenzie River by as much as 20%. The drainage basins of these two rivers are quite large and scavenged mercury (and organic contaminants) entering the Arctic Ocean could increase as a result (Manabe et al., 2004). Depending on the circulation regime, this load would be diverted to the Canada Basin or the Fram Strait, increasing the exposure of the biota and residents of two different areas of the Arctic.

Cadmium cycles geochemically in the surface waters of the marginal areas of the Arctic Ocean and most of the water-borne cadmium enters the Arctic from Pacific Ocean water via the Bering Strait and flows predominantly through the Canadian Archipelago into the Atlantic. The Pacific Ocean has a higher cadmium content due to global biogeochemical cycling (NCP, 2003). Since the 1940s, flow through the Bering Strait has decreased by 15%. Trends in the cadmium content of the Bering Strait water are not known and while sea level rise may increase the inflow, at present it is limited to about one million cubic meters per second by the physical characteristics of the Bering Strait. Cadmium exposure in the Arctic Ocean is likely to be more heavily influenced by upwelling of Pacific Ocean water onto Arctic Basin shelves (due to loss of sea-ice cover) than by increasing flow through the Bering Strait (ACIA, 2005).

Climate is affected by incident UV radiation, which is predicted to increase for at least the next 50 years due to ozone loss in the stratosphere and to the effect of certain greenhouse gases (Schindell et al., 1998). Over the period 1979 to 2000, ozone loss averaged 3% per decade, with a resulting increase in UV radiation (ACIA, 2005). UV radiation is the driving force in the mercury depletion events (MDEs) that take place at polar sunrise in the Arctic. These MDEs result in a dramatic removal of mercury from the sea level atmosphere. Deposition of mercury in near shore and terrestrial environments during these spring-time events coincides with seasonal increases in microbial methylation and lower trophic production as temperatures warm. The effect of thawing permafrost, as well as aquatic plant productivity, can affect the dissolved organic carbon content of terrestrial and near-shore water, which has a more profound effect on UV penetration in water than does the level of ozone depletion currently recorded (NCP, 2003). UV radiation is also known to drive photo-oxidation of mercury in surface waters, which favors gaseous evasion (Lalonde et al., 2001), and to break large organic compounds into smaller simpler compounds which can combine with mercury and enter the trophic web as methylmercury.

Thus, the net effect of UV radiation on mercury is mixed, and the net effect on the mercury budget in the Arctic is difficult to predict. Probably the most important interaction between UV radiation and mercury concerns methylation/demethylation dynamics.

Interaction of UV radiation with oil-spill hydrocarbons increases their toxicity to biological systems. As oil and gas development and transport increase, the likelihood of a spill increases. Increased UV radiation may enhance the risks to health of spilled hydrocarbons (Huovinen, 2000).

2.2.1.6. **Concluding comments**

Arctic climate has historically shown great variability and the ability to change suddenly. The mechanisms and thresholds for these sudden changes are not fully understood. It is clear that the Arctic climate is currently undergoing rapid change. Models for the Arctic generally predict greater warming and

increasing precipitation, although with large variations within regions.

All aspects of contaminant transport and behavior in the Arctic are profoundly influenced by climate. Warmer temperatures and increased precipitation, conditions consistent with a positive AO Index, will result in greater flow of water and surface air into the Canada Basin and thus greater exposure for that region from transported contaminants. A greater extent of ice-free seawater in the Arctic may favor partitioning of some contaminants into seawater from the atmosphere and increase gaseous evasion and removal of others such as HCH.

Increasing concentrations of contaminants in the atmosphere will probably lead to increasing levels of contaminants in the environment and in biota. Contaminant exposures in human populations are harder to predict. The location, population size and availability of marine food species will change as temperatures rise and sea ice retreats. These changes could increase or decrease human exposure depending on the concentrations of lipophilic compounds in food species and the extent to which different food species are consumed.

The structure of the food web might also change as a result of invasive species. Because climate change is rapidly altering temperature, precipitation and sea-ice cover, the Arctic ecosystem is in a rapid state of flux. Some species are moved toward the margin of where they can survive, while conditions become favorable for some species foreign to the Arctic. When an invasive species finds a transport pathway to this new 'favorable' location, species population dynamics can alter rapidly. Transport pathways could include the water, biological populations themselves (mammals, fish, birds) or ballast water from vessels using the North West Passage for transport of goods and supplies.

Mercury emissions related to coal-fired power plants are likely to increase in the near term, and perhaps longer. The atmospheric transport is efficient, and scavenging, methylation, biological uptake, and wildlife tissue levels of methylmercury may all rise in future. If top level marine predators become less available or are less frequently consumed, human contaminant levels may rise more slowly, or decrease. Large predatory fish may show increasing levels and could pose a risk. Local and regional monitoring programs designed to assess trends of contaminants remain the best approach to formulation of public health consumption guidelines.

2.2.2. **Global and regional treaties**

Global and regional agreements to eliminate or control persistent organic pollutants (POPs) and metals now exist and are part of the global effort to lower emissions to the environment and ultimately to lower human exposure to these substances. National legislation is used by countries to implement these agreements and other national policy priorities on POPs and metals. These agreements, and the national implementation of these agreements, represent a substantial effort to reduce risks to health. Chapter 5 of this assessment addresses levels of contaminants in human blood and breast milk as part of the AMAP effort to determine trends throughout the Arctic. Chapter 5 also provides information on whether these global and regional initiatives are ultimately effective in lowering human exposures (lower human tissue concentrations). Chapters 6, 7, and 8 address toxic effects and health outcomes of populations exposed to POPs and metals that are currently, or could become, part of these global and regional control agreements.

2.2.2.1. **Stockholm Convention**

The Stockholm Convention on Persistent Organic Pollutants is the major international and legally-binding instrument for the management of POPs. This 'global' agreement came into force in May 2004 and has been ratified by more than 160 countries to date (March 2009); however, some major producers of chemicals have not yet ratified the Convention (UNEP, 2008a). Among Arctic countries, only the United States and the Russian Federation have signed but not ratified the Convention. Countries which have signed the Convention must develop and submit for scrutiny, National Implementation Plans (NIPs) that fully address issues related to the management of chemicals (e.g., legislative capacity to manage chemicals, stockpiles, wastes, production, use) prior to ratifying the Convention and so becoming 'Parties' to the Convention.

The Convention currently lists 12 substances for elimination or control under its Annexes (Table 2.1) and has provision for the addition of other substances. To date, Parties to the Convention have nominated 12 new substances to be added to the Annexes (Table 2.1).

Table 2-1. Chemicals currently listed under the Annexes to the Stockholm Convention (UNEP, 2008b) and chemicals proposed to be added to the Convention Annexes. Source: UNEP (2008c).

Chemicals currently listed	Chemicals proposed for addition (*see footnote page 14*)
Aldrin [a]	PentaBDE [b, d]
Chlordane [a]	Chlordecone [a, d]
Dieldrin [a]	HBB [b, d]
Endrin [a]	Lindane [a, d]
Heptachlor [a]	PFOS [b, d]
HCB [a, b]	OctaBDE [b, d]
Mirex [a]	PeCB [b, d]
Toxaphene [a]	SCCP [b, e]
DDT [a]	α-HCH [a, d]
PCB [b]	β-HCH [a, d]
PCDD [c]	Endosulfan [a, e]
PCDF [c]	HBCDD [b, e]

HCB: hexachlorobenzene; DDT: dichloro-diphenyl-trichloroethane; PCB: polychlorinated biphenyls; PCDD: polychlorinated dibenzo-*p*-dioxin; PCDF: polychlorinated dibenzo-furan; PentaBDE: pentabromodiphenyl ether; HBB: hexabromobiphenyl; PFOS: perfluorooctane sulfonate; OctaBDE: octabromodiphenyl ether; PeCB: pentaclorobenzene; SCCP: short-chained chlorinated paraffins; α-HCH: alpha-hexachlorocyclohexane; β-HCH: beta-hexachlorocyclohexane; HBCDD: hexabromocyclododecane.

[a] pesticide; [b] industrial chemical; [c] industrial by-product; [d] considered a POP and risk management evaluation complete; [e] under consideration.

At present, nine are determined to be POPs (i.e., the substance is ... 'likely as a result of its long-range environmental transport to lead to significant adverse human health and/or environmental effects such that global action is warranted'). Risk Management Evaluations for these nine substances have been completed and recommendations have been provided to the Parties to the Convention for their addition, with appropriate exemptions, to the Convention Annexes[1]. One of the three remaining substances (hexabromocyclododecane) is under review to determine if it warrants a more detailed review (development of a risk profile) and the two others (short-chained chlorinated paraffins and endosulfan) are at the detailed risk review phase to determine if they are POPs as defined by the Convention.

Countries that are already Parties to the Convention will be able to choose individually whether to implement restrictions on new substances added to the Annexes of the Convention; other countries will have to accept all restrictions for all substances found in the Annexes at the time they become Parties to the Convention.

2.2.2.2. **UNECE POPs and Metals Protocols to the LRTAP Convention**

The Convention on Long-range Transboundary Air Pollution (LRTAP) supported the development of two protocols for the management of substances in the mid-1990s: one related to POPs and the other to heavy metals (UNECE, 2008a,b). The POPs Protocol and the Heavy Metals Protocol under the United Nations Economic Commission for Europe (UNECE) were both signed in 1998 and came into force in 2003. Both have now been ratified by 29 countries (as of December, 2008).

Table 2·2. Chemicals and metals listed under the Annexes to the UNECE Protocols on POPs (UNECE, 2008a) and Metals. Source: UNECE (2008b).

Chemicals currently listed	Metals currently listed
Aldrin [a, b]	Cadmium
Chlordane [a, b]	Lead
Chlordecone [a, b]	Mercury
DDT [a, b]	
Dieldrin [a, b]	
Endrin [a, b]	
Heptachlor [a, b]	
HBB [b, c]	
HCB [a, b, c, d]	
HCH [a, e]	
Mirex [a, b]	
PAH [d, f]	
PCB [b, c]	
PCDD [d, f]	
PCDF [d, f]	
Toxaphene [a, b]	

DDT: dichloro-diphenyl-trichloroethane; HBB: hexabromobiphenyl; HCB: hexaclorobenzene; HCH: hexaclorocyclohexane; PAH: polyaromatic hydrocarbons; PCB: polychlorinated biphenyls; PCDD: polychlorinated dibenzo-*p*-dioxin; PCDF: polychlorinated dibenzo-furan.

[a] pesticide; [b] no production or use permitted; [c] industrial chemical; [d] limits on emissions; [e] restrictions on use; [f] industrial by-product.

Table 2·3. Chemicals 'newly' identified by the parties as POPs and awaiting assignment to an annex(es) of the POPs Protocol, and chemicals nominated by a party for review to determine whether they are POPs under the definition of the POPs Protocol. Source: UNECE (2009).

Newly identified chemicals awaiting assignment	Chemicals nominated for review
HCBD	Dicofol
OctaBDE	Endosulfan
PCNs	PCP
PentaBDE	Trifluralin
PeCB	
PFOS	
SCCP	

HCBD: hexachlorobutadiene; OctaBDE: octabromodiphenyl ether; PCNs: polychlorinated naphthalenes; PentaBDE: pentabromodiphenyl ether; PeCB: pentachlorobenzene; PFOS: perfluorooctane sulfonates; SCCP: short-chained chlorinated paraffins; PCP: pentachlorophenol.

Sixteen POPs and three heavy metals are currently covered by the two protocols (Table 2.2).

The protocols identify bans and restrictions, emission limits, and codes of best practice related to POPs and metals for the member countries of the UNECE that have ratified the Protocols. All Arctic nations have ratified the two protocols except for the United States and the Russian Federation.

The Executive Body to the Convention is currently considering the addition of seven substances considered to be POPs according to the definitions of the POPs Protocol and reviewing another four to determine whether they should be considered POPs under the Protocol's definitions (Table 2.3).

2.2.2.3. **EU Agreements**

The most recent regulations related to chemicals and metals management in the European Union are incorporated in the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) agreement managed by the EU Environmental Chemicals Agency (ECHA) (REACH, 2007). REACH entered into force on 1 June 2007 to streamline and improve the former legislative framework on chemicals of the European Union. This integrated program was operational by mid-2008 and enables restrictions and authorizations to be put in place for a wide range of substances.

Through REACH all producers and importers of chemical substances in the EU must 'register' their substances with ECHA (i.e., specify risks related

[1]In May 2009, at its fourth meeting, the Conference of the Parties to the Stockholm Convention decided to list all nine substances (together with appropriate exemptions) to Annexes A, B, or C of the Convention. These substances are those with footnote 'd' in Table 2·1.

to the substance, the amount of the substance produced or imported and information about the producer or importers, including their name and address). Registration forms are managed by ECHA in cooperation with national authorities of member states. Documentation received is 'evaluated' with specific replies to the producers or importers about problems related to the substances. Based on a determination by ECHA, those substances with significant health and environmental risk may only be used in an approved manner or not at all.

2.2.2.4. **North American Agreement on Environmental Cooperation**

The North American Agreement on Environmental Cooperation (NAAEC) was created as a side agreement to the North American Free Trade Agreement of 1994. One component of the NAAEC, signed by Mexico, Canada and the United States in 1994, was the creation of the (North American) Commission for Environmental Cooperation (CEC). The CEC put in place a Sound Management of Chemicals initiative in 1995 and successfully coordinated, through the three Parties, the elimination of use of all 12 original substances listed under the Stockholm Convention on a continent-wide basis by 2004. It also developed a North American environmental monitoring and assessment plan (CEC, 2008). Action taken by the three countries is shown in Table 2.4. The initiative was re-oriented in 2006 to address three key items: (1) to foster tri-national collaboration for the sound management, throughout their lifecycles, for the full range of substances of mutual concern, including tri-national aspects of high production and high volume (HPV) chemicals; (2) to provide consistent, compatible and comparable data for decision-making in North America; and (3) to build capacity for sustained environmental monitoring and assessment.

Table 2·4. Activities and substances addressed through the North American Commission for Environmental Cooperation initiative on the Sound Management of Chemicals. Source: CEC (2008).

Substance	Action
NARAP required	
Chlordane	Production and use eliminated
DDT	Production and use eliminated
Lindane	Production and use eliminated
PCB	Production ended, no new uses, phase out and destruction
PCDD, PCDF, HCB	Best practices and waste management
Environmental monitoring and assessment	Consistent, compatible, comparable environmental and health monitoring data
NARAP not required	
Dieldrin	Substance not in use in North America
Aldrin	Substance not in use in North America
Endrin	Substance not in use in North America
Heptachlor	Substance not in use in North America
HCB	Substance not in use in North America
Mirex	Substance not in use in North America
Toxaphene	Substance not in use in North America
α-HCH	Substance not in use in North America
β-HCH	Substance not in use in North America

NARAP: North American Regional Action Plan

2.2.2.5. **Russian Agreements**

In 2003, Russia announced the 'Key Provisions of the State Policy to Ensure Chemical and Biological Safety of the Russian Federation for up to 2010 and for the Longer Term'. The announcement defined the aims, key principles, priorities, objectives and state support actions for the policy which focuses on ensuring chemical and biological safety of individuals, society and the state. There are over 15 codes and federal laws underpinning the policy (Eco-Accord, 2003).

Russia has participated in the development of five key international agreements related to chemicals and/or metals management. It has signed and ratified the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal. It has signed but not ratified the Stockholm Convention on Persistent Organic Pollutants and is completing its National Implementation Plan (required for ratification) (see section 2.2.2.1). It has also signed but not ratified the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. Russia has been actively involved in the Strategic Approach to International Chemicals Management (SAICM). In 2006, Russia agreed to 'achieve the sound management of chemicals throughout their life-cycle so that, by 2020, chemicals are used and produced in ways that lead to the minimization of significant adverse effects on human health and the environment'. Russia was also an active participant in the development of the LRTAP POPs and Metals Protocols but has not yet signed and ratified these protocols.

2.2.2.6. **Concluding comments**

Sound management of persistent, bioaccumulative, and toxic chemicals and metals which can travel long distances from their sources is essential for reducing human exposure to contaminants in the Arctic. Effective control of these substances will be a significant factor in global reductions in environmental and human residue levels. All the Arctic countries are supporters of domestic and international action to effectively manage substances which can harm health and the environment; however, not all Arctic countries have ratified the key international instruments currently in force.

Monitoring will be essential to determine whether national, regional and international controls are effective in reducing contaminant loading to the Arctic and

concentrations of contaminants in the food chain and in human tissues.

2.3. Influences of local activities on contaminant exposure and community well-being

Mining, oil and gas exploration and extraction activities, and waste sites have the potential to contribute to loadings of POPs and metals in the Arctic region. These activities can also lead to community stress through in-migration and out-migration of workers, disease introduction and vector transport, socio-economic issues, and other impacts on health determinants. Individuals under stress may be more vulnerable to the effects of contaminants.

2.3.1. Mining

2.3.1.1. Alaska

In Alaska, current large-scale mining operations consist of a single coal mine and an open pit lead-zinc mine. Both are located in remote regions, inhabited only by mine employees, whose health is the responsibility of U.S. Federal and State regulatory agencies. Regional rivers that are potentially impacted by mine activities are tested for compliance with health and safety regulations and there are no reports of adverse impacts on human health.

Abandoned, inactive mine sites are found in many parts of Alaska, and are sometimes the cause of health concerns among regional residents. Other than routine testing of the water supply, few sites have been intensively investigated. In one case, lead levels, and in another case mercury levels were tested in local residents and both were found to be below a level of concern (Middaugh, 2001).

2.3.1.2. Canada

Mining of gold in the Canadian Arctic has a long history. New mines have been appearing over the last 12 years following the discovery of economically-viable deposits of several minerals and diamonds in the North West Territories (NWT). There are currently five operational mines in northern Canada; three diamond mines (Ekati, Diavik, Snap Lake) and one tungsten mine (Cantung) in the NWT and one gold-copper mine (Minto) in Yukon (O'Neill, P., pers. comm., 2009). Releases of arsenic into water bodies have been reported near some goldmines; however, information on wastes from mines past and present was not readily available for this assessment. There are currently 20 abandoned mines that are being assessed or remediated in the NWT, Nunavut and Yukon by the Contaminated Sites Program in Canada (Nahir, M., pers. comm. 2009).

Smelting of metals does not take place in the Canadian Arctic; however, the Voisey Bay mine near Nain, Labrador is a mining and smelting center for nickel sulfide and copper sulfide (Vale Inco, 2009).

2.3.1.3. Greenland

Mining in Greenland has also expanded in recent years. There are three active mines in Greenland and others are in the planning stages: (1) a goldmine near Nanortalik which also has amounts of copper and arsenic in the ore; (2) a zinc-lead-silver mine near Uummannaq that was active for 20 years, closed for 2 years, and then reopened in 2007 because melting of the icecap had increased access to the ore; and (3) a magnesium-iron-silicate mine near Maniitsoq.

Because most of the drinking water supply for communities in Greenland comes from icecap melt waters, waste from mines is unlikely to become a source of human exposure to metals.

2.3.1.4. Russian Federation

The Russian Federation possesses a significant percentage of the world's mineral resources and in 2000 accounted for about 14% of the world's total mineral extraction. The main resources are aluminum, bauxite, cobalt, diamonds, nickel, platinum, tin, copper, lead, gold, molybdenum, tungsten, zinc, silver, and iron. Nickel production in Arctic Russia has been the most important historically and politically. The nickel industry in the border zone between Russia, Norway and Finland played a very important role before and during the Second World War. Nickel deposits were first discovered by a Finnish expedition, developed and extracted by INCO of Canada, and finally taken over by Russia when the Second World War ended. In recent time, the nickel refineries in Nikel and Monchegorsk have become symbols of the types of environmental disasters that can be related to industrialization. Environmental and human health studies have been undertaken following concern for the effects of the smelting operations in these areas (see also Chapter 8).

2.3.2. Oil and gas activities

AMAP has undertaken a detailed and wide-ranging assessment of the implications of present and future oil and gas activities in the circumpolar Arctic (AMAP, 2009). Oil and gas exploration, extraction, and shipping are all likely to increase dramatically over the next 20 years based on the increasing demand for oil and gas worldwide combined with more interest in and access to Arctic resources, the latter due to climate change and reductions in the extent and thickness of sea ice. While oil, drilling fluids and drill cuttings can contain mercury, cadmium and lead in varying amounts and occasionally some POPs and radionuclides, quantities are very small and most wastes in modern operations are now 'contained' (e.g., through the use of on-site tanks, holding ponds, down-hole dumping). Ocean platforms do discharge some wastes but not in quantities that are considered deleterious by national regulatory bodies.

The main health conclusions of the AMAP oil and gas assessment (AMAP, 2009) indicate that there are unlikely to be any major impacts of exploration and extraction activities on local Arctic populations unless there are

major spills. Transport of oil in the Arctic region is likely to increase, making spills a greater possibility; however, even large spills are not expected to contribute significantly to human exposure to metals or POPs because concentrations in oil are extremely low and very few communities are likely to encounter oil spills. Past oil and gas activities in parts of Arctic Russia may have led to some health impacts; however, peer reviewed documentation is unavailable.

Social impacts of oil and gas activities associated with increased disposable income, an influx of workers from outside the Arctic, more community revenue, and changes in social and cultural integrity may occur and could influence health outcomes both positively (better health and educational services) and negatively (social disruption). They may also interact as a determinant factor with contaminant-related health outcomes.

2.3.3. **Waste management**

As climate changes and permafrost thaws, current waste sites (chemical and mixed domestic wastes) may begin to leak their contents into water systems and onto land masses. Burning of domestic waste may also increase. These events could increase human exposure to POPs (e.g., PCBs and some pesticides leaking from waste sites and dioxins and furans from waste burning) and could influence health outcomes.

2.3.3.1. **Waste management in rural Alaska**

In the Arctic and sub-Arctic regions of rural Alaska, sewage and solid-waste landfills are routinely contained by permafrost. With continued Arctic warming, the active layer of the permafrost is now deeper in the summer, with the potential to allow subsurface migration of pathogens and contaminants into nearby surface water and rivers, where they could affect human users and local biota. To date, there has been no systematic evaluation of this potential problem.

Abandoned military dump sites exist in Alaska, the largest being on the southern tip of St. Lawrence Island in the northern Bering Sea. Local wildlife, mostly aquatic and marine organisms, has been found to contain low levels of contaminants related to the dump site. Human tissue levels of local residents are similar to those found in other subsistence communities in the Bering Sea and North Pacific Aleutian Islands (Middaugh, 2003). Thus far, no human tissue levels of contaminants have indicated movement from a dump site into local residents; however, clean-up efforts are in the planning stage for the St Lawrence Island site.

2.3.3.2. **DEW line sites in Arctic Canada**

Primary sources of PCBs within the Canadian Arctic include operational and abandoned mining and industrial sites, waste disposal sites, and abandoned military sites (Stow et al., 2005). It is most likely that the abandoned military radar stations which formed the Distant Early Warning (DEW) line stations have been the most significant. The DEW line covered about 5000 km and comprised 63 radar stations, of which 42 were on Canadian soil. The DEW line was put in place by the United States and Canada during what was termed the 'Cold War' (1956 – 1991). Twenty-one of these sites were abandoned in 1963 and the remaining 21 were taken out of operation in the late 1980s. Considerable amounts of waste material, oil drums, PCBs in transformers and paint, and other hazardous chemicals were left at the sites.

Macdonald et al. (2000) and Pier et al. (2003) called the local influence of these sites on contaminant levels in the surrounding environment 'the halo effect'. The halo of influence appears to range from 5 to 27 km in radius and probably averages 10 km at a typical site (Stow et al., 2005), and transport of PCBs into the halo region is primarily by particulate movement. Macdonald et al. (2000) suggested that local sources represent a relatively minor contribution to the overall burden of Arctic PCB contamination beyond this halo region; representing less than 1% of loadings from remote, long-range sources.

From the average levels of PCBs in soils at the 21 primary DEW-line sites, total PCB loading is estimated to have been about 1000 kg. Early site investigations at the remaining 21 intermediate sites suggest that levels of PCB contamination are significantly lower and possibly about 250 kg (Reimer, K., pers. comm., 2009). Resolution Island (Nunavut) and Saglek (Labrador) are two abandoned military sites that were not included in either of these estimates but which had contaminated soils accounting for over 5000 kg and 4200 kg of PCBs respectively (Gregor et al., 2003; DIAND, 2004). The amount of contamination at these sites was unique among Canadian Arctic military sites and both were cleaned up under stand-alone remediation projects.

Clean-up of the Canadian DEW-line sites has been slow due to the immense cost of collecting the wastes, testing the contents, measuring remediation success and transporting the wastes out of the sites (usually by aircraft). Soil clean-up at the primary sites in Canada is almost complete, with 14 sites finished and the remaining seven to be completed by 2012. The 21 intermediate sites are to be assessed and remediated under Canada's Federal Contaminated Sites Program.

Clean-up of contaminated soil appears to be an effective means of preventing further redistribution of PCBs from these sites. Stow et al. (2005) concluded that this clean-up will be protective of the ecosystem and will reduce the effect on country foods that may be harvested by members of the communities that are closely located to the zone of influence that once extended across the Canadian Arctic.

2.3.3.3. **Waste management in Greenland**

Domestic household waste in Greenland is generally land-filled. This includes scrap metal, plastics and glass. However, Nuuk has a modern waste incinerator which co-generates warm water for community use. Some communities and homeowners burn refuse outdoors.

Dangerous substances such as oils, paints, chemicals and batteries are sent to Denmark for disposal. Wastewater from factories, offices and homes is discharged to sea; the contamination from a population of 57 000 people along the thousands of kilometers of Greenland coastline is considered to be negligible.

2.3.3.4. **Waste management in Arctic Russia**

According to the Waste Classification Guidelines of the Russian Federation, natural organic waste includes about 100 categories of waste from ten major sectors of the economy (manufacturing and consumer consumption). There are 200 to 250 million tonnes of total waste per year (WASMA, 2005). Some of this has been accumulating in neglected waste sites and may be a local source of POPs.

It has been estimated that over 12 million 45-gallon drums had been left in the Russian Arctic by the end of the Soviet era (Efremenko, 2007). The specific contents of the drums are generally unknown, but are thought to include spent oils, lubricants and waste fluids from mechanical equipment and contaminated water. Abandoned drums are most frequently located near coastal communities of indigenous Arctic residents and can be a source of significant local contamination. The drums contain both persistent and biodegradable substances. How they may interact to affect health and well-being is unclear and difficult to measure.

Managing such wastes and in such locations is problematic for Arctic communities and for private businesses involved in waste disposal. The capacity for waste recycling in Russia is low, not because the technology is deficient, but because there is a poor underlying institutional framework, especially in the lack of strong legislative support. Waste recycling success can only be achieved through rigorous and comprehensive state and local regulations, as shown by Russia's own recycling experience during the Soviet period and as experienced by countries with well-supported waste management and recycling programs (Deviatkin, 2007).

Waste stream analysis and reuse/recycling programs are key to reducing waste generation in Russia (WASMA, 2005). Public understanding and commitment are also essential for changing waste management practices. Several Arctic communities in Russia have indicated a readiness to act on waste clean-up. The Indigenous Peoples Community Action Initiative has been developed to implement measures to reduce risks associated with human exposure to persistent toxic substances. This is being achieved through improvement of sanitation and decontamination of neglected waste sites in selected indigenous communities in Russia's Nenets and Chukotka regions. Selection of the indigenous communities was based on the elevated levels of persistent substances measured in the blood of residents of those communities identified in the Persistent Toxic Substances study (AMAP, 2004b). A central focus of this initiative was improving human health, sharing of new information and developing integrated strategies for environmental solutions through the creation of models to address the environmental legacies at the community level.

Ongoing work in these indigenous communities includes use of best practices and model behavior to establish environmental justice. The main partners in the initiative are the Russian Association of Indigenous Peoples of the North (RAIPON) and the Arctic Contaminants Action Program (ACAP) of the Arctic Council of Ministers. The initiative has focused first on the Nenets and Chukotka Autonomous Okrugs to examine their waste management problems and practices. Impressive results in waste recycling have been due largely to a broad information campaign and to many years of effort by local authorities to educate the public. As a result, the public has become aware of the need to get personally involved in domestic waste management and has adopted new, more responsible behavior patterns relating to domestic waste disposal.

Efforts have been made to develop inventories of obsolete and banned pesticides in the Russian Arctic and to store them safely (ACAP, 2006). Over 1306 tonnes of obsolete pesticides have been inventoried and placed into safe storage (sub-surface storage or disposal in large trenches) in six priority regions: Komi Republic, Tyumen, Omsk, Altai Republic, Magadan, and Arkhangelsk. Additional work is underway to inventory and store pesticides in Altai Krai, in particular because of the risks associated with their potential release to the thousands of rivers that flow through the region.

2.3.3.5. **Concluding comments**

Most mining activities within the Arctic are unlikely to add significantly to the body burdens of mercury, lead or cadmium of Arctic residents. Levels of nickel in the environment have been found to increase in the vicinity of the refineries in Nikel and Monchegorsk and the results of extensive environmental monitoring activities and health are discussed later in this assessment (see Chapters 5 and 8).

Oil and gas exploration and extraction can affect health but usually only following a large spill. The most significant impacts are psychological and social and these could affect how individuals and communities respond to exposures to contaminants from sources unrelated to oil and gas activities.

The entry of workers into the Arctic to support exploration and extraction activities related to oil, gas and minerals can lead to the introduction and spread of disease between workers and among communities (AMAP, 2009). While this is not a POPs and metals issue, poorer general health can affect how individuals respond to contaminants from other sources.

Waste clean-up at known sites of persistent substances and metals has progressed well or is underway in Alaska, Arctic Canada and Russia. Information for other countries is not available. Significant PCB contamination at DEW-line sites across Alaska and Canada may have influenced local levels of PCBs within a 10 km radius of each site; however, the overall contribution to Arctic loadings for

the region is probably less than 1%. Contamination of local areas and surface waters associated with other domestic waste and possibly chemical storage sites may become a local problem as climate changes and permafrost thaws. Exposures of communities to some POPs and metals held at these sites could increase through seepage and run-off into surface waters. Local food species could also become contaminated by substances from waste sites, leading to potential increases in human exposures depending on the types, amounts and seasonality of traditional food use.

2.3.4. **Social and cultural influences on exposure**

The sharing of food and material wealth is a cultural value that ensures that families or individuals are provided for in times of need. The exchange of country food within a community is an important element of social well-being and is intrinsic to local culture. The various social and cultural values that create additional incentive to consume country food influence the extent and nature of an individual's and a community's exposure to contaminants. The social health and cultural norms of a community can also affect how money is spent, how and how much alcohol and tobacco are used, trust in health care providers and use of health care facilities, breast feeding of newborns, the importance of education through elders' teachings and more formal school-based learning. These are all determinants which can reduce or exacerbate the impacts of contaminant exposures on overall health.

2.3.4.1. **Exposure to POPs and metals in traditional food**

The consumption of local renewable resources in the Arctic varies depending on geographic location, age and other factors (for details see Chapter 3, section 3.1). Many northerners consider country food to be a cultural anchor and its use is often important to individual and community identity. For example, a number of participants in a recent study conducted in Cape Dorset, Nunavut, Canada emphasized that their cultural connection to the land continues to develop through the harvest and consumption of country food and that the associated practices reinforce their identity as Inuit. One of the male participants stated that:

> *The land is important to my health because even with all the changes that have gone on for us we still depend on the land for survival. Going out on the land has a lot of importance. It has a lot of meaning for us. The land and local food like seal, caribou and char are part of who we are* (Donaldson, S., pers. comm., 2009).

Use of country food within social networks plays an important role in the health and well-being of Arctic Peoples. The sharing of country food is integral to the maintenance of bonds within social networks. The processes associated with the sharing of country food involve a complex set of social rules that are codified in a culturally-specific way. The key tenets of sharing within a social network include norms and expectations of supportiveness, generosity and reciprocity. One of the other male participants from the Cape Dorset study stated that:

> *My culture teaches us to share with anyone who needs it. For example, a hunter will go over the community radio to let community members know that he has country food to give away. This is important for us. Sharing country food helps the community out. I think sharing is a value that makes Inuit different from those living outside of Nunavut* (Donaldson, S., pers. comm., 2009).

Diet is the single most important predictor of contaminant exposure in the Arctic populations. Traditional foods are an excellent source of nutrients and energy and contribute to good social, spiritual and physical health; however, they are also the primary source of POPs and metals. Diets are changing. Concern about contaminants, cultural values, and the availability of traditionally-hunted species due to climate change, all play a role in influencing the types of traditional foods consumed, the frequency of their consumption, and the exposure of Arctic populations to contaminants (see section 2.2.1.6). Chapters 3 and 5 of this assessment provide an update on the influence of diet on exposure and how diets are changing in the Arctic.

2.3.4.2. **Breast feeding**

Transfer of lipid-soluble contaminants from mother to infant by breast milk is well-documented. Maternal levels of contaminants in women who have breast fed are significantly less than those of women of the same age, who have not. Nevertheless, any risk incurred by the breast-feeding infant from contaminant exposure, by this route, is primarily theoretical. Benefits of breastfeeding, however, are very well-documented, and there is a large public health literature to support this. For this reason, at this time, known maternal POPs levels in Scandinavia, Iceland, Greenland, and North America do not justify any other public health recommendation than to continue breastfeeding as the optimal form of infant nutrition.

Information on the relationships between breast-feeding, health and contaminants has been provided in previous reports (AMAP, 1998, 2003) and is further discussed in this assessment in Chapters 3, 5, 6 and 8.

2.3.4.3. **Concluding comments**

Social factors can affect health outcomes and should be considered carefully in risk assessments related to contaminants. Previous reports have discussed the impacts of excessive smoking, alcohol and drug use, and crowding and underemployment on health (AMAP, 2003). How individuals interact within their communities and families can be affected by a variety of environmental circumstances, for example, knowledge

of the extent of contamination of traditional food; accidental contamination of the land, water or air; and individual concern over contaminants in breast milk.

2.4. Conclusions and recommendations

While most Arctic contamination by POPs and metals is from long-range transport, there are several potential sources of contaminants from within the Arctic that could add to loadings of metals and POPs. Human population exposure comes primarily from country food consumption and local sources of contamination have the potential to contribute marginally to food contamination.

Climate change is almost certain to affect the biogeochemical fluxes of contaminants within the environment. This will cause increases and decreases in current human exposures. Current climate trends and future model predictions illustrate the incomplete understanding of the interactions between contaminants and climate. Not all Arctic regions will be affected to the same extent or in the same way. Climate change is also likely to change exposures to pathogens such as viruses and bacteria, and to insect vectors. Climate change can also make human populations more vulnerable. Climate-related 'stress' associated with changes in diet, lack of access to traditional prey species and foods, loss of traditional hunting, changes in community practices and changes in occupation can affect psycho-social health. The combination of changing exposures and vulnerability has the potential to affect health and well-being significantly.

The only practical adaptive response for evaluating the implications of climate change on contaminant fluxes is continued monitoring of humans and key wildlife species to directly assess tissue levels of contaminants. In this way, dietary information would be directly available to human residents and alternative and culturally appropriate food choices could be made which preserve cultural traditions, and the benefits of the traditional diet. Research into climate and contaminant interactions should continue to assist policy development of regionally appropriate adaptation strategies.

Knowledge of how climate and local weather affect contaminant distribution and redistribution and the rates at which these occur are in the early stages of development.

Detailed knowledge of climate-mediated transport pathways is also a relatively new field of investigation. Continued research in this area, coordination between researchers, and careful development of joint research plans is a critical need for future progress in the climate–contaminant transport–human exposure research effort, because it has a direct bearing on how exposure and health will be affected in the future.

Arctic countries need to continue to support the implementation of international and regional agreements to control chemical and metal releases to the environment. The United States and Russia have yet to ratify some key environmental agreements that are important for the protection of the Arctic and its people.

Monitoring programs to assess the success of national, regional and global control initiatives currently in place are essential. Without information on where and how levels are changing and which populations are most at risk, it is impossible to revise control actions to make them more effective.

Mineral exploration and extraction could lead to contamination of the local environment with mine tailings. Depending on the amount, type and location of the contamination, these activities could increase human exposures to some metals of significance through the intake of local foods, air, water and wildlife. The in-migration of workers to oil, gas and mining operations can lead to the introduction and spread of disease if health monitoring and treatment are not adequate. General health is a significant determinant in evaluating how an individual may respond to contaminant loads. This assessment has not undertaken a thorough review of mining activity in the circumpolar Arctic to assess how mining activity may co-contribute to current human exposures to mercury, cadmium and lead.

Oil and gas exploration and extraction activities are likely to increase in the Arctic, but have the potential to contribute only very small amounts of POPs and metals to the environment. Most on-site wastes are contained and managed to similar high standards. A large oil spill could contaminate a large area; however, it would not add appreciably to the entry of POPs or metals into the environment. A large spill could lead to significant social disruption which can influence mental health and affect individual responses to current exposures to POPs and metals received primarily through diet. A detailed review of the health implications of oil and gas exploration and extraction in the Arctic has been undertaken by AMAP (2009).

The security and integrity of domestic and chemical waste sites in the Arctic is important, especially under the conditions of a changing climate. Most military sites in the Arctic which had caused contamination in local areas have now been cleaned up or are in the process of being cleaned up. These and other waste sites need to be monitored to ensure that they do not affect community water and food supplies as the permafrost thaws. Leaking waste sites have the potential to add to local population exposure to chemicals, metals and pathogens that are likely to impact negatively on health.

Social factors can affect health outcomes and should be considered carefully in risk assessments related to contaminants. Excessive smoking, alcohol and drug use, and crowding and underemployment can affect health. How individuals interact within their communities and families can be affected by their knowledge of the extent of contamination of traditional food, breast milk and the local environment.

Chapter 3

Food, Diet, Nutrition and Contaminants

Arild Vaktskjold, Bente Deutch, Kelly Skinner, Shawn G. Donaldson

Summary

This chapter presents recent research findings concerning food sources and diet in Arctic populations, and explores how food choices and availability influence human nutritional status and exposure to contaminants. Other factors influencing human exposures to contaminants were addressed in Chapter 2. The term *traditional food* is used to represent foods that originate in the populations' habitat (generally foods such as seal, whale, caribou and fish from the land); other foods are called *imported food*.

In the Arctic, traditional food is beneficial to indigenous populations for cultural, social, psychological, and economic well-being, however, foods from mammals, birds and fish have been documented as the main source of human exposure to contaminants. Changes in food sources and food choice can influence the nutritional quality, density, and security of the diets of indigenous populations. In addition, the incidence of food-borne botulism and trichinosis is associated with the preparation and consumption of local meat. As a result, studies in Canada indicate that food insecurity is more prevalent among indigenous populations than non-indigenous populations. One of the observed consequences of the changes in diet and lifestyle is an increased prevalence of overweight and obesity.

In indigenous populations where most of the dietary energy was provided from imported food before the turn of the millennium, this pattern has remained the same or increased further. In Russia, on the other hand, the socio-economic changes and deterioration of the farming and livestock system in the northernmost parts after the dissolution of the former Soviet Union seems to have led to increased use of local foods in some populations. In indigenous populations, the trend towards a higher proportion of imported foods in the diets of young people has continued, and appears particularly strong in Alaska, Yukon, and among the Canadian Inuit. Sweet and fatty store-bought food is becoming the main source of energy for children in this region, which has also contributed to an inverse relationship between nutrient density in the diet and age group. In the future, the low consumption of traditional food in the young age groups may perpetuate itself as they grow older and contribute to additional decreases in the consumption of traditional food. The overall contribution of traditional foods to energy intake in indigenous populations of Arctic Canada ranges from 10% to 36%, with an average of 22%; this figure is lower among children. Within that proportion there have also been reports of changes in food choice, for example more fish and fewer marine mammals are being consumed. In southern Greenland (Inuit) and northwestern Alaska, local food constituted a lower proportion of the diet than in Canada. In Greenland, studies indicate that the consumption of local food among the Inuit has been reduced by about 50% over the last 30 years, and today the community-level proportions among adults range from 11% to 22%. Women in most indigenous populations in Alaska, Greenland and Arctic Canada generally consume proportionally less traditional food than men. Consumption is positively associated with the proximity of settlements to a coast or river, but varies with season. Education above elementary school level tends to lead to the consumption of more imported food. Alcohol consumption tends to be underestimated or not accounted for when estimates of energy consumption are made. Thus, the true proportions of energy intake from traditional foods among adults, especially men, are likely to be lower than those reported.

In general, the decreasing proportion of traditional foods in the diet has had a negative impact on the intakes of most nutrients, but imported foods appear to have contributed positively to the intake of vitamin C, folate, and possibly calcium. According to measurements of blood and dietary intakes, nutritional deficiencies of vitamin A, iron, calcium, and magnesium are prevalent in some communities. However, the amount of calcium provided through consumption of local foods is insufficiently researched. In terms of vitamin A, the types of imported foods consumed do not seem to provide the recommended amounts. The transition to diets mainly based on imported foods in the indigenous populations is likely to have led to insufficient intakes of other nutrients as well, especially in the young age groups. Nutritionally, the problem is not the imported food itself, but rather the widespread replacement of traditional food by a diet that is high in sugar and other foods with low nutrient density. However, updated, accessible and comparable information about nutritional intake is relatively sparse from circumpolar populations outside Alaska, Greenland and Arctic Canada. Information concerning populations in Russia, where the majority of indigenous and non-indigenous people live, has become more available and accessible since the previous AMAP assessment of human health in the Arctic (AMAP, 2003), but still relatively little is known.

Contaminant levels in the Arctic, including levels in dietary items of fish, birds, seals and whales, are in most cases lower than in more densely populated and industrialized regions. This geographic difference is especially pronounced for the organochlorines. Nevertheless, based on measured levels in Arctic biota and food samples, and based on studies of total dietary intakes of contaminants, it is apparent that dietary exposure to persistent contaminants and metals in Arctic indigenous communities is higher than in neighboring

non-indigenous communities. The main explanation is that indigenous populations consume tissue from marine top predators that are not normally eaten in other parts of the world. Within the Arctic, there is therefore a higher exposure to contaminants through the diet in coastal dwelling ethnic communities that eat traditional foods such as marine mammals and some bird species, than in inland dwelling communities that eat reindeer/caribou and freshwater fish.

However, for the contaminants investigated the levels in local food sources appear to be decreasing for some compounds in some areas, for example polychlorinated biphenyls (PCBs) and DDT in Arctic Canada and Russia and PCBs in Greenland, whereas mercury (Hg) seems to be increasing in Arctic Canada and northwestern Greenland. The overall picture for chlordanes, toxaphenes, hexachlorohexane (HCH) and Mirex is uncertain; their levels appear to be decreasing in Arctic Canada, while increasing levels have been measured in Greenlandic food items and high levels of β-HCH were found in both animal biota and human plasma in the eastern part of Arctic Russia.

The research findings presented concerning exposure to contaminants through food consumption indicate that food items from marine mammals have the highest contaminant levels. But other marine foods, such as burbot (*Lota lota*), Greenland shark (*Somniosus microcephalus*) and liver from Greenland halibut (*Reinhardtius hippoglossoides*), and birds such as marine gulls and fulmars (including their eggs) also have relatively high levels of contaminants. Thus, further research and monitoring is needed for these species and for others with a similar role in the food chain. However, the levels of contaminants in the biota vary to a large extent within and between populations and within and between areas of the circumpolar Arctic. Exposure also depends on the amount of local foods consumed.

3.1. Diet

This section provides an overview of the importance of and factors guiding traditional food consumption in the Arctic, dietary surveys, and the implications associated with a diet shifting from traditional food to imported food among those living in the circumpolar region. Information about food and dietary interventions is provided in Chapter 9.

3.1.1. The role of traditional foods in well-being

In general, indigenous peoples living in the Arctic tend to take a holistic view of health and well-being. Definitions of health among those living there, however, are very different. This section does not provide a detailed discussion of the different definitions of health held by those living in the Arctic. The brief overview that follows is only intended to provide the reader with a general understanding of the important role of traditional food.

Indigenous peoples have stated that traditional foods provide the following health benefits (Watt-Cloutier, 2000; Van Oostdam et al., 2005):

- Traditional food is a cultural anchor and its use is often important to the identity of indigenous peoples.
- The sharing of traditional food plays a role in the maintenance of social norms and expectations.
- Given the high cost of living in most Arctic communities, traditional food saves many families money.
- There are important spiritual aspects associated with traditional food use.
- Traditional foods provide substantial nutritional benefits.
- There are many physical health benefits associated with harvesting traditional food.

Health benefits associated with harvesting traditional food play an important role in the overall health and well-being of indigenous peoples. Nevertheless, there are many other factors that influence the health and well-being of indigenous peoples that also need to be considered, such as the influence of Western culture and to varying extents development projects such as mining, oil and gas activities, and fishing. In many cases, communities are also shifting away from a traditional diet toward a diet of imported food.

3.1.2. Factors influencing the choice of traditional and store-bought foods

The bioaccumulation of environmental contaminants in species used as traditional food and the lack of affordable, accessible, and culturally acceptable substitutes for traditional food in many Arctic regions raise issues that transcend the traditional confines of the public health field and cannot be resolved by dietary advice or food substitution alone. Food choice studies are considered necessary to formulate culturally appropriate dietary advice. Food choice studies can also highlight potential avenues for public health intervention to maximize the benefits and minimize the risks associated with a traditional diet (Sparks and Shepherd, 1994; Furst et al., 1996; Jack et al., 1998; Furgal et al., 2003; Donaldson et al., 2006).

A number of food choice studies have been conducted in the circumpolar region. Curtis and Pars (2006) combined qualitative and quantitative methods to explore the reasons why Greenlanders eat traditional food. These studies found that access followed by variation, taste, and health influenced decisions to eat traditional Greenlandic food. In Arctic Canada, three key food-choice studies have been completed. The first study (Kuhnlein et al., 2003) explored the factors that influence food choices among women and children in three Dene and Métis communities (Fort McPherson, Tulita, Fort Resolution) and two Yukon First Nations communities (Old Crow, Carcross). The study found that the most important factors influencing family

food choices were costs associated with imported food and availability of traditional food. The second study (Furgal et al., 2001, 2003) found that food choices in Nunavik and Labrador were influenced by the perceived ease or difficulty of obtaining traditional food, beliefs about the consequences of eating traditional food, and personal values. The third study (Donaldson et al., 2006) found that the most influential determinants of traditional food consumption among Inuit living in Cape Dorset, Nunavut (Canada) were accessibility, personal preferences, and personal values. Results on intention to consume imported food show that the most influential determinants are: accessibility, convenience, and personal values.

Concerning the influence of environmental factors on food choice in the Arctic, many analyses have shown that respondents living in Greenland were aware of environmental contaminants in traditional food (Curtis and Pars, 2006), but that this awareness did not seem to have any great influence on intentions toward choice of food because the positive perception of traditional food seems to outweigh the possible health impacts.

Furgal and co-workers found that contaminants are not a significant factor when making choices about traditional food in Nunavik and sub-Arctic Labrador. However, in parts of the western Arctic, contaminants may influence decisions to eat traditional food. Kuhnlein et al. (2003) found that more than 40% of women gave 'concern for contaminants' as a reason for why they did not serve traditional food more often. Furthermore, the study by Donaldson and co-workers found that environmental contaminants are not a direct factor influencing food choice. However, they found that environmental contaminants indirectly influenced the participants' food choices. Inuit and their ancestors have made extensive observations of Arctic biota for thousands of years. All the hunters that raised concerns about the safety of the Arctic food chain relied on Inuit knowledge to assess whether an animal is safe for human consumption. If a hunter assesses an animal and it is considered to be contaminated, it is not eaten:

> *"We can tell if an animal is sick from pollution. Usually there are green spots on the liver. Also, sometimes, there are patches of hair missing from their coat. When I find an animal that is sick I leave it on the land or I take it to the Hunters and Trappers Association. We do not eat these animals. We make decisions like this on a case-by-case basis. Each animal is inspected."* (Donaldson, S., pers. comm., 2009).

As suggested by this narrative, hunters are confident in their own knowledge about whether traditional food is safe to consume. For this reason, it is important to consider their observations and knowledge of animal health, especially when communicating about contaminants. If a hunter suspects that an animal is contaminated, based on smell, taste, coloration, or texture, it is typically discarded on the land or taken to the Hunters and Trappers Association for testing. Thus, an increase in discards influences access to traditional food as there is less available in the community to be shared per unit hunter.

The direct and indirect influences of contaminants on traditional food choice raise concerns because of the known nutritional (Kuhnlein and Dickson, 2001; Kuhnlein et al., 2001, 2004), social, economic, and cultural benefits of traditional food use (Wenzel, 1995; Collings et al., 1998; Donaldson et al., 2003, 2006; Sparks and Shepherd, 1994; Van Oostdam et al., 2005).

The results of food choice research in the Arctic highlight that access is a primary determinant of traditional food and imported food choice. To date, research suggests that food access is strongly associated with its availability within the participants' social network and the extent to which it is shared. In these cases individual dietary intakes commonly reflect the type of food chosen by other people in their social network.

Because the majority of people living in the Arctic have limited financial resources and their food choices largely depend on the type of foods that they have access to, health promotion strategies that seek to reduce exposure to environmental contaminants by focusing on changing people (i.e., changing beliefs, knowledge, habits) stand little chance of success. Rather, strategies that focus on changing the availability of food choices stand the best chance of success. As Furgal et al. (2003) stated 'the provision of health information alone would have little chance in changing behavior if this traditional/wild food was available for free through sharing networks or other sources in the community (i.e., people do not choose their food solely on the basis of their value to health)'. The likelihood of successfully reducing exposure to environmental contaminants from a traditional diet would be significantly increased if culturally-acceptable dietary alternatives were made available at the same time that dietary advice was provided.

Food choice research has tended to be limited to Arctic Canada. Additional research is required on this topic in other circumpolar regions. Such data are important to the development of dietary advice about environmental contaminants in traditional food and to make improvements to overall diet.

3.1.3. **Dietary surveys in Arctic populations**

This review describes dietary studies which have been carried out in the circumpolar region since 2002 and references earlier studies when appropriate to add context.

3.1.3.1. **Alaska**

The Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study assessed the genetic and environmental, including dietary, contribution to cardiovascular disease among Alaska indigenous people living in seven Norton Sound communities. The diet of 850 adult Iñupiat (age 17 to 92 years) was assessed using a

quantitative food frequency questionnaire (Howard et al., 2005). Traditional foods were found to contribute 15% of the dietary energy and to contribute disproportionately more protein, total fat, monounsaturated fat, polyunsaturated fat, n-3 fatty acids, vitamin B12, and iron. Younger adults consumed even less traditional food (10% to 13% energy) and still obtained 16% to 64% of these same nutrients from traditional food. However, the younger age groups had lower intakes of all nutrients. Seal oil and salmon were shown to be the main sources of n-3 fatty acids for all groups. Some trends were observed regarding age, for example the proportion of fat increased and the proportion of carbohydrate intake decreased with age increase (Nobmann et al., 2005).

A detailed cross-sectional study, called the Alaska Traditional Diet Project (ATDP), was carried out in 13 rural communities of Alaskan indigenous people in three different ecological zones. The objective of the project was to identify types and amounts of traditional and imported store-bought foods as a first step in evaluating potential exposure to contaminants (Ballew et al., 2006). In 2002, 665 participants aged 13 years and above participated in a one-year recall food frequency and portion size questionnaire. A detailed list of traditional food and imported food intake is presented. In four of the five study regions, traditional food accounted for approximately 20% of total energy intake. In all regions, traditional food intake explained at least 40% of the protein consumed, 75% of the vitamin B12 consumed, and 90% of the n-3 fatty acids consumed. In four out of five regions, traditional food accounted for 40% of the vitamin A in the diet (Ballew et al., 2006). Fiber and calcium intakes were below recommended levels. Folate, iron, and n-3 fatty acids were reported as below the Estimated Average Requirement (EAR) for less than 40%, 36% and 20% respectively, of the population. The authors compared their results with all past studies involving Alaskan indigenous peoples between 1962 and 2003. They described the synopsis as being that a considerable amount of variation between region and season has been reported. Their study confirmed the trend of increasing imported food and sugared beverages with time.

The Center for Alaska Native Health Research (CANHR) was established in 2001 to address the increasing health disparities observed between Alaskan indigenous and non-indigenous populations. The center supports interdisciplinary research investigating genetic, nutritional, and behavioral risk factors for chronic disease among Alaskan indigenous people (Boyer et al., 2005). Seven rural communities in the Yukon Kuskokwim River Delta participated in a dietary survey. Twenty-four hour recalls and three-day food records were collected from 548 Yup'ik Inuit (age 14 to 95 years) to assess the nutritional and health benefits of traditional foods (Bersamin et al., 2007). Overall, the study found that participants consumed a mixed diet including traditional food and imported food. Traditional food comprised 22% of total energy (range 7.1% to 43%), which was reported to be consistent with other studies from the same area (Heller, 1967; Nobmann et al., 2005). The study also reported that the older age groups surveyed, as well as the rural groups, had a significantly higher intake of traditional food than the younger age groups or urban dwelling groups. Although individual species were not mentioned, 90% of traditional food intake was made up of fish and roe, animal fat, game meat, and game fowl. Around 69% of traditional food energy intake was from marine sources (fish and seal oil) (Bersamin et al., 2007).

3.1.3.2. **Canada**

A study completed in 2000 and 2001 surveyed children from five communities including Fort McPherson, Tulita, and Fort Resolution in the Northwest Territories and Old Crow and Carcross in Yukon Territory. Two publications have come out of this study detailing traditional food and imported food use and extent (Nakano et al., 2005a) and anthropometrics and nutrient intakes (Nakano et al., 2005b). Height and weight measurements as well as 24-hour recalls were used to collect the data. Of the traditional food consumed, 86% comprised land animals, 11% fish, 2% birds, and 1% berries. Twenty-eight traditional foods were reported, although caribou (*Rangifer tarandus*), moose (*Alces alces*) and whitefish (*Coregonus* spp.) made up 95% of the energy intake from traditional food. In children 10 to 12 years of age, traditional food contributed 4.3% to 4.7% to total energy (Nakano et al., 2005a). On days when children consumed traditional food, they had a higher intake of protein, iron, zinc, copper, magnesium, phosphorus, potassium, riboflavin, and vitamins E and B6 than on days when they did not. Children from the northern communities consumed more traditional food and had a lower intake of fat, saturated fat, and sodium (Nakano et al., 2005a). The children were deemed to be probably adequate in their intake of vitamins B6 and C, riboflavin, zinc, iron, copper, selenium, manganese, carbohydrate, and protein; and probably inadequate in their intake of vitamins A, D, and E, phosphorus, magnesium, calcium, n-6 fatty acids, and n-3 fatty acids. A similar study measured energy intake in Dene-Métis adults in 1997. Traditional food contributed 11.4% to 29.9% energy in women and from 16.0% to 28.5% in men (Receveur et al., 1997).

The most comprehensive survey conducted in Canada to study the traditional food intake and body burden of contaminants among women of child-bearing age is the Monitoring Temporal Trends of Human Environmental Contaminants Study in Northwest Territories, known locally as the Monitoring our Mothers study (MOMs). MOMs was undertaken in the Inuvik region, which is located in the Mackenzie Delta, from September 2003 to July 2006. The surrounding communities, served by the Inuvik Hospital, comprise Inuvialuit, Gwich'in, Métis, and Dene people as well as non-indigenous individuals. The study involved recruiting pregnant women, and then collecting maternal blood samples, hair samples, and information on lifestyle and diet. The project had three main objectives: (1) to establish the trend for environmental contaminants in blood and hair of women

Table 3·1. A comparison of the participation and demographic characteristics of the Inuvik Regional Human Contaminants Monitoring Program (the Baseline Study) conducted 1997 to 2000 and the Monitoring Our Mothers Study (MOMs) conducted in 2003 to 2006. Source: Baseline study (Butler Walker et al., 2003, 2006) and MOMs study (Armstrong et al., 2007).

	Baseline study	MOMs study
Total participants	104	86
Surveys completed	104	79
Blood samples (maternal)	95	83
Blood samples (cord)	90	0
Hair samples	73	79
Age (mean years, (min – max))	25.9 (15 – 45)	25.9 (16 – 40)
Inuvialuit	33 (32%)	54 (68%)
Dene/Métis	46 (44%)	18 (23%)
Other/non-indigenous	25 (24%)	7 (9%)
Current smokers	54 (52%)	53 (67%)
First-time mothers	35 (34%)	28 (35%)
Parity >1, mothers who previously breastfed	54 (78%)	41 (80%)

living in the Inuvik region; (2) to evaluate maternal exposure to contaminants from diet and selected lifestyle factors; and (3) to contribute to international blood monitoring programs, including the Global Monitoring Plan under the Stockholm Convention.

The methodology used was similar to that of a baseline study conducted between 1997 and 2000 known as the Inuvik Regional Human Contaminants Monitoring Program (Butler Walker et al., 2003, 2006). This study also involved recruiting pregnant women and collecting maternal and umbilical cord blood samples, hair samples, and information on lifestyle and diet. Participation and demographic characteristics of the two studies are shown in Table 3.1. The objective of the study was to establish baseline data for specific heavy metals and organochlorines in the blood of women and their newborns from communities in the Inuvik region. Women in both studies were asked to rate themselves as high, medium, or low consumers of traditional foods. The results are presented in section 3.1.4.

3.1.3.3. **Greenland**

A cross-sectional dietary study took place among the Inuit of Greenland in 2004 in Uummannaq in the north and in 2006 in Narsaq in the south. Thirty members of each community participated in the study which included blood samples, semi-quantitative food frequency questionnaires, and nutrient analyses of meals from three days using the duplicate portion method. Results were compared to data collected in Uummannaq in 1976. Top consumed traditional food in both communities included seal meat and blubber, dried narwhal (*Monodon monoceros*) meat, narwhal or minke whale (*Balaenoptera acutorostrata*) skin (known as *muktuk*), Greenland halibut, catfish, capelin (*Mallotus villosus*), and Greenland cod (*Gadus ogac*); and also in Narsaq, Arctic char (*Salvelinus alpinus*), and reindeer (*Rangifer tarandus*) (Deutch et al., 2007b). The proportion of traditional food in Narsaq was 10.8% by weight and 9.4% of total energy. The figures for Uummannaq were 22.9% by weight and 13.4% of total energy. In a comparable study carried out in the same district in 1976, traditional food constituted 59% of consumption by weight and 41% of total energy. Meal nutrient analysis, using all three data collections, revealed that those with a low traditional food : imported food ratio had lower micronutrient contents than those with a high ratio (Deutch et al., 2007b).

A study investigating factors contributing to overweight was carried out in 1999, 2000 and 2003 in five Inuit communities (Deutch et al., 2005). The communities included Ittoqqortoormiit and Tasiilaq in the east and Uummannaq, Qaanaaq, and the town of Sisimiut in the west. A cross-sectional study design with 410 participants was used to test whether the nutritional transition was the cause of overweight in Greenland. Food frequency and lifestyle questionnaires and blood samples were used to collect data. Thirty-five traditional food items were on the questionnaire and marine mammals and fish were popular items consumed. Traditional foods made up 21% of total energy. The authors found no significant link between traditional food or imported food consumption and Body Mass Index, but rather with increasing age and economic status. The n-3 : n-6 fatty-acid ratio was found to be 2- to 3-fold higher than in the Danish population. Compared to a former study in Greenland (Bjerregaard, 1995), the prevalence of obesity had increased 5- to 6-fold in less than 10 years in two of the communities (Deutch et al., 2005).

A cross-regional study using qualitative and quantitative data collection was carried out in Nuuk and Denmark (Rejnmark et al., 2004). The study aimed to compare the effects of latitude, season, diet, and ethnicity on vitamin-D status, plasma para-thyroidhormone (PTH) levels, and bone turnover. Data were collected from 145 Inuit from Nuuk and 43 Danes in the form of a three-month dietary recall interview and blood samples. The authors found that a diet high in traditional food and particularly the summer season was associated with higher vitamin-D plasma levels. The study also found that Inuit from Greenland had lower plasma PTH and calcium levels compared to ethnic Danes (Rejnmark et al., 2004).

3.1.3.4. **The Nordic countries**

Brox and co-workers (2003) compared youths (13 to 14 years) from a coastal Norwegian community (Hammerfest) with an inland, mostly Sámi, community (Kautokeino) for hemoglobin, iron, nutrition, and traditional food intake. Data collection tools included blood samples, anthropometrics, food-frequency and lifestyle questionnaires, and a three-day food registration. Regional traditional food previously reported in the area included saltwater fish on the coast and reindeer meat. The study found that fish is now

rarely eaten by youth, but traditional meat is consumed at a greater rate in the inland Sámi community. The authors concluded that the traditional diet has been maintained in the inland community to a certain extent and that it contributes to nutrient intake. The study indicates that fish consumption in the adult community is much higher than in the youth population with 55% of adults in the coastal community and 38% in the inland community consuming fish on a regular basis.

Another study reconstructed diet data for 24 Sámi and Norwegian municipalities in Norway (Brustad et al., 2008a). A cross-sectional cluster analysis was carried out on 3024 Sámi and 4590 Norwegian participants in order to investigate traditional food dietary patterns during childhood and by ethnicity. Food-frequency and lifestyle questionnaires were used to collect data in 2003 and 2004. Diets were classified as dominant in imported food, traditional food, or mixed. Traditional foods reported by the study include fish and roe, reindeer, blood products, mutton, wild berries and wild plants. Significant differences were found in diet composition according to ethnicity. Inland Sámi consumed diets consisting of reindeer and blood products or ate a modern diet. Coastal Sámi had a diet consisting of fish and mutton or imported fish. Inland Norwegians mostly consumed imported food and coastal Norwegians had a diet containing an equal mix of fish, imported fish, and imported food. For information on other dietary studies see Trondsen et al. (2004) and Arkkola et al. (2008).

3.1.3.5. **Russian Federation**

In Russia, the vast majority of indigenous peoples of the north are taiga and tundra nomadic or semi-settled hunters and fishermen. Thus, few groups obtain their traditional food from the ocean (this occurs mainly in the northeast) (Kozlov et al., 2007), which also means that the general exposure to contaminants in Arctic Russia is different to that in coastal populations of Greenland and Arctic Canada. Kozlov et al. (2007) provided a thorough overview of dietary studies in indigenous populations in the north of Russia.

Sorensen et al. (2005) carried out a cross-sectional study in 2001 among Sakha or Jakut peoples in Siberia. Two hundred and one people from six communities including Dikimdye, Asyma, and Berdygestiakh (rural) and Khorobut, Maia and Nižny Bestakh (mixed urban/rural) participated. Cardio-vascular disease is the main cause of death among the Jakut, and the aim of the study was to investigate the diet and lifestyle determinants of plasma lipids in the Jakut. Traditionally, the Jakut herded cattle and horses and hunted and fished. Reindeer herding also took place in the extreme north. After the collapse of the Soviet Union, the Jakut returned to a traditional subsistence lifestyle due to a lack of jobs and money. Three dietary patterns were found, characterized by dominance in traditional food or imported food or mixed, and people in rural areas ate more traditional food. The traditional foods included cattle, horse, reindeer, milk products, berries, and mushrooms.

In 2001/02, Dudarev and co-workers collected information through interviews about diet and food consumption in the Chukotka Peninsula (unpublished). The main food sources of coastal Chukchi and Inuit (256 individuals) were marine mammals (~100 kg wet weight/capita/year) and fish (~70 kg), mainly polar cod (*Boreogadus saida*), smelt and salmon, while reindeer meat (~70 kg) and fish (~90 kg) were the main foods among inland Chukchi (208 individuals residing on the bank of the river Kanchalan). The coastal groups consumed more birds and wild plants, while the consumption of berries was higher in the inland groups. The relative consumption of the different traditional foods varied with season. Store-bought food constituted a smaller proportion of the total food consumed than traditional foods. The main imported foods in the diet were macaroni (~14 kg), grains (~10 kg), and sugar (~11 kg). Further details are provided in Figure 3.1.

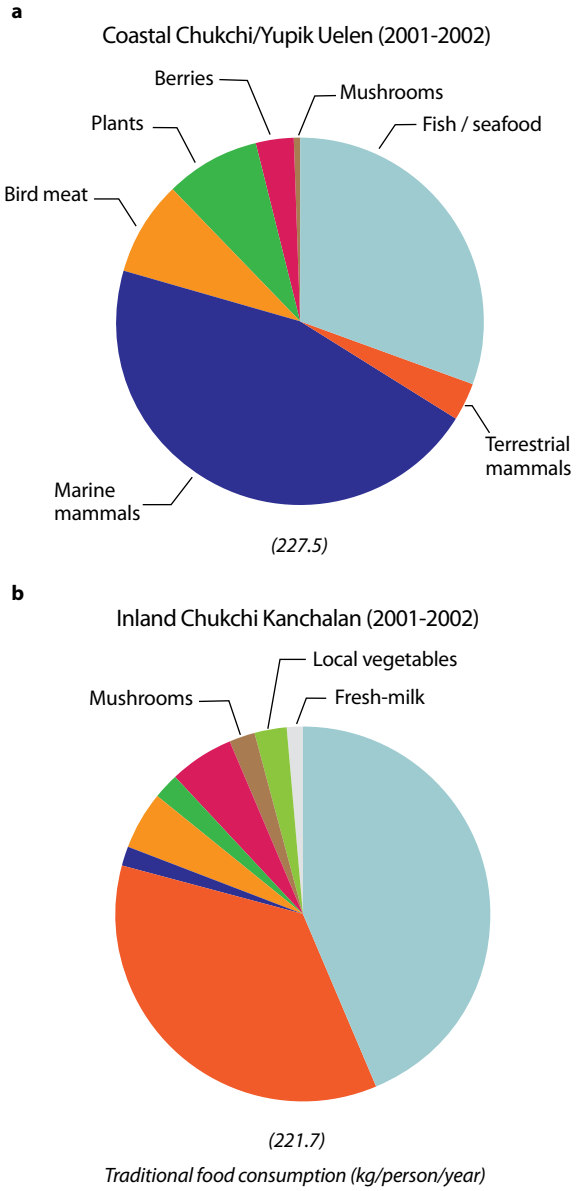


Figure 3·1. Annual consumption of traditional food in (a) Uelen (coastal Chukchi and Inuit) and (b) Kanchalan (inland Chukchi), on the Chukotka Peninsula, north-east Russia. Diagram provided by A. Dudarev (unpublished).

Table 3·2. Traditional food consumption (kg/person/year) (mean, standardized) [minimum, median, maximum] of the Inuvialuit and Dene/Métis in the Inuvik Regional Human Contaminants Monitoring Program (the Baseline Study) conducted 1997 to 2000 and the Monitoring Our Mothers Study (MOMs) conducted in 2003 to 2006. Source: Baseline study (Butler Walker et al., 2003, 2006) and MOMs study (Armstrong et al., 2007).

	Inuvialuit		Dene/Métis	
Food	Baseline, n = 33	MOMs, n = 54	Baseline, n = 45	MOMs, n = 18
All fish / seafood	8.0 (8.1) [0, 6.1, 35.8]	27.1 (34.8) [0, 16.9, 225.0]	9.4 (12.2) [0.2, 4.3, 50.4]	21.3 (31.6) [0, 5.9, 01.3]
Land mammal meat	30.1 (22.4) [0.3, 29.8, 74.5]	34.2 (24.5) [0, 35.1, 113.9]	30.9 (28.3) [0, 16.6, 94.9]	26.8 (31.6) [1.4,17.0, 75.2]
Marine mammal meat	1.4 (4.9) [0, 0, 28.3]	5.2 (18.1) [0, 0, 114.4]	0.0 (0.1) [0, 0, 0.7]	1.1 (0.2) [0, 0, 0.7]
Marine mammal fat	4.3 (10.0) [0, 1.2, 50.4]	1.4 (2.4) [0, 0, 13.5]	0.2 (0.4) [0, 0, 1.2]	1.1 (0.3) [0, 0, 1.2]
Bird meat	3.5 (2.9) [0, 0, 10.8]	14.9 (24.5) [0, 4.7, 106.7]	7.9 (14.8) [0, 3.0, 84.3]	8.1 (21.3) [0, 2.4, 92.4]
All plant	4.0 (6.1) [0, 0, 30.5]	1.9 (2.5) [0, 0, 10.0]	3.8 (4.4) [0, 2.0, 18.1]	2.1 (2.2) [0,1.8, 7.2]

To determine the extent of traditional food use in the Chukotka Peninsula, 1461 indigenous Chukchi and Yup'ik took part in a study in 2000 and 2002 (Kozlov, 2004). Kozlov used interviews with hunters, food and lifestyle questionnaires, and reviewed government data. The overall consumption of traditional food increased and imported food decreased between 1985 and 2000, probably due to an out-migration of non-indigenous people from the area and a food crisis due to the major societal change in Russia. Compared to 1985, consumption of marine mammals increased. Overall meat intake from traditional food increased from 55% to 89%. Furthermore, 76% of those under 30 years of age expressed a preference for a traditional food diet, compared to 66% of those over 30 years of age (who grew up during the Soviet period).

3.1.4. **Changes in dietary habits**

As in other circumpolar regions, the contemporary Alaska indigenous diet is one of mixed traditional and imported foods and there are notable differences in the reliance upon traditional foods by region (Hamrick and Smith, 2004; Risica et al., 2005; Bersamin et al., 2006, 2008). For the Bering Straits region, the indigenous diet had higher amounts of protein intake (partially attributed to traditional food intake) compared to southern U.S. populations (Risica et al., 2005). However, large variations in study methodology, including geographic region covered and sample characteristics, preclude direct a comparison of results between the studies. Nevertheless, the studies did provide evidence that traditional food intake has declined since pre-contact times and that 'westernization' has precipitated major changes in food sources and the intake of many nutrients among Alaskan indigenous people. Studies of age as a factor consistently found differences in common food sources by age. Traditional food sources comprised a greater proportion of the diet of elders than youth. The CANHR study found that traditional foods accounted for 22% of energy intake overall. This varied by age, educational attainment, and geographic location (Bersamin et al., 2007).

In comparison with communities in eastern Russia (Kamchatka and Chukotka), indigenous people residing in western Alaska, including the Aleutian Islands, had a greater reliance upon traditional food and a greater percentage of their dietary protein from traditional food sources than their Russian counterparts (Hamrick and Smith, 2004). However, in Yup'ik Inuit surveyed in three remote Alaskan villages, the predominant source of energy was from imported food sources, and the quality of the diet was considered to be poor for 63% of Yup'ik Inuit surveyed based upon the Healthy Eating Index, and based upon imported and traditional nutrient intake obtained from 24-hour recalls (Bersamin et al., 2006).

In the MOMs study in Inuvik (Canada) the level of traditional-food consumption was calculated for the two ethnic groups (Inuvialuit and Dene-Métis) in order to compare with the baseline study. In such a comparison, it is important to consider the distinctions between eating habits of the groups, because Inuvik is a region representing different ethnic, historical, and cultural backgrounds. In addition, climatic conditions and traditional food diets vary throughout the region. Overall categories of traditional-food consumption for the Inuvialuit and Dene-Métis are shown in Table 3.2. Women in the MOMs study reported higher consumption of traditional foods compared to women in the baseline study six years earlier. The findings are presented in Figure 3.2. It must be noted however, that the differences in communities surveyed and the distribution of ethnicities may contribute to the differences in reporting. In their interviews, the women confirmed that elders and family members had indeed shared with them the importance of eating traditional food, especially during their pregnancy. From the baseline study to the MOMs study, respondents reported increasing their traditional-food consumption, although the amount and type varied considerably by community and population. For the Dene-Métis, the

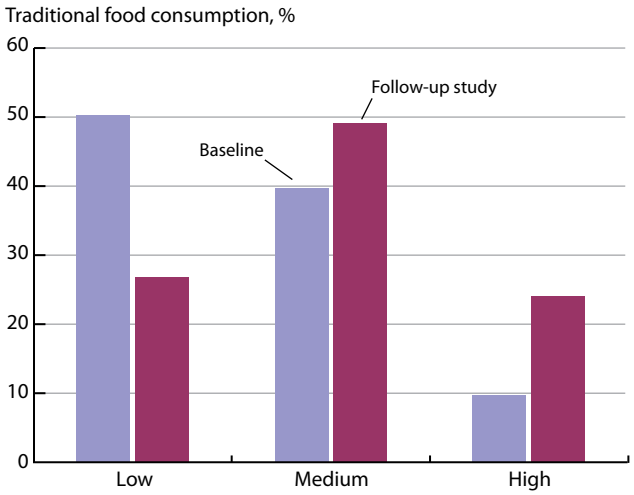


Figure 3-2. Self-reported level of traditional food consumption (low, medium, and high). Comparison between baseline (1998/1999) and MOMs study (2005/2006).

amount of traditional food use in 2006 was similar to that of 2000, except for the amount of fish consumed, which had doubled. The increase in fish consumption was up to three-fold higher among the Inuvialuit. The Inuvialuit also reported eating more seal meat, but the consumption of marine mammal fat (particularly beluga, *Delphinapterus leucas*) decreased by a factor of three (Butler Walker et al., 2003, 2006). This decrease could be a positive reflection of the message communicated by health professionals, which suggested decreasing intake because contaminants often build up in fat. The positive message of traditional-food consumption should continue throughout the communities.

For adults in general, much variability was noted in the percentage of energy from traditional food within each of the three territories in Canada and average consumption ranged from less than 10% to greater than 30% in Yukon communities, from 6% to over 30% in Dene-Métis communities, and from 12% to as high as over 40% in Inuit communities (Kuhnlein et al., 2005). In the Inuit in Canada, the highest proportion of local fish and meat consumption appears to be in Nunavik and Baffin (Statistics Canada 2001; Egeland et al., 2004). Differences in traditional food consumption have also been noted by age within the same regions and communities, with younger generations consuming less traditional food than older adults (Egeland et al., 2004; Kuhnlein et al., 2004). The implications for human health can be substantial if nutrients associated with traditional food are not replaced by nutrient-rich imported food sources.

In a study from Greenland comparing countrywide dietary surveys from the period 1999 to 2006 with dietary studies from 1945 to 1987 (Deutch et al., 2007b), it was found that the proportion of traditional food had already decreased in the larger towns (Illulissat and Qaqortoq) by 1950 whereas the proportion of traditional food in the villages remained high until the late 1970s. Among the adult population, the present country average of the traditional food ratio ranged from 11% in the south to 22% in the north. Thorough reviews of the changes in dietary habits that have taken place in Greenland and in indigenous populations in northern Russia have been published elsewhere (Kozlov et al., 2007; Hansen et al., 2008).

3.1.5. Health implications associated with changes in dietary habits

A decrease in traditional food in the diet may have negative health consequences through the corresponding changes in nutritional quality of the diets and food gathering and eating patterns. Lifestyle changes influence the prevalence and extent of obesity and the health consequences may have been manifested through an increased occurrence of diabetes, cardiovascular disease and other illnesses. Concerns in terms of obesity and an overview of the disease situation are provided in Chapter 8.

3.1.6. Summary

Traditional food use is culturally specific and varies widely over the many communities and regions in the Arctic. Its diversity depends on many factors. Game meat and fat, fish, marine mammals, dairy products, and edible plants and berries were consumed in different quantities depending on latitude, proximity to a major center and water, age, and culture. For example, the findings from eight studies in Arctic Canada reporting the contribution of traditional food to total dietary energy ranged from 4.3% to 89% with a median of 17.5%.

Traditional food provides better nutrients despite a low contribution to energy. In almost all studies, traditional food consumption was associated with higher levels of most nutrients in the diet. Studies that compared present intake to past intake found a decline in traditional food use; or a shift to increased fish consumption and decreased marine mammal fat consumption. Furthermore, younger generations consume less traditional food than older generations. The level of nutritional transition is dependent on the ratio of market food to traditional food and the food items consumed.

Decreasing intake of traditional food also increases the risk of obesity, which is associated with increased risk of chronic disease. In general, the evidence supports the increasing rates of overweight and obesity among children and adults in the circumpolar north and adds to the cumulative evidence of a global shift in adiposity with significant health implications. While data suggest that adiposity may not have the same magnitude of association with metabolic syndrome risk factors for Inuit as for Caucasians, adiposity is related to increased insulin resistance among Inuit.

There are still knowledge gaps, and future research is required to study the diet in the Arctic within the context of overall health and well-being, disease

prevention, and health promotion. In particular, additional research is needed on: (1) regionally-specific sources of contaminants in country foods; (2) the relationship between changes in risk of cardiovascular disease and changes in diet among Arctic indigenous populations; and (3) the impacts of climate change on country food safety and availability, and general food security.

3.2. Nutritional value of Arctic diets and the relationship to contaminants

3.2.1. Context

More than a decade ago, it was observed that market foods contributed most of the dietary energy and a higher proportion of nutrients to the diet of the younger rather than the older age groups among Dene, Métis, and Inuit in Canada (Kuhnlein et al., 1996, 2001; Receveur et al., 1997; Berti et al., 1999; Blanchet et al., 2000). Overall, between 60% and 94% of the total energy intake of indigenous populations came from imported food (Kuhnlein et al., 2001), and also among indigenous populations in Arctic Russia the proportion was over 50% (Leonard et al., 1996). The nutrient profiles in Canada were described as adequate for nutrients associated with fish and meat, and less than adequate for nutrients associated with fruit and vegetables (Kuhnlein et al., 2001). The previous AMAP assessment (AMAP, 2003) concluded that traditional foods were the main sources of protein, fat, most minerals, vitamin D and long chain n-3 fatty acids, while imported foods were the main sources of carbohydrate, water-soluble vitamins, vitamin A, and calcium.

Diet composition, and thereby the nutritional value of the diet and its contaminant content and composition, varies with gender, age, educational level, country, region, population, urban/rural, coastal/tundra, season, and origin and source of the food. These factors also influence the nutritional composition of a diet through the proportion of traditional food items it contains, which also tends to vary substantially with season (Kuhnlein et al., 1996; Receveur et al., 1997; Bersamin et al., 2007). The majority (55% to 81%) of Inuit adults in Canada, and an even higher proportion of their households, harvest country food (Statistics Canada 2001), and the estimates of nutrient intake are therefore further challenged and complicated by the wide variety of animal and plant species in the traditional diet (Nobmann et al., 1994; Blanchet et al., 2000; Kuhnlein et al., 2001; Kuhnlein and Receveur 2007). Men tend to consume more traditional foods in their diet than women, and older age groups tend to consume more than the younger (Leonard et al., 1996; Receveur et al., 1997; Blanchet et al., 2000; Egeland et al., 2004); patterns also found in Russia (Kozlov et al., 2007). Diets based on traditional food are usually more nutrient dense because the imported food consumed often has a high sucrose content (Receveur et al., 1997; Berti et al., 1999; Nobmann et al., 2005).

3.2.2. Energy-providing nutrients

Peoples indigenous to the Arctic have reportedly higher basal metabolic rates compared to populations at lower latitudes. This probably reflects an adaptation to the severe climatic living conditions in the Arctic and causes an increased dietary stress on the people. However, this energy demand is believed to be compensated through other somatic functions and not by an elevated need for dietary energy (Snodgrass et al., 2007). Dietary energy intake varies with sex, age group, and activity level, and the relative contribution of each energy-providing nutrient and the magnitude of intake fluctuate from day to day according to food availability and/or choice. That is, in populations where traditional food is not consumed on a daily basis the energy intake tends to be higher on days when such food is included as a food source (Kuhnlein et al., 2004; Kuhnlein and Receveur, 2007), and the proportions of energy from protein and n-3 fatty acids are positively associated with the intake of traditional food, and thereby also with age group and male gender. An association between source and consumption of total fat and saturated fat, however, is uncertain, because the findings have varied (Receveur et al., 1997; Kuhnlein et al., 2004; Nakano et al., 2005a; Risica et al., 2005; Nobmann et al., 2005; Ballew et al., 2006; Bersamin et al., 2007; Deutch et al., 2007a; Kuhnlein and Receveur, 2007; Egeland et al., in press). However, the relative intakes of carbohydrates, including sugar, are higher from imported foods (Kuhnlein et al., 2004; Nobmann et al., 2005; Bersamin et al., 2007; Deutch et al., 2007b; Kuhnlein and Receveur, 2007) and the reported sugar consumption has been high (Table 3.3) (Nobmann and Lanier, 2001; Nobmann et al., 2005; Lapardin et al., 2006; Ballew et al., 2006; Bersamin et al., 2006; Deutch et al., 2007b), especially among youth (Berti et al., 1999; Brox et al., 2003; Kuhnlein and Receveur, 2007). The amounts of dietary cholesterol and trans-fatty acids consumed tend to be proportional to the proportion of energy from saturated fat (Nobmann et al., 2005), and the intake of traditional food (as a percentage of energy) has been found to have an inverse correlation to plasma levels of trans-fat in the Canadian Arctic (Egeland et al., in press). However, in inland Jakutia (Siberia), traditional food consumption was reported to be associated with higher total cholesterol and low density lipoproteins (Sorensen et al., 2005).

As outlined in Table 3.3, the reported dietary caloric intake, and the proportion of energy from fat, protein, and carbohydrates varies between regions and populations. In some populations, the sources of dietary energy are strongly influenced by season, which may not be captured well in a study. Findings in different studies are not readily comparable because different instruments have been used and different segments of the populations have been studied, however these studies provide valuable information about the relative proportions of energy-providing nutrients within each population studied. The dietary recommendations are not identical in all the circumpolar countries, but

Table 3-3. Mean dietary proportion (%) of energy from protein, carbohydrates, fats, and alcohol.

Location	Population	Strata [a]	Energy intake, kcal	Protein	Carbohydrate	Fat	Saturated fat	Sucrose	Alcohol	Source
Alaska										
Bering Strait	Alaska Native	Men	2273	24	41	35	25	-	-	Risica et al., 2005
		Women	1899	22	43	36	44			
Yukon-Kuskok-wim delta	Yup'ik	Age 14 – 19	2460	14	51	37				Bersamin et al., 2006
		Age 20 –39	2586	17	44	39	-	-	-	
Anchorage	Alaska Native	Women	1804	16	52	31	11	-	0.7	Nobmann and Lanier, 2001
Northwest	Eskimo	Men	3100	15	49	37	13	-	-	Nobmann et al., 2005
		Women	2360	14	48	39	12			
Canada										
Dene/Yukon	Children [b]	With TF	2043	16	56	30	11	18	-	Kuhnlein and Receveur, 2007
		Without TF	1993	13	58	31	11	19	-	
Baffin	Inut, 10 – 15 years	Boys	1817	18	55	26	-	11	-	Berti et al., 1999
		Girls	2088	18	51	31		13		
	Inuit, 16 – 18 years	Boys	2490	21	45	33	-	10	-	
		Girls	1841	16	56	29		19		
Yukon and NWT	Inuit, adults	With TF	2170	34	35	30	9	12	-	Kuhnlein and Receveur, 2007
		Without TF	1857	18	47	36	12	17		
	Dene/Métis, adults	With TF	2261	31	35	34	12	9	-	
		Without TF	2058	20	41	39	14	12		
	Yukon, adults	With TF	2052	31	37	32	11	9	-	
		Without TF	1947	19	41	40	14	11		
Greenland										
Northwest	Inuit, adults		1583	17	49	35	14	17	-	Deutch et al., 2007b
South	Inuit, adults		1172	15	59	28	12	32	-	
North Sweden	Adults	Male	1800	14	47	37	15	-	1.5	Krachler et al., 2005
		Female	1800	14	49	36	15		0.8	
North Finland	Pregnant women		1710 – 1807 [c]	16 – 18	48 – 51	30 – 36	13 – 16	7 – 9	0.1 – 0.2	Soininen et al., 2005
Russia										
Siberia	Nenets, 14 – 17 years	Boys		16	56	27	-	-	-	Vorobjev, 2005
Siberia and northeast	Yupik and coastal Chukchi	Adults		26	48	26	-	-	-	Litovka, 2001 (from Kozlov et al., 2007)
Northeast	Tundra Chukchi	Adults		14	58	28	-	-	-	
Yamalo-Nenets	Indigenous	Men	2272	20	51	28	-	-	-	Ionova and Aglabyan, 2005 (from Kozlov et al., 2007)
		Women	2177	18	52	29				

- : not studied; [a] With traditional food in the diet (with TF) and without traditional food in the diet (Without TF); [b] on days when traditional food was consumed; [c] estimated values for two different methods.

typically it is recommended that a minimum of 12% of dietary energy should come from protein, less than 30% to 35% from fats, with the remainder from carbohydrates (non-added sugars). Pregnant and lactating women, and children, are usually recommended a higher relative intake of protein. A general weakness of the reported studies is that the energy intakes and the proportions from fat, carbohydrates, and protein tend not to have taken into account alcohol consumption (see Table 3.3). In Greenland, alcohol was estimated to account for 14% of the average overall energy intake; whereas the proportion among men was 19.5% (Deutch et al., 2005). The higher the energy turnover (activity level) the higher the likelihood that the food intake will meet the need for essential micro-nutrients. On the other hand, a high food intake relative to body mass also increases the body burden of food contaminants. The high energy intakes reported for Chukotka (Sandanger et al., 2003) and Alaska suggest that large variations in energy intake in the Arctic are due to differences in lifestyle.

In contrast to non-Arctic populations, the indigenous populations of the north have traditionally had fats and protein as the main source of dietary energy due to their abundance in the local biota. Thus, in these populations there has possibly been a long-term adaption to a diet high in fat and protein, and their blood glucose has been comparatively low (Kozlov et al., 2007; Hansen et al., 2008). According to Kozlov et al. (2007) the relatively recent shift towards high levels of carbohydrates from imported foods might have introduced an imbalance between endogenous and exogenous sugars.

Marine food (especially fatty fish, fish oils, and blubber from marine mammals) is rich in n-3 polyunsaturated fatty acids (eicosapentaenoic acid, EPA; docosapentaenoic acid, DPA; docosahexaenoic acid, DHA) (also called omega-3 fatty acids), which are associated with beneficial health effects (Mozaffarian and Rimm, 2006). Thus, a decrease in traditional-food intake tends to lead to a lower n-3 fatty acid intake (Deutch et al., 2006, 2007a). Humans can metabolize the plant oils linoleic acid (LA) (n-6) and linolenic acid (ALA) (n-3) to EPA and DHA, but because the capacity is very limited EPA and DHA are also needed through the diet. The recommended intake of n-3-fatty acids is uncertain, but in Norway has been set to 1% of caloric intake (0.5% is considered a minimum) (Vitenskapskomiteen for mattrygghet, 2006), while the American Heart Association recommends 1 g of EPA and DHA per day compared to 0.5 g by the International Society for the Study of Fatty Acids and Lipids (Leblanc et al., 2006). Although a decreasing consumption has been observed, the northwestern Greenlandic Inuit consume 3 g of n-3 fatty acids per day on average (Deutch et al., 2006); about twice the amount found in the southern Greenland diet (Deutch et al., 2007b). The average intake was also above 1% of caloric intake among Alaska Natives (Nobmann et al., 2005; Bersamin et al., 2007, 2008), which was substantially higher than in Norway (0.4%) (Vitenskapskomiteen for mattrygghet, 2006) and in pregnant Faroese women (0.5%) (Veyhe, 2006). In Alaska, the intake of n-3 fatty acids was several times higher than 1% in the highest quintiles of traditional food intake (Bersamin et al., 2007) and thereby highest among the elderly (Nobmann et al., 2005). In each of the three major indigenous Arctic cultures in Canada, the median usual intake (LA only) was at least 1.3 g among adults, independent of gender and age group (Kuhnlein et al., 2007). Among Dene-Métis and Yukon children, on the other hand, the intake of both n-3 and n-6 fatty acids was low (Nakano et al., 2005b). In a Norwegian diet, the minimum intake can be reached through non-marine foods (such as plant oils), but to reach the recommended 1% of caloric intake it has been estimated that one meal of fatty fish per week is needed. The CALIPSO report (Leblanc et al., 2006) concluded that two fish meals per week (including fatty fish) provide the recommended intake of n-3 fatty acids.

The optimal dietary ratio between n-6 (LA, AA) and n-3 fatty acids is uncertain. In the early 1990s in Chukotka, the ratio was estimated at about 2 in coastal communities and 3 on the tundra (Nobmann et al., 1994). In Norway, the ratio is considered to be relatively high (Vitenskapskomiteen for mattrygghet, 2006), while in Greenland the highest ratio (~3) was reported in the south where non-local food is the most predominant in the Inuit diet (Deutch et al., 2007a), and the proportion has been increasing (Deutch et al., 2006). In Arctic Canada, the median ratio LA : ALA in the diet was above 3 (Kuhnlein et al., 2007). Monounsaturated fat has been recommended to constitute 10% to 15% and polyunsaturated fat 5% to 10% (including the 1% from n-3 fatty acids) of caloric intake (Vitenskapskomiteen for mattrygghet, 2006). Alaska Natives were within the ranges for both types (Nobmann and Lanier, 2001; Risica et al., 2005; Nobmann et al., 2005; Bersamin et al., 2008), while adult Dene-Métis of the Northwest Territories and Inuit children of Baffin were within the recommended range only for polyunsaturated fat (Receveur et al., 1997; Berti et al., 1999). In general, fatty-acid intake was found to be low among Dene-Métis and Yukon children (Nakano et al., 2005b). Among male Nenets teenagers on the Russian tundra, average intake was within the recommended range for monounsaturated fats, but below the recommended range for polyunsaturated fats (Vorobjev, 2005). The latter was also found for pregnant women in the Faroe Islands (Veyhe, 2006) and Inuit in Greenland (Deutch et al., 2007b). As outlined in Table 3.3, the saturated-fat intake tends to exceed the general recommendation of 10% of energy intake. Additional information about fatty acids and their role is given in Chapter 7.

The level and types of contaminants in traditional diets depend on both the location and the type and local sources of the food. Levels tend to be higher in coastal food systems, such as in marine mammals, rather than in land-based systems, but the foods with the highest levels of toxaphene, chlordane and/or PCB tend to be the foods contributing the most protein and essential n-3 fatty acids (Kuhnlein et al., 2001, Sandanger et al., 2003, Deutch et al., 2006). However, levels of contaminant trace elements and PCBs in different species of fish are

not associated with their n-3 fatty acid content (Leblanc et al., 2006), but there is a positive correlation between marine animal fat, n-3 fatty acids, and lipophilic contaminant intakes at a dietary level (Hoekstra et al., 2005; Deutch et al., 2006).

After ingestion, the distribution of the different lipophilic organic contaminants is in a dynamic equilibrium between body tissues. A change in the lipid content of a tissue therefore changes its content of such contaminants, and a post-meal change in serum lipids affects serum levels of the contaminants (Phillips et al., 1989). However, most of the variation in total lipid concentration in the serum can be explained by the concentrations of cholesterol and triglycerides, independent of sex and age (Rylander et al., 2006). An increasing intake of saturated and trans-fatty acids leads to elevated levels of blood lipids, such as low-density lipoprotein (LDL)-cholesterol, so these fatty acids should not exceed 10% of caloric intake. The mean intake in Dene-Métis, northern Sweden, and Inuit in Alaska and northwestern Greenland exceeded this proportion (Krachler et al., 2005; Risica et al., 2005; Nobmann et al., 2005; Receveur et al., 1997; Deutch et al., 2007b), also among those with a high traditional food use (Receveur et al., 1997; Deutch et al., 2007b). Inuit children and adolescents at Baffin obtained on average 9% of their dietary energy from saturated fat (Berti et al., 1999).

In addition to n-3 fatty acids, fish and seafood provide high-quality protein (i.e., provide essential amino acids) and are a rich source of the free-form amino acid taurin (Laidlaw et al., 1990). Dietary fiber intakes tend to be relatively low in diets high in traditional food (Receveur et al., 1997; Kuhnlein et al., 2004; Bersamin et al., 2007) and low in general (Nobmann and Lanier, 2001; Brox et al., 2003; Nobmann et al., 2005; Soininen et al., 2005; Ballew et al., 2006; Deutch et al., 2007b; Kuhnlein et al., 2007).

3.2.3. **Fat-soluble vitamins**

Fat-soluble vitamins (A, D, E) can be of nutritional concern due either to excessive exposure or to sub-optimal intake.

3.2.3.1. **Vitamin A**

A sub-optimal intake of vitamin A was reported to be prevalent among Canadian Inuit (Kuhnlein et al., 1996; Lawn et al., 1998; Berti et al., 1999; Blanchet et al., 2000) and Dene-Métis (Receveur et al., 1997), and traditional foods were considered to have low concentrations of vitamin A (Blanchet et al., 2000). In a study among Inuit women in Baffin in 1987/88, Kuhnlein et al. (1996) revealed substantial seasonal variation in intake from traditional foods, and the variation was not compensated through the intake of imported food. They found that more than 60% of the population fell below two-thirds of the Recommended Daily Allowance (RDA), independent of gender and age group (Kuhnlein et al., 1996). Average intake was also low among children at Baffin, even though they largely obtained their vitamin A from imported food (Berti et al., 1999). Lawn et al. (1998) reported similar findings among Inuit women.

However, Receveur and Kuhnlein (1998) recommended caution in interpreting the estimated intakes due to possible systematic underestimations in the investigations, and in 2001 Kuhnlein and co-workers reported that increasing use of traditional food could improve vitamin A status among the indigenous peoples in Canada. This was later reported from other studies in Canada (Egeland et al., 2004; Kuhnlein et al., 2004; Ballew et al., 2006), as well as in Greenland (Deutch et al., 2007b) and Alaska (Bersamin et al., 2007). Kuhnlein et al. (2004) found a higher dietary intake of vitamin A on days when traditional food was consumed, while Bersamin et al. (2007) revealed that the total vitamin A activity was positively associated with the proportion of traditional food intake in the diet. Seal liver, meat, and organs have been found to be especially high in vitamin A (Deutch et al., 2007b). In Alaska, traditional food provided 20% of the caloric intake but 40% of the vitamin-A intake, and few rural Alaskans had an intake below recommendations (Ballew et al., 2006). On the other hand, the vitamin-A content of food has also been positively correlated with the content of PCB, DDT and Hg (Deutch et al., 2007a).

Although there was an age trend in intake positively related to consumption of traditional foods among the Inuit, imported food was the main source (69% to 90%) of vitamin A in all the studied Inuit groups in Canada, and the majority younger than age 40 was below the Estimated Average Requirement (EAR). On the other hand, 89% of Inuit males and 85% of females in the age group above 40 had a dietary intake above the EAR for retinol activity (7% of males were above the maximum recommendation) (Egeland et al., 2004). The differences between older and younger Inuit were later confirmed. In Yukon, about the same overall proportion met the EAR, but the gender and age pattern was different (Kuhnlein et al., 2007). In 2005, Nakano and co-workers reported low average intake among Dene-Metís and Yukon children (Nakano et al., 2005b), who obtained more than 90% of their dietary energy through imported food (Nakano et al., 2005a), and low intakes were also found among adults, independent of gender and age (Kuhnlein et al., 2007). In Alaska, the majority of female Natives in urban settlements did not meet the recommendations (Nobmann and Lanier, 2001). The same occurred in the general population in the Faroe Islands and southern Greenland (Veyhe, 2006; Deutch et al., 2007b), and among pregnant women in northern Finland (Soininen et al., 2005). Comparable studies concerning vitamin A in Arctic Russia are lacking, but low intakes have been reported in the general population (Martinčik et al., 2005) and high prevalence of deficiency among industry workers in the north (Bojko et al., 2006). In Norway, fish is not considered an important source of vitamin A (accounting for about 1% of total intake). Instead supplements, such as cod-liver oil, contributed more than 20% of the total intake among adults.

The intake of vitamin A from fish and seafood is

potentially excessive only among people who eat fish liver (30% of the general population and 80% in the Sami-populated areas in northern Norway). However, even if the consumption of fish liver is combined with a daily cod-liver oil supplement, it was concluded that intake does not reach the maximum recommended intake (Vitenskapskomiteen for mattrygghet, 2006). In Greenland, on the other hand, Deutch et al. (2007b) estimated that intakes of vitamin A reported in the past could have been borderline toxic due to traditional food diets. A particular risk group for excessive intake of vitamin A in indigenous populations is pregnant women who consume liver on a frequent basis (e.g., from caribou and seals). However, the median retinol content in market-bought liver is comparable (Egeland et al., 2004). The effects of high and low intake of vitamin A might also be magnified by alcohol abuse (Whitby et al., 1994), which is prevalent in northern communities (Deutch et al., 2005; Kozlov et al., 2007). Alcohol binging and poor nutritional habits tend to go hand in hand.

3.2.3.2. **Vitamin D**

Vitamin-D deficiencies are prevalent worldwide and are of particular concern in the far north as endogenous synthesis is constrained for most of the year due to the limited exposure to sunlight (Schroth et al., 2005). In Canada, vitamin D-deficiency rickets has been persistent among children, and recent findings suggest that the incidence is higher in the north of the country (Ward et al., 2007). To assess vitamin-D status, it is necessary to take both dietary intake and exposure to sunlight into account. The common method is to measure the major metabolite $25(OH)D_3$ because the circulating serum levels are the product of the endogenous and exogenous exposures. Thus, a general optimal dietary intake is difficult to set and as a result national recommendations vary. For example, the Nordic recommended intake levels for people younger than 50 years are higher (7.5 to 10 μg/d) than the U.S. recommendations (5 μg/d). In terms of serum concentrations of $25(OH)D_3$, the levels that are considered optimal and deficient are also controversial. The applied vitamin-D deficiency level has varied from less than 20 nmol/L to less than 80 nmol/L (Huotari and Herzig, 2008). Nevertheless, it is recommended to use biomarkers to assess vitamin-D status.

Dietary intake appears to be equivalently associated with the proportion of traditional food in the diet as vitamin A (Blanchet et al., 2000; Kuhnlein et al., 2004; Bersamin et al., 2007). Fish, liver, and fat from seals and whales are rich in vitamin D, while the only plant food containing small amounts are mushrooms (Huotari and Herzig, 2008). However, the average pregnant woman in the Faroe Islands did not meet the recommendations through diet (Veyhe, 2006), and intake was below adequate in Yukon and among Dene and Métis (except for among young Dene-Metís men) (Kuhnlein et al., 2007). Deficiency is a common finding among adolescent girls and the elderly at northern latitudes (Huotari and Herzig, 2008), and has been reported among Canadian First Nations (Smith, 2000). Among Dene-Metís and Yukon children, more than 50% were found have a very low vitamin-D intake (Nakano et al., 2005b). On the other hand, the nutritional requirements of Inuit women appeared to be met (Blanchet et al., 2000; Kuhnlein et al., 2007). Among young adult Inuit in western Greenland, the mean serum $25(OH)D_3$ level was 32 nmol/L in summer and 29 nmol/L in winter (Rejnmark et al., 2004).

In Finland, milk is fortified with vitamin D, but less so than in Canada – where margarine is also fortified. In Alaska, orange juice, bread, and cereals may also be fortified (Huotari and Herzig, 2008). Vitamin-D deficiency during pregnancy (≤35 nmol/L) has been reported in western Finland and in three populations in northern Manitoba (Schroth et al., 2005). A third of the young population in northern Finland has previously been reported as deficient during winter (Huotari and Herzig, 2008), and the average pregnant woman in the north did not meet the recommendations through diet (10 μg/d) (Soininen et al., 2005). However, fortification of milk in Finland (initiated in 2003) appears to have improved vitamin-D status in the younger segments of the population (Laaksi et al., 2006; Piirainen et al., 2007). In Alaska, intake appears high mainly among those consuming a diet high in traditional foods, including fish (Bersamin et al., 2007).

In Norway, where one third of the average consumption of fish and seafood is fish with high fat content, it was estimated that fish and seafood contributed on average 22% of the dietary content of vitamin D in the 1990s, and that about 5% met their dietary needs from fish and seafood alone. Supplements, such as cod-liver oil, contributed 55% of the average intake. Estimates in Norway indicate that it is necessary to take vitamin-D supplements to meet the recommended daily intake when consumption does not exceed one fish-seafood meal per week (27 g/d). Alternatively, one is dependent on sunlight as a source, which is not feasible for a large part of the year – especially in the north. An average intake of 27 g/d corresponds to the 10-percentile consumption in Norway. Thus, a low intake of vitamin D is of concern in the population in Norway that is at the low end in terms of fish and seafood consumption, even though margarine, butter, and low-fat milk is fortified with vitamin D. In the Sami populated areas in the north, 37% responded that they had fish for dinner at least three times per week. The 90-percentile consumption of 119 g on average per day corresponds to a vitamin-D intake that is one fifth of the maximum recommended intake. The conclusion in the report by the Norwegian Committee for Food Safety was that exceeding the maximum recommended intake of vitamin D is not a concern in Norway, even for people who consume fish liver and supplement with cod-liver oil daily. The health authorities in Norway recommend a daily supplement of cod-liver oil to all infants four weeks and older, but less than 50% of the population met this recommendation in their first year (Vitenskapskomiteen for mattrygghet, 2006).

When ingested in excess amounts, vitamin D accumulates in the adipose tissue, and mega doses

cause clinical symptoms, such as hypercalcemia. Circulating serum levels of over 200 nmol/L have been considered toxic. But, as reported above for Norway, such levels are not reached without the intake of vitamin-D supplements (Huotari and Herzig, 2008). In Greenland, concern about excessive intake has been reported for people consuming seal liver, which was common in the past (Deutch et al., 2007b).

3.2.3.3. **Vitamin E**

Vitamin-E intake has also been reported to be positively associated with traditional food consumption (Kuhnlein et al., 2004; Nakano et al., 2005a; Bersamin et al., 2007; Kuhnlein and Receveur, 2007), and for urban Native Alaskan women of whom the majority consumed only imported food the mean intake was below recommendations (Nobmann and Lanier, 2001). Intake was also found to be low in all major indigenous Arctic cultures in Canada (Kuhnlein et al., 2007), including Dene-Métis and Yukon children (Nakano et al., 2005b), and pregnant women in northern Finland, and just below recommendations in Greenland (Deutch et al., 2007b). In Norway, crab meat has been reported to be a particularly rich source of vitamin E (Vitenskapskomiteen for mattrygghet, 2006).

The associations of fat-soluble vitamins with traditional food consumption make intake and dietary adequacy prone to factors associated with the proportion of traditional food in the diet, such as season, age group, and gender (Kuhnlein et al., 1996).

3.2.4. **Minerals and water-soluble vitamins**

3.2.4.1. **Vitamins B and C**

Vitamins that tend to be of relatively low intake in a traditional food diet are vitamin C (Kuhnlein et al., 2004; Ballew et al., 2006; Bersamin et al., 2007) and folate (Receveur et al., 1997; Lawn et al., 1998; Arbour et al., 2002; Kuhnlein et al., 2004; Ballew et al., 2006; Bersamin et al., 2007; Deutch et al., 2007b). The magnitude and relative proportion of vitamin C and folate intake from market foods might be higher in Arctic America than elsewhere because fortification is common in North America (Kuhnlein et al., 2004). Nevertheless, Alaskan women eating imported food only, had a mean intake of folate below the recommended intake (Nobmann and Lanier, 2001). Among rural Alaskans in general, up to 40% was found to have below the recommended intake of folate (Ballew et al., 2006), and across Arctic Canada the situation appeared to be similar (Kuhnlein et al., 2007). The folate recommendations tend to be twice as high for pregnant women. In northern Finland more than three-quarters of pregnant women had a dietary intake below the recommendations, and only one in six women used folate supplements (Soininen et al., 2005). A large proportion of the indigenous populations in Arctic Canada were also below the EAR for vitamin C, and the proportion was particularly high among older men (Kuhnlein et al., 2007). Low intakes of folate and vitamin C have also been reported for Greenland (Deutch et al., 2007b).

One explanation for the low estimated intakes could be that many local foods have not been analyzed for folate content (Ballew et al., 2006). Furthermore, some food items used in traditional diets contain a non-negligible amount of vitamin C (Fediuk et al., 2002). It is also notable that there have been no recent reports of scurvy or other deficiency symptoms in Greenland (Deutch et al., 2007b). In northern Finland, on the other hand, most pregnant women met the recommendations for vitamin-C intake (Soininen et al., 2005).

The population of pregnant women in northern Finland also met the recommendations for all B-vitamins, except for thiamine (Soininen et al., 2005). Intakes of riboflavin and vitamin B6 in Arctic Canada, which tend to be higher on days when traditional food was consumed (Kuhnlein et al., 2004; Kuhnlein and Receveur, 2007), appear to have met the requirements. Widespread intakes on the low side of the EAR were found only for riboflavin and among the Inuit only (Kuhnlein et al., 2007).

3.2.4.2. **Minerals and vitamin B12**

Non-table-added sodium intakes appear to be related to the proportion of imported food in the diet (Kuhnlein et al., 2004). A sodium intake higher than recommended has been reported for Alaska (Nobmann and Lanier, 2001) and northern Finland (Soininen et al., 2005). Intakes of magnesium, phosphorus, zinc, copper, iron, potassium and manganese, on the other hand, appear positively associated with the intake of traditional foods (Kuhnlein et al., 1996, 2004; Receveur et al., 1997; Wein et al., 1998; Berti et al., 1999; Blanchet et al., 2000; Nakano et al., 2005a; Ballew et al., 2006; Bersamin et al., 2007; Kuhnlein and Receveur, 2007), but the main traditional food sources are the same items that contribute most of the organochlorine contaminants (Kuhnlein et al., 2001; Deutch et al., 2007b). In inland communities in northern Norway, the magnesium, thiamine, and iron intake of the youth was positively associated with meat consumption (Brox et al., 2003). For magnesium, however, the association with traditional-food intake has not been consistent (Blanchet et al., 2000) and reported intakes have been low. In Baffin, where the intake of traditional food was highest among Canadian Inuit (Egeland et al., 2004), 37% had an estimated intake of less than two-thirds of the RDA (Kuhnlein et al., 1996). Low intakes of magnesium have been found in all major indigenous cultures in Arctic Canada (Kuhnlein et al., 2007), including Dene-Métis and Yukon children (Nakano et al., 2005b), and by Alaskan women (Nobmann and Lanier, 2001). Yukon children also had low intakes of phosphorus (Nakano et al., 2005b), which together with copper and zinc intakes, were also very low among teenage male Nenets in the tundra of Russia and Russian girls in the northeast of the Russian Federation (Vorobjev, 2005). On the other hand, in the general population in the Far East of Russia the intake

of copper and zinc is reportedly in accordance with recommendations (Lapardin et al., 2006; Lugovaja and Maksimov, 2007).

Nevertheless, there are concerns about the nutritional mineral status of the Russian population in the north (Kubasov et al., 2007; Gorbačov et al., 2007), and iron deficiency anemia has been increasing in indigenous populations (Kozlov et al., 2007). Alaskan women and Inuit children and adolescents in Baffin had inadequate intakes of iron and zinc (Nobmann and Lanier, 2001; Berti et al., 1999); up to 36% of rural Alaskans had an iron intake below recommendations (Ballew et al., 2006). In northeastern Norway, 16% of the women studied had iron deficiency, four-fold higher than among men (Broderstad et al., 2006); 40% of pregnant women had iron deficiency anemia (Hodgins et al., 1998), which has also been reported from northwestern Russia (Vaktskjold et al., 2004a), and the recommended dietary iron intake was not met by the average pregnant woman in the Faroe Islands and northern Finland (Soininen et al., 2005; Veyhe, 2006). More than one in three infants (6 to 12 months of age) and about 50% of children in the age group 9 to 14 months in Nunavik were anemic (Hodgins et al., 1998; Willows et al., 2000). A relatively high prevalence has also been revealed among children (4 to 18 months old) in Nunavut and northern Ontario, mainly due to iron deficiency (Christofides et al., 2005). Adults in Greenland, on the other hand, had a high intake of iron (Deutch et al., 2007b), which suggests a high intake of food from marine mammals. The intakes of iron, as well as phosphorus, copper, manganese, and zinc appeared to be adequate among adults in the Canadian Arctic (Kuhnlein et al., 2007), and most pregnant women met the recommendations for magnesium, phosphorus, iodine, and potassium in northern Finland (Soininen et al., 2005).

Calcium is a nutrient which has tended to be below the recommended level in a traditional food diet and intake has been prone to seasonal variations. Data from the late 1980s indicate that more than 60% of the Inuit population in Baffin, regardless of gender and age group, fell below two-thirds of the RDA (Kuhnlein et al., 1996). Low intakes were also reported elsewhere among the Inuit (Lawn et al., 1998). Intake was lowest among women and imported food provided several times higher intake than traditional foods, regardless of the seasonal proportion of traditional food in the diet (Kuhnlein et al., 1996). Among Dene-Métis and Nunavik and young Baffin Inuit the pattern was similar, but calcium intake was low even among people with high imported food use (Receveur et al., 1997; Berti et al., 1999; Blanchet et al., 2000).

However, Receveur and Kuhnlein (1998) expressed concern about possible systematic underestimations in the conducted investigations (Receveur and Kuhnlein, 1998), such as methodological insufficiency to measure the contribution of calcium from bone and bone marrow in the traditional food diet (Blanchet et al., 2000) and local foods that have not been analyzed for calcium content (Ballew et al., 2006). Nevertheless, recent studies have also found that the estimated calcium intake was highest in the groups with the lowest proportion of traditional food in their diet (Ballew et al., 2006) and lower on days when such food was consumed (Kuhnlein et al., 2004), and that the overall intake is low in most of the Arctic (Nobmann and Lanier, 2001; Nobmann et al., 2005; Ogloblin et al., 2005; Ballew et al., 2006; Korčina, 2006; Lugovaja and Maksimov, 2007; Gorbačov et al., 2007; Kubasov et al., 2007; Deutch et al., 2007b; Kuhnlein et al., 2007). For teenage male Nenets living in the tundra the intake was estimated to be about two-thirds of the Russian recommendations for the age group (Vorobjev, 2005). In the Faroe Islands and northern Finland, where the diet consists mainly of store-bought food, calcium requirements appeared to be met by the average pregnant woman (Soininen et al., 2005; Veyhe, 2006).

Traditional foods are excellent sources of a number of nutrients, but are not appropriately classified into the Healthy Eating Index (HEI) food groups. As an example, the milk group was designed in part to measure calcium. An important source of calcium among Yup'ik in Alaska is fish, which does not contribute to the milk score. Despite the insensitivity of the HEI to measure the contribution of traditional foods to diet quality, low scores among the majority of participants indicated that there is cause for concern (Bersamin et al., 2006). On the other hand, the recommendations might overestimate the dietary intake needed in indigenous populations because of a possible genetic adaptation to dietary constraints. This may predispose to nephrolithiasis or nephrocalcinosis if standard nutritional guidelines are followed (Sellers et al., 2003).

Iodine deficiency is widespread globally; especially in areas where table salt is not fortified (de Benoist et al., 2003). Such deficiency and thyroid disorders have been prevalent in northern populations of Russia (Christoforova, 2004; Sibileva, 2004; Korčina, 2006; Kubasov et al., 2007; Gorbačov et al., 2007). The content of iodine is high in marine animals, and so the traditional Greenlandic diet was assumed to provide an intake more than ten times the minimum recommended level (Hansen, 2000) and almost 40 times the intake on a diet based solely on imported food (Andersen et al., 2002b). However, a more recent study of iodine content in typical traditional food items, tap water, and beverages in eastern and western Greenland suggested that the iodine intake with a traditional diet is just slightly above the recommendations (Andersen et al., 2002b), which is in accordance with a report of low incidence of thyroid disorders in these populations (Andersen et al., 1999b). In Norway, iodine intake appears to be in accordance with the recommendations for men and small children, but is generally low among adolescent girls. Fish provides 20% of the overall intake in Norway and is the main natural source of iodine, but milk, milk products and salt provide the most due to fortification (Dahl et al., 2004). A high consumption of

non-fatty fish (90-percentile in Norway) may provide three to four times the daily recommendation, but is still far below the maximum recommended intake (Vitenskapskomiteen for mattrygghet, 2006).

Fish may also be an important source of selenium, vitamin B12, and ubiquinone (coenzyme Q_{10} – an important co-factor in our energy production). Other sources rich in selenium are whale skin, birds, and seals (Hansen et al., 2004). Thus, selenium and vitamin B12 intakes are positively correlated with traditional food consumption and thereby also with PCB, DDT, and Hg intakes (Ballew et al., 2006; Deutch et al., 2007b). In Norway, fish contributed about 33% of the total intake of vitamin B12 among adults and 14% to 25% among children (the proportion decreasing with decreasing age). Proportions were similar for selenium. However, because there are also other good animal sources of B12 and selenium these nutrients are generally not of concern for low-fish consumers, for instance, in Norway (Vitenskapskomiteen for mattrygghet, 2006). Traditional foods supplied sufficient selenium in the diets of Nunavik Inuit women (Blanchet et al., 2000); and intake has appeared adequate across Arctic Canada and among Greenland Inuit (Hansen et al., 2004; Deutch et al., 2007b; Kuhnlein et al., 2007), and very few rural Alaskans were found to have intakes below the recommendation, which is contrary to previous findings (Ballew et al., 2006). Very high intakes of selenium in some parts of Greenland have raised concern, but no clinical signs have been recorded (Hansen et al., 2004). On the other hand, low selenium status has been reported in northwestern Siberia and in the European north of Russia (Korčina, 2006, 2007). Antioxidants are discussed in Chapter 7.

3.2.5. **Region-specific summary**

3.2.5.1. **Alaska**

The GOCADAN, CANHR, and ATDP studies all found that traditional foods accounted for only about 20% of energy intake, but that these foods contributed appreciably to protein, vitamin A, vitamin B12, iron, and n-3 fatty acids. The study of Alaskan Natives living in seven Norton Sound communities (GOCADAN) found that intake of traditional foods differed significantly by age group, with the youngest age group (17 to 39 years) consuming the least. Mean traditional food contribution of energy in all ages combined was 15%. Traditional foods provided 23% to 34% of protein, less than 5% of carbohydrate and 15.5% to 20.9% of fat intake, depending on age and sex. Traditional foods also contributed more than 50% of n-3 fatty acids and vitamin-B12 intake.

In western Alaska, the degree of dietary westernization contributes to nutrient intake, both positively and negatively, in a dose-response manner. Participants in the highest quintile of traditional food intake consumed significantly more vitamins A, D and E, and iron and n-3 fatty acids than participants in the lowest quintile. Intake of vitamin C, calcium, and total dietary fiber decreased with increased consumption of traditional foods.

3.2.5.2. **Canada**

Diet and nutrient intakes are well mapped in Canada. Local foods constitute less than 40% of the energy intake of adults and less than 15% among children. In general, the consumption of traditional food is highest in communities that are settled in close proximity to a coast and/or a river, higher among men than women, and higher in the older age groups. The transition to a diet high in imported foods in Arctic Canada has led to observed changes in intake levels of vitamins A, C, D, and E as well as iron, calcium, folate, n-3 fatty acids, and fiber. There is nutritional concern, especially for the groups with the lowest consumption of traditional foods, and the intakes of vitamins A, D and E, magnesium, folate, and calcium appear low. Among indigenous children, iron-deficiency anemia appears to be relatively prevalent.

3.2.5.3. **Greenland**

Among Inuit, traditional food consumption has been associated with a higher proportion of dietary energy from protein and fat, a high n-3 fatty acid and iron intake, and sufficient vitamin-A intake. Vitamin C and folate intake is reportedly low, but vitamin-C deficiency symptoms have not been observed in recent times. However, the overall nutritional picture is blurred by high alcohol consumption, especially among men. There are also regional differences in traditional food consumption, nutrient intakes, and nutritional status.

3.2.5.4. **Other Nordic countries**

Studies about food and nutritional intake are lacking in Iceland and in the Arctic parts of Sweden. In Norway, it is known that cod-liver oil and fish are important sources of n-3 fatty acids and vitamin D in the diet. Studies including both Sámi and non-Sámi communities in northern Norway found distinct differences in diet between Inland Sámi, Coastal Sámi, and Norwegians. Fish from the sea was mainly consumed in the two latter groups, but not by the youth. The nutritional status of the youth was found to be adequate for all nutrients except vitamin D and fiber. In northern Finland, large segments of the population appear to have an insufficient intake of vitamin D. The only study conducted in the Faroe Islands reported low intakes of polyunsaturated fat, iron, and vitamin A in the pregnant population.

3.2.5.5. **Russian Federation**

There have been insufficient comparable and standardized scientific investigations to draw conclusions about nutritional status in the Russian Federation, especially for indigenous population groups. This is further complicated by the extensive and rapid socio-economic changes that have occurred and are still taking place. However, in some populations economic hardship and deteriorated infrastructure may have induced an increased use of local foods in

the diet compared to previous decades. Several Russian studies have raised concern about the mineral status of the inhabitants of the north; particularly in relation to calcium, iron, and iodine. The prevalence of high alcohol consumption among men inevitably influences the general nutritional status.

3.3. Contaminants in single food items and total diets

This assessment has focused on several persistent organic pollutants (POPs), such as dichloro-phenyl-trichloro-ethane (DDT) and polychlorinated biphenyls (PCBs), and metals that are potentially of concern to human health in the Arctic. The POPs and some of the metals are to a large extent transported to the Arctic by air and ocean currents and by northward-flowing rivers. Once in the Arctic, they tend to accumulate in biota and biomagnify through marine food chains with the highest levels present at the top of the food chain. Traditional food can be a significant source of exposure to environmental contaminants for humans and some Arctic populations have exceeded the tolerable daily intakes of certain contaminants, for example the chlordane derivatives oxychlordane and *trans*-nonachlor; toxaphene and PCBs (AMAP, 1998, 2003).

Chapter 5 lists the compounds addressed in the two previous AMAP assessments of human health in the Arctic (see for example section 5.1 and Box 5.1) and several emerging contaminants that are now being found in traditional foods and peoples of the Arctic (section 5.2). A larger range of compounds is presented for some regions and populations, such as Arctic Russia and parts of Alaska, because this will allow more comprehensive comparisons for regions and populations that were not included in the previous assessments.

The following text reviews human dietary exposure to contaminants within different population groups in the circumpolar countries, based mainly on studies published since the last AMAP assessment (2003). Because some circumpolar countries have not performed dietary studies in their Arctic communities, findings from studies in other population groups or the general population are also included. However, it is beyond the scope of this work to consider contaminant levels in the many Arctic wildlife species; a topic addressed by a previous AMAP assessment (AMAP, 2004a). The general conclusions from that assessment were that PCB and total DDT levels were declining slowly; levels of chlordane-related compounds appeared to be declining; levels of the sum of hexachlorocyclohexanes (HCH) remained stable; whereas levels of β-HCH seemed to have increased, but that the variation in environmental levels was large. However, to assess overall human exposure to such contaminants, in addition to information about levels in biota, it is necessary to obtain information about dietary intakes to assess the relative contribution from food. Interactions between contaminants and nutrients are addressed in Chapter 7 and interactions with genes in Chapter 6. Non-dietary factors influencing human exposures to contaminants were addressed in Chapter 2.

3.3.1. Alaska

3.3.1.1. Organochlorines in food items

In a study in the three northernmost Alaskan towns, edible tissues from local marine and terrestrial mammals and fish were compared to store-bought (imported) food items (O'Hara et al., 2005; Hoekstra et al., 2005). In general, imported foods had lower concentrations of organochlorines (ΣPCB, ΣDDT, ΣHCH, ΣCHL and hexachlorobenzenes, HCB) than some tissues of local marine animals (especially blubber and *muktuk*). Tolerable Daily Intake (TDI) limits were calculated for tissues in different species. The most restrictive limits for daily intake were set at 300 g *muktuk* and 67 g blubber from bowhead whale (*Balaena mysticetus*), and 78 g *muktuk* and 32 g blubber from beluga. For blubber in bearded (*Erignathus barbatus*) and ringed (*Phoca hispida*) seal and liver in burbot the limits were more than ten times higher. However, some imported foods; namely sardines, smoked and canned salmon, milkfish, beef tongue, and reindeer meat and marrow had higher levels than some wildlife tissues (e.g., whitefish, pink salmon, Arctic char). The authors concluded that switching from a traditional diet to imported food would not always reduce exposure to organochlorines. The study did not provide estimates of total intake of food and contaminants.

3.3.1.2. Mercury in food items

Dietary surveys in 1999 to 2002 by the Alaskan Department of Fish and Game in northwestern Alaska showed that the average composition of subsistence harvest by rural residents comprised 60% fish, 14% marine mammals, 20% land mammals, and 2% each of plants, birds, and shellfish (Jewett and Duffy, 2007). In non-fish consumers the blood values of Hg were less than 1 μg/L, while in people that consumed large amounts of fish the level could be higher than 4.2 μg/L. Thus, the meat of fish and marine mammals that are high predators is a major contributor of Hg, whereas their liver and kidney have high cadmium (Cd) levels. Studies measuring stable isotope ratios of carbon and nitrogen in marine animals subsistent in Alaska and Chukotka have shown that polar bear (*Ursus maritimus*) is the highest predator followed by beluga and pilot whales (*Globicephala melaena*), whereas bowhead and grey (*Eschrichtius robustus*) whales are at a lower trophic level (Dehn et al., 2006). This is reflected in the total and methyl Hg (MeHg) levels in the consumed parts, and bowhead and grey whale can be considered safe for consumption. Ringed and bearded seals are also at high trophic levels, and Hg levels in their muscles are higher than in bowhead and grey whales, but lower than in dogfish and beluga (Dehn et al., 2005).

Among fish, the piscivorous and long-lived northern pike (*Esox reicheti*) contained muscle Hg levels that often exceeded the guidelines for food consumption,

and the level increased with age and length of the fish but varied between different regions of Alaska. Exposure assessments were conducted on several types of mature fish in Alaska: northern pike, Arctic grayling (*Thymallus arcticus*), whitefish and chinook (*Oncorhynchus tshawytscha*), burbot, chum (*O. keta*), coho (*O. kisutch*), sockeye (*O. nerka*) salmon and others. Only pike exceeded the USFDA action level of 1.0 mg/kg and the critical value for human consumption of 0.3 mg/kg. The estimated limit for consumption of pike was about one monthly meal. In contrast, methyl Hg concentrations in the most frequently consumed fish, such as salmon, cod, halibut, pollock, sole, and herring were very low.

3.3.2. **Canada**

3.3.2.1. **Organochlorines in food items**

In Arctic Canada, the main human exposure route to organochlorines is the consumption of marine mammals at high trophic levels; such as polar bear, walrus (*Odobenus rosmarus*), seal species, and toothed whales (e.g., beluga) from which blubber is the main source. Braune et al. (2005) reported on blubber levels of ΣPCB, ΣDDT, ΣHCH and ΣCHL in ringed seal, beluga, polar bear, and some types of fish (e.g., turbot). Levels of both organochlorines and Hg, measured by stable isotope ratios of nitrogen ($\delta\ ^{15}N$), are correlated with the trophic level of the animal. It was concluded that concentrations of most organochlorines declined in Canadian Arctic biota between 1970 and the late 1990s, and are today about half the levels seen during the 1970s. Decreasing temporal trends were found for PCBs and DDT in fish and ringed seal in some locations, and also for HCH and CHL. Using archived material from the 1970s and 1980s, decreasing trends in blubber from male beluga and polar bear were also found for PCB, HCH, DDT, and toxaphene from 1980. However, levels of other POPs, chlorobenzene, endosulfan and the 'emerging' chemical, polybrominated diphenylethers (PBDEs), have been increasing rapidly over the same period. Traditional-food intake is highest in Inuit communities followed by Dene and Métis in the North West Territories and First Nation people of Yukon. As previously mentioned, intakes of traditional food by Inuit seem not to have changed over the past 20 years. Monitoring and assessment of the intake of organochlorines within these groups are warranted (Muir et al., 2005).

3.3.2.2. **Mercury in food items**

The Hg level is high in animals from Arctic Canada compared to other Arctic areas, but varies between different locations (Braune et al., 2005, Muir et al., 2005). There is good evidence that Hg levels have increased from pre-industrial times to the present. However, data for Hg in beluga whales, ringed seals, moose, seabirds and fish from the last 20 to 30 years show conflicting results in terms of temporal trends, due to high variations in average levels. Both year-to-year variability and within-year variability have been observed. However, a steady increase in Hg in seabirds in Lancaster Sound suggests that there has been an increased delivery of Hg into the Arctic marine food web. On the other hand, only some animal species showed an increase in Hg levels. At present, it is therefore not possible to conclude whether anthropogenic Hg is increasing in Canadian biota or not.

Traditional-food intake is highest in Inuit communities followed by Dene, Métis and First Nations of Yukon. Among the Inuit, intake of traditional foods does not seem to have changed much over the last 20 years. Variations in human Hg blood levels therefore mainly reflect environmental levels. In Nunavik for example, Hg levels in blood appear to have varied markedly from year to year due to variation in the levels in the biota used as traditional food (Dewailly et al., 2001b).

3.3.2.3. **Contaminants in total diet**

Dietary surveys have shown that the most frequently eaten traditional foods among the Dene, Métis, and in Yukon were caribou, moose, salmon, whitefish, grayling, trout and ptarmigan (*Lagopus* spp.); whereas in the Inuit communities caribou, seal, char, musk ox (*Ovibos moschatus*), *muktuk* from narwhal and beluga were most frequently consumed. The percentage of energy derived from traditional food ranged from 10% to 32% in Yukon, 5% to 32% in Dene and Métis, and 12% to 40% among the Inuit. Differences in intakes of traditional food were reflected in the mean levels of human plasma contaminants. In the Inuit communities, Baffin, Inuvik, Kitimeot, Kivaliq and Nunavik, plasma levels of most organochlorine pesticides were 8- to 10-fold higher than in Dene, Métis, and Caucasians, whereas the PCB levels were about 5-fold higher (Van Oostdam et al., 2003).

Based on data collected in the late 1990s, the intake by Dene and Métis were below provisional TDI values for chlordanes and toxaphenes, whereas Inuit communities exceeded these TDI levels. The TDI for Hg was also exceeded in some Inuit communities (Kivaliq and Baffin). In Qikiqtarjuaq, the provisional TDI values for chlordane, HCB, HCH, Mirex, PCBs, and toxaphenes were exceed by 5% to 50% of the population. The calculated daily intakes (measured in μg/kg body weight per day) of most organochlorines dropped by about 30% between 1987/88 and 1998/99. Toxaphenes, on the other hand, had increased five-fold, and Hg had not changed. The study also showed that the main proportional contributions by food items to chlordane and toxaphene intake were beluga and narwhal blubber. The main sources of Hg intake in five Inuit regions were caribou meat, ringed seal meat, beluga *muktuk*, lake trout, and Arctic char flesh. It was also reported that marine mammals contain mainly inorganic Hg whereas fish contain mostly organic Hg, and that to account for this would make a risk assessment more accurate.

The Canadian Total Diet Study (Rawn et al., 2004) was a national survey to determine the level of chemical contaminants in the Canadian food supply. The study involved the retail purchase of foods representing 99%

Table 3·4. Studies of contaminants in the 'total diet'. Average daily intakes of key contaminants (μg/d) and percentage of the study populations exceeding the TDI values in parentheses.

	Study group and sampling year	PCB aroclor 1260	DDT	Chlordanes	Mercury	Source
TDI [a], μg/d		60	1200	3	12.2	
Canada	Whitehorse (1998). Average Canadian diet analysed for organochlorine compounds (no traditional foods included)	-	0.36 (0)	0.06 (0)	-	Rawn et al., 2004
Greenland [b] (NW)	Uummannaq (1976). 180 day-portions	36.8 (10)	22.5 (0)	9.4 (97)	83.8 (100)	Deutch et al., 2006
	Uummannaq (2004). 90 day-portions	12.1 (3.3)	8.8 (0)	7.1 (40)	33.6 (50)	Deutch et al., 2006
	Narsaq (southwest) (2006). 90 day-portions.,	5.4 (0)	1.8 (0)	1.3 (10)	8.6 (20)	Deutch et al., 2007a
Greenland (W)	Dietary survey (1995) combined with organochlorine compounds and heavy metal levels in animals. Spring and autumn, respectively.	23.0 [c] 22.9 [c]	32.0 25.4	17.8 14.7	41.6 41.6	Johansen et al., 2004b
Sweden	Four cities, 4000 persons (1998). Market basket, dioxin PCDD, PBDEs.	0.62 (0)	0.52 (0)	0.12 (0)	-	Darnerud et al., 2006
Finland	Four cities, 4000 persons (1998). Market basket, dioxin PCDD, PBDEs.	1.2 (0)	-	-	-	Kiviranta et al., 2004

- :not available; [a] based on a TDI in μg/kg body weight/day (PCB = 1.0, DDT = 20, chlordanes = 0.05); [b] the three sample years represent different compositions and percentages of local food; [c] sum of 10 PCBs.

of the average diet for an individual city. Each year, samples were collected from a different city as part of the total diet cycle. In a study of food samples collected in 1998 in Whitehorse and Yukon supermarkets, 132 food composites were analyzed for the concentrations of 61 pesticides. Using the concentration data, dietary contaminant intakes were calculated by multiplying their concentration by the estimated consumption of the particular food item. Finally, the total intake was calculated by summing intakes from all the foods containing residues. The findings are summarized in Table 3.4. Organochlorine insecticides were the only group of pesticides detected in fish composite samples. Seven insecticides were detected in freshwater fish, and six in canned composites of salmon and tuna. Dichlorodiphenyl-dichloro-ethylene (DDE), dieldrin, and HCB, now rarely used as pesticides, were detected in marine composites of cod and haddock. ΣCHL and ΣHCHs were below reporting limits in shellfish and marine fish. The measured ΣDDT in composites of freshwater fish was 1.67 ng/g; of canned fish 6.60 ng/g; and of marine fish 0.43 ng/g. In general, the pesticides in food composites were well below the maximum residue limits of the Canadian Food and Drug Regulations, and the dietary intakes of any of the pesticides were not above acceptable daily intakes in any gender and age-specific group. The low contaminant loads reflected that the study included common supermarket food and not traditional Arctic foods.

3.3.3. **Greenland**

In Greenland, human dietary exposure to organochlorine compounds and heavy metals has been assessed in several ways: by measuring contaminant levels in daily food portions from three sub-population groups with different dietary composition (Deutch et al., 2006, 2007a,b); by calculating theoretical estimates of human exposure from dietary surveys and contaminant levels determined in consumed animals (Johansen et al., 2004a,b); and by combining a country-wide dietary survey with individual blood and plasma levels of contaminants to identify dietary predictors for the level of each contaminant (Deutch et al., 2007a).

3.3.3.1. **Contaminants in the total diet**

A comprehensive study of contaminant concentrations in the local diet in Greenland (Johansen et al., 2004a) included Cd, Hg, selenium, PCB, DDT, chlordane, HCH, chlorobenzenes, dieldrin, and toxaphene levels in the major animal species and tissues consumed by Greenlanders. Tissue from about 25 animal species was included in the study and as a generalization contaminant levels were very low in terrestrial species and in muscle tissue of many marine species. High organochlorine concentrations were typically found in marine mammal blubber and high metal levels in seabird liver and in liver and kidney of seals and whales. The study also found that contaminant levels in the Greenland environment, including dietary items, were lower than in more densely populated and industrialized regions of the northern hemisphere. This geographic difference was very pronounced for most of the organochlorines and Hg levels were also generally lower in Greenland. In contrast, Cd concentrations were much higher in biota from Greenland (and other Arctic areas) than from temperate European marine

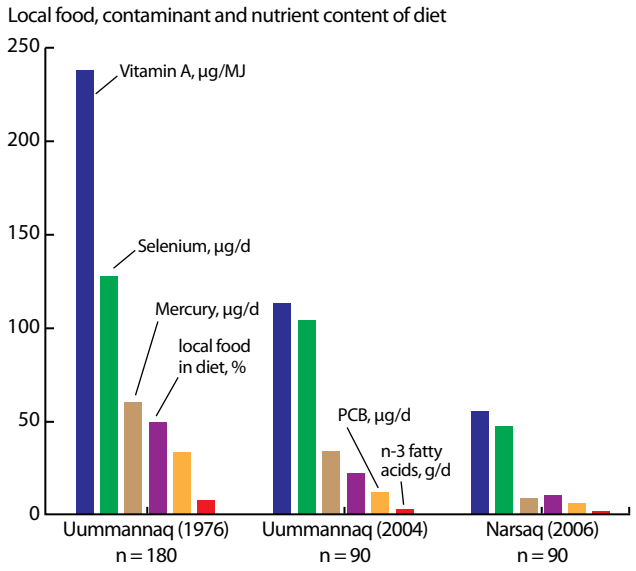


Figure 3·3. Local food percentage, contaminant and nutrient content measured in duplicate meal portions from Uummannaq, Greenland in 1976 and 2004 and Narsaq, Greenland in 2006.

environments. Based on studies by Dietz et al. (1990), a MeHg intake of 38 µg/d per person was calculated by Johansen et al. (2004b) in autumn and 54 µg/d per person in spring in the diet study in Disko Bay. This is a high intake, significantly exceeding the European Food Safety Authority's TDI of 0.23 µg/kg body weight per day and the U.S. EPA Reference dose of 0.1 µg/kg body weight per day (Hansen and Gilman, 2005).

In an AMAP-associated study (Deutch et al., 2006, 2007b), dietary composition and nutrients and contaminants were compared between 180 traditional meals collected by the 'duplicate portion method' in Uummannaq (northwest) in 1976, and 90 meals sampled in Uummannaq in 2004 and Narsaq (south) in 2006 under similar conditions. Eleven pesticides, 14 PCB congeners, heavy metals, selenium, and fatty acids were analyzed in both the meals and blood samples from the participants. Contaminant levels were compared between locations and collection years after adjustment for n-3 fatty acids, marking local food content. Large changes occurred between the dietary composition in 1976 and the meals from 2004 and 2006. The percentage of local food decreased from about 40% in 1976 to 22% (Uummannaq) and 12% (Narsaq), and with it the intake of n-3 fatty acids from 8.5 g/d, to 3.5 g/d and 1.7 g/d, respectively. The consumption of seal products decreased in particular (from > 400 g/d in the 1976 samples to < 100 g/d in the 2004 to 2006 samples). Both the contaminants and several important nutrients had decreased together with the intake of local food (see Figure 3.3). Daily organochlorine and Hg intakes, and percentage of participants exceeding TDI values, are shown in Table 3.4.

Calculated as daily intake, all but three contaminants (chlordanes, mirex, and toxaphenes) decreased. This could be explained to a large extent by the lower intake of local food. As the contaminant intakes decreased, so did the nutrient intakes originating from traditional food items. After adjustment for n-3 fatty acid content, a decline in concentration in the local food was evident only for PCB and lead (Pb), whereas for Hg, DDTs and chlordanes the levels were unchanged, and for HCB, mirex, and toxaphenes the levels increased. Thus, with the exception of PCB and Pb, contaminants in local food items are in general not decreasing in Greenland, but their intake is decreasing due to changing dietary habits (Deutch et al., 2006).

Figure 3.4 shows the relative contribution to contaminant exposure of different types of seafood that occurred in meal portions. It shows that a dietary composition based on imported food, without local marine mammals and fish, presents a very low contaminant load. The intake of seal blubber was the most important determinant for high contaminant exposure even if the intake of seal blubber was only 8 – 20 g per meal on average.

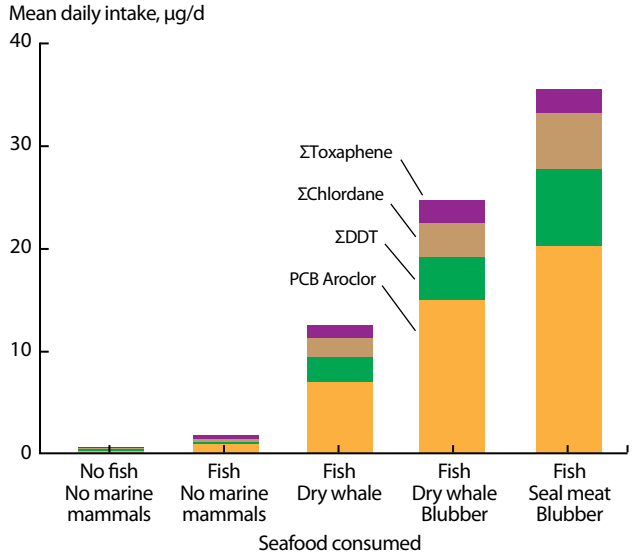


Figure 3·4. Daily intake of POPs in 90 daily food portions as a function of seafood types present in the diet.

3.3.3.2. Dietary survey and calculation of exposure from animal data

A dietary survey using a food frequency questionnaire (FFQ) performed in western Greenland in 1995 (spring and autumn) with 300 participants (Pars, 2000), analyzed contaminant levels in muscle, liver, kidney, and blubber from animals hunted within the same area and grouped the results into categories of very low to very high contaminant levels. The daily average intake of the various tissues was calculated and multiplied by the contaminant level measured in the tissues, thereby providing an estimated total daily contaminant intake. It was found that the mean intake of Cd, chlordanes and toxaphene exceeded the TDI values by a factor of 2.5 to 6. Mean intakes of Hg, PCB, and deldrin exceeded the TDI values by up to about 50% (note that the PCBs measured were the sum of ten PCBs, therefore lower than the PCB Aroclor 1260 TDI), while intakes of DDT,

HCH, and chlorobenzenes were well below the TDI values. The percentage of participants exceeding the TDI values was not reported (Johansen et al., 2004a,b). Levels are presented in Table 3.4.

3.3.3.3. **Dietary survey and blood levels of contaminants**

A dietary survey by semi-quantitative FFQ was performed as part of the ongoing AMAP study covering eight locations in Greenland (n = 600) (Deutch et al., 2007a). Blood levels of heavy metals and a number of lipophilic POPs were measured, including 10 pesticides, 14 PCB congeners, and 5 toxaphene congeners, and the associations between self-reported monthly food frequencies and the levels and ratios of plasma phospholipid fatty acids as indicators of local food were assessed. The resulting relative solid weight of local products ranged from about 25% in Qaanaaq (N) and Uummannanq (NW), to about 12% in Sisimiut (W), Nuuk (SW), and Narsaq (S). The relative energy intake was almost the same as the relative solid weight. It was found, not unexpectedly, that the intake of local Greenlandic products was higher in the north, and that the intake and versatility of imported Danish products was higher in the southern and southwestern parts of the country (Deutch et al., 2007a).

Reported food intakes (traditional and market food) were found to be very similar between men and women in the smaller towns, but in the bigger towns the women appeared to be more 'westernised' and consumed more market foods than the men (Deutch et al., 2004, 2006). The relative intake of local food was strongly correlated with plasma n-3/n-6 levels, and this ratio was used as an indicator of marine food intake. Positive associations were found between n-3 fatty acids in human lipid fractions and blood levels of both Hg and all organochlorines. This makes the connection between intake of marine mammal fat (e.g., blubber) and organic pollutants highly probable.

3.3.3.4. **Organochlorines**

Organochlorine levels in blood and plasma data are presented in Chapter 5. All the plasma organochlorine levels were positively associated with the reported monthly intake of Inuit meals and, not surprisingly, several were inversely correlated with the intake of Danish meals. Meals including seal meat were correlated with PCB, chlordanes, HCB, and Mirex. Meals which included seal products (meat, blubber, liver) were correlated with plasma levels of all organochlorines (Deutch et al., 2004). Polar bear intake was correlated with all organochlorines, except DDE and Mirex, and so was intake of musk ox. However, intake of musk ox is only common in Ittoqqortoormiit and may be a marker of intake of polar bear or ringed seals (Deutch, 2003b; Johansen et al., 2004a,b). Bird intake was correlated with PCBs and toxaphenes, and fish intake was correlated with all organochlorines. Seal and whale blubber were the major contributors to relative exposure from all organochlorines, about 50% and 40%, respectively. Among women from Nuuk and Sisimiut, who only ate seal and whale once or twice a month, the PCB and Hg exposure levels were as low as in young Danish women (Deutch, 2003b).

It was also found that smoking, independent of the other factors, was correlated with the plasma levels of organochlorines. The magnitude of the effect of smoking was quite considerable, to the extent that a typical 50-year old male smoker could have double the PCB level of a comparable non-smoker. Tobacco itself is not a source of organochlorines, whereas Cd and Pb concentrations in blood are both correlated with smoking because tobacco is a direct source of these elements, especially Cd. The higher levels of all measured organochlorines among smokers in Greenland suggest that nicotine or other substances in tobacco smoke influence the metabolism of these xenobiotic substances (Lagueux et al., 1999; Deutch and Hansen, 2000; Deutch et al., 2003). Because of the uneven spatial distribution in local predatory animals, district (municipality) is a predictor of contaminant levels. The different spatial distribution of human exposure indicates that not all organochlorines have the same geographical distribution and that the external sources of organochlorines may vary from place to place, but the differences in human exposure also stem from differences in dietary composition in the different districts.

In Greenland, as in Arctic Canada, the main human exposure to organochlorines is consumption of marine mammals at high trophic levels. Polar bear is an important food source on the east coast particularly during the winter months, and the organochlorine levels in polar bear were very high, especially for PCB (Riget et al., 2004). The high PCB levels in Ittoqqortoormiit were highly correlated ($p < 0.0001$) with polar bear consumption (Deutch et al., 2003, 2004). Contaminant data for polar bears indicate such high levels that polar bears would be the predominant source of PCB contamination in areas where it is consumed. From the analysis of hunted animals, including polar bear, it appears that PCB and DDT levels are decreasing (Johansen et al., 2004a,b, Riget et al., 2004).

There is less documentation of a temporal trend in human tissue. However, among pregnant women from the Disko Bay area over a 12-year period (1994 to 2006), decreases of oxychlordane, *p,p*-DDE, and CB153 were found in plasma and for Pb in whole blood, but not for Hg. These decreases can partially be explained by different dietary and smoking habits (further details provided in Chapter 5, Table 5.7) (Deutch, unpublished data). Multiple linear regression analyses, which were performed using natural logarithms of lipid-adjusted POPs as dependent variables showed that the following factors were all strong indicators of human plasma levels of organochlorines: age, gender, district, intake of marine mammals, smoking status (present, previous, or never) or plasma cotinine level, and in particular the plasma n-3 : n-6 fatty acid ratio. So identification of individuals

at risk of accumulating a high organochlorine burden is not just a simple question of dietary exposure, but is complicated by other behaviors as well as by interacting genetic and biochemical factors.

3.3.3.5. **Heavy metals**

The plasma n-3 fatty acids and blood levels of heavy metals were strongly correlated; Hg in particular ($r = 0.54$, $p < 0.001$). However, the blood levels of Hg were very high in Uummannaq and Qaanaaq in northwestern Greenland (Deutch et al., 2007a) and the ratio between Hg levels and n-3/n-6 fatty acids was higher there than in all other districts (different correlation coefficients in different districts). This could mean that the dietary sources have higher Hg levels than in other districts and could point to a special environmental Hg problem in northwestern Greenland (see also Canada), which cannot yet be explained. Riget et al. (2004) found that Hg levels are increasing in northwestern Greenland in animal biota. But animal data are not consistent between locations or species. The Hg blood levels were correlated with selenium levels ($p < 0.001$) indicating the same external source.

Estimates of human exposure to bioavailable Hg indicate that seal and whale meat are the biggest contributors, by about 40% and 20%, respectively. In contrast, the high inorganic Hg levels in animal liver and kidney tissue are much less bioavailable (less than 10%), and therefore not important sources (Deutch, 2003a,b). Blood levels of Hg and Pb were correlated with the intake of meat from seal and whale, but a multiple linear regression also revealed an association with age, gender, district, plasma n-3 fatty acids, and smoking. Cadmium levels, on the other hand, were not correlated with seal and whale consumption and age, but with n-3/n-6 fatty acids, gender, district and smoking. See also section 3.3.3.1.

3.3.4. **Faroe Islands**

3.3.4.1. **Organochlorines in food items (gull eggs)**

Eggs from fulmars (*F. glacialis*) constitute part of the traditional diet for a part of the population and may contribute to the high levels of organic contaminants found in the blood of pregnant Faroese women. In general, fulmars, and fulmar eggs, muscle, and subcutaneous fat were found to have high levels of several organochlorines, namely PCBs, HCB, and DDT. Levels were higher in adults than in young birds. Fulmar eggs also contained PBDEs, but in much lower concentrations than PCBs, and also much lower than in guillemot eggs from East Greenland or the Baltic. PCB concentrations in fulmar eggs and muscle were in the same range as for pilot whale blubber. However, the total fulmar egg consumption per year was only about 10 000 among a population of 50 000. Nevertheless, humans that eat fulmars and their eggs are exposed to noteworthy PCB levels in addition to exposure from pilot whales (Fängström et al. 2005a,b). No other dietary studies of contaminant contents in food items have been published for the Faroe Islands.

3.3.5. **Norway**

3.3.5.1. **Organochlorines in food items (gull eggs)**

Top level predators in the Arctic, such as polar bears, Arctic foxes (*Alopex lagopus*), and some gull species, accumulate high levels of several fat-soluble POPS. Gulls deposit high levels of these pollutants in their eggs, which are part of the traditional diet in northern regions (Pusch et al., 2005). Seagull eggs were collected from four gull species (*Larus argentatus*, *L. marinus*, *L. fuscus*, *L. hyperboreus*) at 12 locations in northern Norway, the Faroe Islands, and Svalbard. Although levels were highest in the northernmost location, Ny Ålesund, and the mean burden varied by location, it did not vary in a systematic geographic manner. The total burden (the sum of mono-*ortho* PCBs, non-*ortho* PCBs, polychlorinated biphenyl dioxins (PCDDs), and polychlorinated biphenyl furans) varied from 22 to 107 pg TCDD equivalents (TEQ) per/g ww with an average of 65.5 pg TEQ dioxin and PCB per g ww. It was calculated that by eating eight eggs per year, an adult of 60 kg would exceed the Tolerable Weekly Intake (TWI) of 14 pg TEQ/ kg body mass per week, while a child of 20 kg would exceed the TWI by eating three eggs per year. Based on these results, it was recommended that children, young women, and pregnant and nursing women should not eat gull eggs, and that other people should limit their intake. There is reason to believe that consumption of seagull eggs declined markedly after the National Nutritional Council issued a warning, and the retail sale of eggs stopped altogether in 2000.

3.3.6. **Sweden**

3.3.6.1. **Organochlorines in the total diet**

A 'market-basket' study was carried out in Sweden in 1999 by Darnerud et al. (2006) using a similar approach and technique as the Finnish study in section 3.3.7.1. It covered four cities in different geographic areas, with the city of Sundsvall at the Baltic Sea coast the northernmost (61.4° N). Thus, none were actually in the Arctic. Average daily consumption was derived from national statistics. The consumed food items were divided into 15 groups (market baskets); fish, meat, dairy, fats, cereals, etc. Fish was the major contributor to TEQ intake (34%). While PCBs and DDTs showed the greatest intake by weight, the dioxin intake, although lower by weight, is perhaps of higher potential risk. More than 10% of the Swedish population is estimated to have an intake above the TDI of 2 pg total WHO-dioxin-TEQ/ kg body weight. The results were compared to a recent Swedish food study using individual food consumption data, and the resulting intake levels of organochlorines were similar. The authors concluded that the market-basket method is an efficient monitoring instrument that can be used in contaminant trend studies. A follow-

up of the market-basket study was performed in 2005 (Ankarberg et al., 2007) and showed that calculated average per capita intakes of persistent organochlorines and toxic equivalents had decreased between 1999 and 2005 for PCDDs, PCB, and total TEQ, ΣPCB, and ΣDDTs. The total TEQ had decreased by 48%, ΣPCBs by 41%, and ΣDDTs by 31%. It was also confirmed that fish consumption was still the major source, contributing 49% of the total TEQ intake. Commercial fishers from the Baltic Sea with high consumption of fatty fish (salmon and herring) had the highest TEQ intake /kg/d; five times the average intake.

3.3.7. **Finland**

3.3.7.1. **Organochlorines in the total diet**

A Finnish food-basket study, based on the average consumption figures from four major cities (non-Arctic), compared the contaminant contents of almost 4000 individual food samples divided into ten market baskets (milk products, fish, meat, eggs, fats, cereals, potatoes, vegetables, fruits, beverages) (Kiviranta et al., 2004). PCDD, PCDD/Fs, dioxin TEQs, and various PCB congener fractions were measured. The average daily intake by this representative population sample was assessed based upon the 'total market basket content' (see Table 3.4). It was found that fish was the major contributor of several contaminants (80% of PCB, 72 – 94% of PCDD and PCDD/Fs, and 94% of dioxin-TEQs) although the average intake was only 27.4 g/d (or 1.4% of total food consumption). The exposure contribution from fish was about 50 times the contribution from meat and eggs; 100 times the contribution from milk products; and about 1000 times the contributions from vegetables, fruit, berries and beverages.

The Finnish daily intakes and dioxin exposure were compared to ten other European countries, Japan, China, and the United States. The total daily intakes of WHO-TEQs, PCB-TEQs, and PCDDF-TEQs did not differ much between the countries compared, and were of the same order of magnitude. However, sources varied between countries. In several of the other European countries, meat and dairy products contributed more than fish to the contamination load. Only Japan, which is known to have a high fish intake, had almost the same relative contribution from fish as in Finland.

3.3.7.2. **Organochlorines in food items**

During the 1990s, the pollutants in foods in Lapland (Arctic Finland) were analyzed and compared to levels in foods from the rest of Finland (Soininen et al., 2005). DDT, PCB, HCB, and BHC were on average low in all food items tested, including all freshwater fish.

3.3.7.3. **Metals in food items**

In the same study, a number of metals regarded as nutrients (copper, zinc, selenium) and pollutants (arsenic, Cd, Pb, Hg, nickel) were measured in local food items in Lapland (vegetables, potatoes, berries, mushrooms, reindeer, game, local fish) and compared to levels in food items from the rest of Finland (Soininen et al., 2005). In general, levels of pollutant metals were low (and below the Finnish reference values) in most food items except reindeer liver, some of which exceeded the reference values for Cd and Pb. Likewise, Hg levels were low in most food items, including most fish species except fish from new water reservoirs where levels exceeding 1 mg/kg were found in old burbot and pike. Based on a dietary FFQ the average dietary Hg intake was estimated to be 4.4 μg/d, corresponding to 15% of the provisional TWI and basically equivalent to the situation in the rest of Finland.

3.3.8. **Russian Federation**

3.3.8.1. **Organochlorines in food items**

In all studied regions of Arctic Russia, the concentrations of organochlorines in venison and fish (marine, migratory, and freshwater) were low. In birds, the levels were 2 to 4 times higher than in reindeer and fish, but 10 times lower than the RFSL. Levels in birds decreased based on feeding habit: molluscivorous > omnivorous > piscivorous > meadow feeding; the species with the lowest concentration was ptarmigan. Levels in marine mammal meat, liver, and kidney in Chukotka were low, but accumulated in fat tissue. Nevertheless, PCB levels in the fat of walrus, seals, and whales were 20 times lower than the RFSL, while DDT and HCH levels in fat only slightly exceeded these limits.

Thus, from a food safety perspective, there should be no concern about eating venison, all types of fish, and fish liver. But indigenous northern peoples are recommended to restrict (to various extents) the amounts of specific types of local foods; for example liver and kidney of reindeer, meat of waterfowl, and in coastal Chukotka, meat, liver and kidney of seals, liver and kidney of walruses, whale liver, and the fat (including *muktuk*) of whale, walrus, and seals. Based on the maximal concentrations of persistent toxic substances in traditional food products, the values of maximal daily intake were calculated for each product – both for inland and coastal communities (Dudarev et al., 2005).

3.3.8.2. **Organochlorines in food items, and additional sources of food contamination**

In the Russian Arctic, a double contamination of food products during storage, souring, processing, and cooking was found (Dudarev and Chashschin, 2004, Dudarev, 2007a), a phenomenon not found in other circumpolar countries. It was concluded that indoor sources of PTS were likely to have contributed to the high blood levels of contaminants among indigenous peoples of the Russian Arctic, particularly Chukotka natives. It was observed that all the houses of indigenous peoples studied were contaminated by organochlorines, mostly by PCBs and DDT. Home-produced ready-to-eat

local food had much higher levels of contamination by persistent toxic substances than fresh products obtained directly from the natural environment. It was established that household use of insecticides and other chemicals for combating insects and pests, technical oils and liquids for the imbuing of wood and other construction materials, second-hand use of wasted technical containers and barrels for souring of plants and vegetables, home-made alcohol fermentation, and water keeping, are subject to additional contamination during processing in the household environment. High risk of food contamination is specifically associated in Chukotka with prolonged fermentation of meat and fish in ground pits that are not protected from accidental contamination by leakage of drainage waters and contaminated soils due to poor sanitation and general environmental neglect of native communities (Dudarev and Chashschin, 2004, Dudarev, 2007b).

The findings from the investigations in Russia have been realized in recommendations and nutritional advice aimed at reducing organochlorine exposure though food by indigenous peoples without intervening in their basic traditional lifestyle and cultural identity. A colored brochure aimed at indigenous population groups providing information on how to avoid secondary contamination of food was disseminated. However, no evaluation of the effect of recommendations and the information campaign has been undertaken.

3.3.8.3. **Dietary survey and human plasma levels of organochlorines**

On the Chukotka Peninsula, where the population depends heavily on marine mammals, plasma levels of organochlorines among the study population (Sandanger et al., 2003) were correlated with data obtained in a dietary survey (Dudarev et al., unpublished) (see section 3.1.3.5). The dietary survey was performed using a FFQ covering the locally-consumed food items, of which the 18 most common were reported. Consumption of seal, walrus, and whale was common, and so was consumption of blubber, as well as Arctic char, salmon, and duck. Polar bear was consumed, but infrequently (it is illegal to kill polar bears). Although the intake of marine mammals, particularly of their blubber, was higher than in East Greenland (Deutch, 2003b), the human plasma levels of ΣPCB and ΣDDTs were lower than in eastern and northwestern Greenland and lower than in Nunavik (northern Quebec). This indicates that levels of these compounds are lower in marine mammals from the eastern Arctic. On the other hand, β-HCH plasma levels were higher than in any of the

Table 3·5. Russian Food Safety Limits (RFSLs) and allowable daily intakes. Source: Public Health Ministry of Russia (2002, 2003a,b).

Contaminant	Raw food (fresh or frozen products)	Russian food safety limits	
		Concentration in food, mg/kg	Allowable daily intake, mg/kg body weight per day
HCHs	Fish, meat of marine mammals	0.2	0.01 (adults); 0.005 (children)
	Fish liver	1.0	
	Meat and poultry	0.1	
DDTs	Fish, meat of marine mammals	0.2	0.005 (adults); 0.0025 (children)
	Fish liver	3.0	
	Meat and poultry	0.1	
HCB	Cereals	0.01	0.0006
PCBs	Fish, meat of marine mammals	2.0	not established
	Fish liver	5.0	
	Fat of marine mammals	3.0	
Lead	Meat and poultry	0.5	not established
	Liver of mammals and birds	0.6	
	Kidneys of mammals and birds	1.0	
	Fish, fish liver, meat of marine mammals	1.0	
Cadmium	Meat and poultry	0.05	not established
	Liver of mammals and birds	0.3	
	Kidneys of mammals and birds	1.0	
	Fish, meat of marine mammals	0.2 – 0.6	
	Fish liver	0.7	
Total Mercury	Meat and poultry	0.0	not established
	Liver of mammals and birds	0.1	
	Kidneys of mammals and birds	0.2	
	Fish, fish liver, meat of marine mammals	0.3 – 0.6	

Table 3·6. Studies concerning single food items and contaminants.

	Study	Food items	Source
Alaska	Comprehensive study of POPs in Arctic local food items	Marine biota and store-bought food items	Hoekstra et al., 2005; O'Hara et al., 2005
Canada	Comprehensive study of Arctic local food items and their POPs and heavy metal levels	Marine biota	Braune et al., 2005
Iceland	Selected single food items, but no human consumption data, POPs levels	Six species of waterfowl	Olafsdottir et al., 2001
Faroe Islands	Selected single food items, POPs levels	Fulmars and eggs	Fängstrom et al., 2005a,b
Norway	Selected single food items, correlations between specific food items and POPs levels in breast milk	Seagull eggs	Pusch et al., 2005
Russia	Comprehensive study of heavy metal and POPs levels in Arctic local food items	Marine biota, terrestrial biota and store-bought food	Dudarev et al., 2005; AMAP 2004b

native populations from Greenland, Canada, and the Faroe Islands, for both men and women. The β-HCH levels in men were 4 times higher than the highest levels reported for East Greenland. The sum of the self-reported consumption of blubber from seal, walrus, and whale was an indicator of plasma concentrations of ΣPCB, but only borderline for chlordanes and DDT.

3.3.8.4. **Metals in food items**

In a summary of Russian data regarding persistent organic substances in Arctic food products, it was concluded that the overall levels of Pb and Hg in venison were low in the four main studied regions of Arctic Russia (Kola Peninsula, Nenets Autonomous Okrug, Taymir APO, Chukotka AO) (Dudarev, unpublished). However, in some regions the Hg levels in reindeer kidney exceeded the food safety limits in Russia for commercial and wild foods (RFSL) by up to 50%. In waterfowl, Hg levels were 2 to 3 times higher than the RFSL. For Cd, venison and reindeer liver and kidney exceeded the RFSL by up to 100% (see Table 3.5). Lead levels in reindeer liver and kidney were below the RFSL everywhere, this was also the case for birds – except when lead shot was found inside. Cadmium levels in birds were also low. In all regions, levels of metals in fish (including marine, migratory, and freshwater fish) did not exceed the RFSL, including burbot liver.

In Chukotka, levels of Pb in all tissues were below the RFSL in all species of marine mammals. In meat, Cd levels were also low. Liver levels of Cd, on the other hand, exceeded the RFSL by 5 to 15 times in whales, walrus, and seals. All species of seal were more contaminated with Hg than terrestrial mammals, birds and fish. For Hg, levels in seal meat exceeded the RFSL by 3 to 10 times; seal kidney by 10 times; and seal liver by 20 to 100 times. The highest Hg levels were observed in bearded seal, particularly in the liver. Meat of walrus and grey whale is less contaminated with Hg, with levels lower than the RFSL. However, kidney and liver of walrus had Hg levels 2 to 4 times higher than the RFSL. In whales, on the other hand, Hg levels in kidney are below the RFSL and the liver level is similar to the RFSL. The percentage of the population exceeding the RFSL levels was not reported.

3.3.9. **Summary**

Ideally, total exposure based on total diet measurements or calculation of exposure from dietary surveys should have been combined with measurements of contaminant levels in foods. However, only a few of the published studies facilitated this. Within the Arctic populations, total diet studies with analysis of contaminants have been performed only in Greenland and Canada. Large population market-basket studies have been performed in Finland (Kiviranta et al., 2004) and Sweden (Darnerud et al., 2006), but not within indigenous populations in the Arctic. In Alaska, local food items from various indigenous communities have been analyzed for contaminant levels, and the investigated items have been compared to TDI values or reference dose levels, but total dietary exposure has not been estimated (Hoekstra et al., 2005). In Russia, a large study determined contaminant levels in indigenous domestic food and residences, and a large number of food items were compared between different provinces and relative to safety limits and/or reference doses (AMAP, 2004b; Dudarev et al., 2005). Simultaneously, contaminant levels were also determined in humans, both in maternal and cord blood and in the general population, and were compared between provinces. However, these measurements were not directly related to estimated dietary exposure. As a part of the study, human plasma levels of organochlorines were measured and dietary information collected by a questionnaire in Uelen (Chukotka), and blubber from seal or walrus was identified as the main dietary predictor for high organochlorine levels. A summary of studies of single food items is provided in Table 3.6.

Based on the very heterogeneous material reviewed in this chapter, it is difficult, if not impossible, to make direct comparisons between total dietary contaminant exposures in the different Arctic countries and population groups. For instance, the different studies have used different methods and have not focused on the same set of contaminants, although there are some overlaps.

For most of the Arctic areas concerned, the major dietary sources to high human exposure come from the same animal groups (usually high trophic level marine

predators). Nevertheless, the contaminant levels may vary from place to place, with large spatial differences both between and within countries. Therefore, it still appears important to caution the intake of certain animal tissues that are a part of the traditional diet. One approach could be to categorize key local food items into groups of relative safety. However, any advice should be based on local food habits and contaminant levels.

3.4. Food security

Food security is 'the assurance that all people at all times have both the physical and economic access to the food they need for an active, healthy life. It means that the food itself is safe, nutritionally adequate and culturally appropriate and that this food be obtained in a way that upholds basic human dignity' (Canadian Centre for Policy Alternatives-Mb, 2004; WHO, 2006). Food security is based on three basic components: food availability (i.e., sufficient quantities of food available on a consistent basis), food access (i.e., having sufficient resources or income to obtain appropriate foods for a nutritious diet), and food use (i.e., appropriate use based on knowledge of basic nutrition and care) (WHO, 2006). A fourth concept that is beginning to be included is the risk of climatic fluctuations, conflict, job loss, and epidemic disease, all of which can disrupt any of the first three factors (Webb et al., 2006). In addition to food availability and access as an issue for nutrition in the Arctic, food safety and hygiene have been reported to be compromised in Arctic populations, resulting in food-borne illnesses and the incidence of zoonotic infectious diseases passed from animals to humans.

3.4.1. Food security in the Arctic context

Data on food security in the Arctic are scarce and primarily available for the Canadian Arctic and Alaska. These data have only been collected in a few discrete communities and not across the expanse of Arctic North America. More data are needed for Arctic North America as well as for other circumpolar countries and regions to provide a better overall view of this issue.

Previous dietary surveys have found that food security is a concern in northern Canadian communities (Lawn and Langer, 1994; Lawn and Harvey, 2001), findings which are now corroborated by additional reports on food insecurity in northern Canada (Lawn and Harvey, 2003; Ledrou and Gervais, 2005; Chan et al., 2006; Lambden et al., 2006; Egeland et al., in press).

Food security in the Arctic involves unique and more complex issues than food security in southern populations. Arctic communities rely heavily on traditional food, which plays a critical role in the health of people living in the Arctic. Not only does traditional food provide significant nutritional health benefits, the lifestyle for procuring and consuming traditional food is important for maintaining cultural values, identity, and social well-being (Chan, 2006). In many Arctic communities, traditional foods are an economic necessity as well as a vital element for good health. As a result, contamination of traditional food raises problems not only with respect to consumption and toxin exposure, but also by affecting the cultural way of life (Kuhnlein, 1995; Van Oostdam et al., 1999; Kuhnlein and Chan, 2000). In addition to the three common levels of food security (individual, household, community), Power (2007) suggested 'cultural food security' as a fourth level relevant to indigenous people in northern Canada, and probably also to other Arctic populations. Cultural food security might include indicators such as: traditional food knowledge, access to traditional food systems, and safety of traditional food (Power, 2007). Key factors affecting food security in the Arctic include: poverty and unemployment; food sharing networks; environmental contamination and global climate change; access to the land; traditional knowledge; cost, availability and quality of commercial market foods in remote communities; and the processing, marketing, and sale of traditional food (Kuhnlein and Chan, 2000; Duhaime, 2002; Paci et al., 2004; Guyot et al., 2006; Lambden et al., 2006; Power, 2007; Luick, 2008).

Studies in a few isolated indigenous communities in Arctic Canada have shown high prevalence of food insecurity, from 40% to 83% (Lawn and Harvey, 2003, 2004a,b; Boult, 2004), compared to 9% in non-indigenous households in 2004 (Health Canada, 2007). About 30% of Native American and Alaska Native households were food insecure, a value twice as high as for the rest of the U.S. population (Nord et al., 2007).

Food costs in most remote communities are easily double that of costs in accessible southern Canadian cities. Prominent barriers to food security mentioned by focus group participants included the costs of hunting, the limited income available after bills were paid, inadequate government support and involvement, as well as the many societal and individual changes that have occurred in recent times (Chan et al., 2006). In a survey evaluating access to traditional and imported food in 44 communities across the three Canadian territories involving Yukon First Nations, Dene, Métis, and Inuit women (n = 1771), some degree of food insecurity was noted throughout the communities surveyed. There was, however, considerable regional variability in the percentage of respondents indicating that they could afford adequate food (Lambden et al., 2006). Altogether, the literature speaks to the vulnerability of indigenous women to food insecurity and that factors associated with poor affordability of imported food, lack of accessibility to hunting and fishing equipment, and/or lack of a hunter in the family contribute to food insecurity.

3.4.2. Food hygiene

Climate change may affect the incidence of food-borne diseases in the Arctic as higher temperatures may result in increasing temperature-sensitive food-borne infections such as botulism. Animal populations may

also increase with a warmer climate and influence the spread of zoonotic infectious diseases to humans. Bears, walrus, certain types of seal, foxes and other wild animals can carry *Trichinella spiralis* (Appleyard and Gajadhar, 2000). If humans eat improperly cooked meat from these animals they may acquire trichinosis.

Food-borne botulism is caused by eating contaminated foods that contain a nerve toxin that is produced by the bacterium *Clostridium botulinum*. High incidence of botulism in Arctic areas of Canada, Alaska, and Greenland was accounted for by the preparation of traditional fermented foods, such as fish, seal, and whale (Parkinson and Butler, 2005). There is a hypothesis that there may be increases in food-borne botulism in these Arctic regions as a result of warmer ambient temperatures associated with climate change (Parkinson and Butler, 2005).

Cases of trichinosis have been reported in the medical literature in Arctic areas of Canada (Margolis et al., 1979; MacLean et al., 1989; Schellenberg et al., 2003), Greenland (Kapel, 1997; Møller et al., 2005) and Scandinavia (Kapel, 1997). A recent dissertation by Møller (2007) reported two small human outbreaks of trichinosis in Greenland in 2001/02. Risk factors associated with seropositivity of *Trichinella* included: age (+40 years), high intake of traditional food and polar bear meat, and living in hunting areas (Møller, 2007). The study also found a decline in seroprevalence over time and suggested that this was a reflection of the transition from consumption of game meat to industrialized food products. A primary prevention program for trichinosis was introduced in Nunavik in 1992 and led to the successful resolution of a trichinosis outbreak in 1997 (Proulx et al., 2002). For this program, all municipalities in Nunavik were offered the opportunity to test samples of meat from newly harvested walrus for the presence of *Trichinella* larvae. The samples were flown to a research center and results were communicated to the community as quickly as possible. Hunters were advised not to distribute or consume any of the meat until the samples had been analyzed. A pamphlet and video were also widely distributed to inform the public about trichinosis and hunters were trained in sample-collection procedures (Proulx et al., 2002).

In western Siberia, the prevalence of the helminth parasite (*Opistorchis felineus)* exceeds 50% in some populations. The larval form is spread through the consumption of some types of fish (Kozlov et al., 2007).

3.5. Conclusions and recommendations

Progress has been made in assessing the nutrient status, nutrient intakes, dietary quality, and exposure to food-borne contaminants in traditional food diets since the previous AMAP assessment of human health in the Arctic (AMAP, 2003). This progress has also been due to improvements in assessment quality (see Chapter 4). One result is that the view concerning traditional foods' contribution to the supply of vitamin A has become more favorable, but that the estimated intakes of vitamins A, D, and C, magnesium, iron, calcium, and folate in the indigenous populations tend to be lower than recommended, and nutritional deficiencies are prevalent in some Arctic populations.

Updated, accessible, and comparable information about nutritional intake is sparse from Arctic circumpolar populations outside Alaska, Greenland, and Canada, especially from Russia. Nevertheless, the decreasing proportion of traditional foods in the studied diets has had a negative impact on the intakes of most nutrients; usually accompanied by a negative cultural, social, psychological, and economic impact. On the other hand, imported foods appear to contribute positively to intakes of vitamin C, folate, and calcium, but underestimates of intake from traditional diets have been likely due to the wide variety of animal and plant species that such diets usually contain. Future studies concerning nutrient intake should also include assessments of consumption and nutritional contents of locally harvested plant food. Nevertheless, the nutritional status and intake appear to be of concern for children and youth; groups for which there has been widespread replacement of traditional food by a diet high in sugar and other foods with low nutrient density.

Ideally, information about nutrient and food intakes should be combined with assessments of dietary exposure to contaminants and contaminant levels in foods. However, total dietary assessments that include analyses of contaminant levels have only been carried out in Greenland and Canada. The findings indicated that large proportions of the studied populations in Greenland exceeded the TDI values set for chlordanes and Hg. Studies in other Arctic regions, undertaken on single food items from game, revealed relatively high levels of contaminants in marine mammals, especially polar bears and some seabird species. Organic contaminant levels in marine mammals are highest in the blubber, while Hg was found in highest concentrations in liver and kidney. Little is known about levels of contaminants in the liver of most fish species. The investigated contaminant levels in local marine food sources appear to be decreasing for PCBs and DDT in Arctic Canada and Russia and for PCBs in Greenland, whereas Hg seems to be increasing in Arctic Canada and northwestern Greenland.

It is not feasible to provide specific dietary recommendations that apply to all Arctic populations because the diet and local food sources, their role, amount consumed, and levels of contaminants in the biota vary to a large extent within and between populations and within and between areas of the circumpolar Arctic. More food-choice research in Arctic populations is needed in order to be able to provide effective dietary advice. In general, traditional foods, including fish, should be recommended and dietary advice about this food should be based upon local conditions and exercised with prudence, especially in indigenous populations, but people should be

informed about how they may lower their intake of contaminants. However, the use of Pb for ammunition should cease. Particular attention, both to nutritional quality of diet and exposure to contaminants through foods, should be given to children and pregnant women, who are at particular risk for adverse effects. Thus, additional item-specific and dietary-exposure studies and monitoring are needed in more populations and regions. A thorough discussion about public health relevance is provided in Chapter 9.

Chapter 4

Analytical Quality Assurance and Quality Control

Kristín Ólafsdóttir, Torkjel M. Sandanger, Jean-Philippe Weber

Summary

For more than two decades, researchers from AMAP countries have relied on the data produced by various laboratories to determine the exposure of Arctic populations to persistent organic pollutants (POPs) and heavy metals. In order to establish meaningful temporal trends and spatial distributions in exposure levels, the uncertainties resulting from variations in laboratory performance over time or among laboratories should be as low as possible. Given the analytical difficulties, variations of 20% or less are considered acceptable. If there are significant variations in the accuracy of results, the biases should be estimated, so as to enable the application of correction factors, or such data should at least be flagged.

Laboratories should therefore participate in intercomparison exercises on a regular basis to determine their performance, relative to that of their peers, in an objective manner. Several international external quality assessment schemes (EQAS) exist for metals in human biological fluids and laboratories should participate actively in one or more. This was not the case for POPs in human serum however, where no ongoing intercomparison program existed when the AMAP Ring Test was initiated in 2001 (with the exception of The German EQAS based at the Institute and Out-Patient Clinic of Occupational, Social and Environmental Medicine of the University Erlangen-Nuremberg). Laboratories producing AMAP data were required to participate in the AMAP Ring Test. Results indicated that performance between 2001 and 2007 was generally acceptable. Some biases were identified, however, especially when new compounds were introduced. It was shown that lipid determinations were very method-dependent, with gravimetric methods yielding significantly underestimated results.

The difficulties inherent in comparing data from several laboratories, with different detection limits, were illustrated by reference to the new Russian data on persistent toxic substances. The use of appropriate statistical techniques was crucial in allowing meaningful comparisons.

Emerging persistent compounds create new challenges for laboratories, requiring new analytical technologies and lower detection limits. To ensure comparability of data produced by different laboratories it is essential that EQAS be developed for these substances.

It is recommended that AMAP takes a more proactive role in ensuring that good quality data are produced by all contributing laboratories. AMAP should determine, promulgate, and enforce formal performance requirements for the measurement of POPs, including emerging compounds, and in future should accept data only from laboratories conforming with these performance requirements. It is also recommended that serum lipids be measured using standard enzymatic methods rather than gravimetric methods.

4.1. Introduction

Reliability of analytical data is essential to correctly assess health effects as well as to interpret temporal trends and spatial distributions. A number of laboratories from the AMAP countries are reporting contaminant levels in human samples. It is therefore essential to establish the quality and comparability of the data provided by these laboratories. The quality and comparability of the samples analyzed by the different laboratories is equally important; this issue lies outside the scope of the present chapter, however.

4.1.1. Demonstrating the quality of laboratory data

Two questions should be asked:

1. Does the laboratory have the potential for producing good quality data?

   This will include adequate infrastructure, appropriate equipment, trained personnel, and appropriate administrative and operating procedures, which can be verified by onsite inspection. Accreditation by the laboratory to a recognized standard, such as ISO/IEC 17025 (ISO, 2005), will ensure that the laboratory is in a position to produce good quality data.

2. Is the laboratory actually producing good quality data?

   The laboratory must be able to demonstrate that the procedures by which the data are generated are reproducible over time and that the data are accurate.

4.1.2. Precision versus accuracy

Precision and accuracy are two terms that may appear to convey the same information. However, in the field of measurement they have very specific and different meanings. 'Precision' refers to the repeatability or reproducibility of a measurement whereas 'accuracy' is the degree of conformity with the true value. An often-used illustration is the target, such as is used for darts. Precision is achieved when darts are closely grouped, wherever they lie on the dartboard. Accuracy describes closeness to the bullseye. For laboratory results, Figure 4.1 provides a more meaningful illustration of these two concepts.

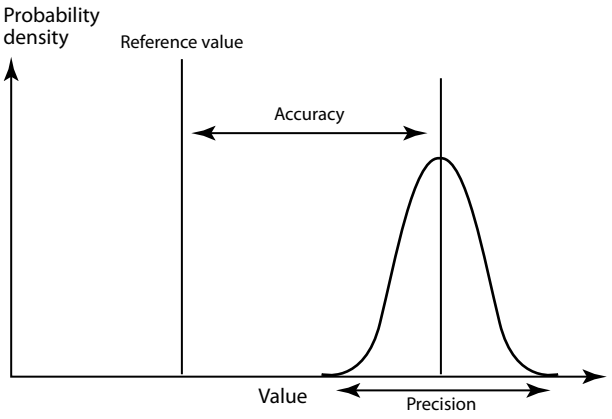


Figure 4·1. Comparison of precision and accuracy.

Laboratories are able to determine the precision of their analyses by repeatedly measuring the same sample under specified experimental conditions. 'Repeatability' is determined by performing the measurement under the same conditions (within a short time frame, on the same instrument, by the same operator). 'Reproducibility', a more meaningful parameter for estimating the precision attainable by the laboratory, requires that the measurements be performed under varying conditions (over several weeks, by different operators). A minimum of 20 replicates is considered adequate to estimate reproducibility.

Accuracy on the other hand, can only be determined by reference to an external standard (the reference value). There are two generally accepted means of determining the accuracy of a laboratory for a given analysis. The first is through the use of reference materials. A reference material is defined as a material for which one or more of its property values (e.g., concentration of the relevant analyte) are sufficiently homogeneous and well established that the material may be used to calibrate a piece of apparatus, to assess a measurement method, or to assign values to materials. Certified reference materials (CRMs), accompanied by a certificate, have one or more of their property values certified by a procedure which establishes its traceability to an accurate realization of the unit in which the property values are expressed and for which each certified value is accompanied by an uncertainty at a stated level of confidence.

Certified reference materials are available from producers such as the National Research Council of Canada, the U.S. National Institute for Standards and Technology, and the Institute for Reference Materials and Measurements (formerly the European Bureau Communautaire de Référence). By analyzing a CRM, a laboratory can compare its result with the certified concentration and thus determine its degree of accuracy. There are two potential problems with this approach: (1) an appropriate CRM (matrix-matched with analytes at relevant concentrations) may not be available, and (2) CRMs cannot be used to demonstrate a laboratory's accuracy objectively, because the target concentration was known by the laboratory prior to performing the analysis.

The second means of determining the accuracy of a laboratory for a given analysis is through participation in an EQAS, also known as a proficiency testing or interlaboratory comparison program. An EQAS functions by having a central laboratory, known as the scheme organizer, prepare batches of test material, aliquots of which are distributed to the scheme participants. Participants are allotted a certain period in which to analyze the samples and report their results to the organizer. Results from the participating laboratories are compiled and analyzed and a report is produced. The report evaluates the performance of the laboratories, which remain anonymous and are identified only by a code number.

4.2. Synthesis of quality assurance data obtained from the AMAP Ring Test, 2002 – 2007

The AMAP Ring Test is an EQAS that was initiated in 2001, with the objective of providing a means of comparing the quality of data produced by laboratories involved in the measurement of POPs in samples of human origin from Arctic countries (Weber, 2002).

4.2.1. A brief history of the AMAP Ring Test

The AMAP Human Health Assessment Group, concerned with the accuracy and comparability of data originating from laboratories, recommended in 2000 that a quality assessment (QA) program be established for POPs in human samples.

Owing to its 22-year continuous experience in organizing interlaboratory comparison programs for heavy metals in human biological fluids (Weber, 1996), the Centre de Toxicologie du Québec, was selected to implement the program. Initial funding was provided by Health Canada.

Preliminary trials were successfully undertaken with three laboratories: The Canadian Centre de toxicologie of the Institut national de santé publique du Québec, the American National Center for Environmental Health at the Centers for Disease Control and Prevention, and the Norwegian Institute for Air Research. A first round was conducted in 2001, with 32 participating laboratories recruited. To ensure high participation, this first exercise was free of charge. Three serum specimens were prepared; each spiked with PCB congeners 28, 118, 138, 153, 170, and 180 as well as DDT, DDE, and Mirex, and sent to laboratories in May. The initial deadline for reporting results was extended from 20 June to October, to enhance the response. Analysis of the data indicated good overall performance for this first round of the AMAP Ring Test, although some problems were apparent, notably with DDT and Mirex.

In 2002, a permanent structure was given to the AMAP Ring Test, including a published annual schedule of three rounds with specified deadlines. To ensure a sufficient pool of reporting laboratories, participation was extended to all interested laboratories regardless

of their involvement with AMAP. Oxychlordane and β-hexachlorocyclohexane (HCH) were added to the list of analytes, and Mirex was removed. Quantitative scoring criteria were introduced for formal evaluation of performance. The application of fees, necessary for self-funding of the program led to a decrease in participation. The performance of the remaining laboratories was generally very good. One of the samples sent to participants was actually NIST (National Institute of Standards and Technology) Serum Standard Reference Material 1589 for POPs in serum. Analysis of results from participants showed convincingly that some of the NIST-certified values were inaccurate. NIST was informed and eventually revised its certificate.

The most notable change in 2003 was the addition of toxaphene congeners Parlar 26 and 50. Excellent performance was observed for most participants. In 2004, participants were offered the option of reporting lipid results. It was noted that lipid results were significantly higher for laboratories using enzymatic methods, compared to those using gravimetric methods. A decrease in participation coincided with an increase in fees, despite the modest nature of this increase (around 20%).

In 2005, four new analytes were added, including two polybrominated diphenylethers (PBDEs) congeners (BDE47 and BDE99) and two organochlorine pesticides, *trans*-nonachlor and hexachlorobenzene (HCB). Although initially poor, the performance for PBDEs improved significantly after three rounds. No modifications were brought to the Ring Test for 2006 and overall performance remained at the same level.

There was a major overhaul of the program in 2007 with the introduction of several new analytes, bringing the total to 32. The new analytes were:

- Perfluorinated compounds (perfluorooctanoic acid [PFOA] and perfluorooctane sulfonate [PFOS])
- Three new PCB congeners (CBs 74, 99, 105)
- Six new PBDE congeners (BDEs 23, 100, 153, 154, 183, 209)
- Individual lipid components (free and total cholesterol, phospholipids, triglycerides)

To better analyze the new wealth of data generated, modifications were required to the scoring system. In line with other EQAS, the zonal scores were replaced by z-scores from which composite z-scores, the Rescaled Sum of z scores (RSZ) and the Sum of Squared z-scores (SSZ), could be calculated for each class of analytes, thereby enabling a better appreciation of the laboratories' strengths and weaknesses. Details of the calculation and interpretation of these two performance indicators are given in Appendix 4.1.

4.2.2. **Results from 2002 – 2007**

4.2.2.1. **Participation**

Participation has fluctuated over the years (Figure 4.2). Currently, 28 laboratories are registered participants.

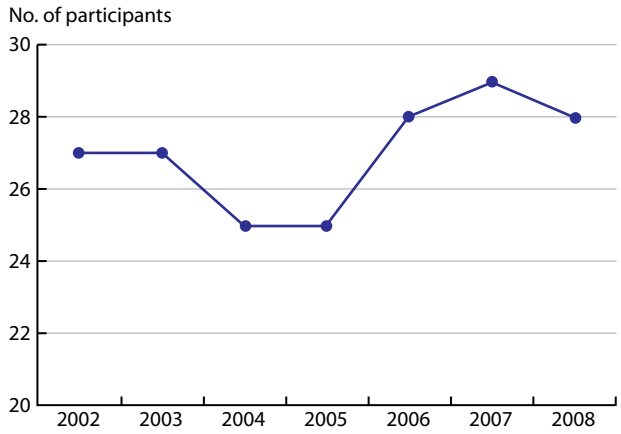


Figure 4·2. Trend in participation in the AMAP Ring-tests.

Of these, 21 are from AMAP countries, but only 12 are actually providing data for use by AMAP. It is also possible that some data provided to AMAP are produced by non-participating laboratories.

4.2.2.2. **Analytes**

Analytes for which performance is compiled are those for which a sufficient body of data exists.

4.2.2.3. **Performance (for each analyte) and overall performance trends**

Evolution of performance over time is illustrated for CB28 (Figure 4.3) and CB138 (Figure 4.4), using the Ring Test's criteria for good (within 20% of target) and acceptable (within 40% of target). Details of the performance calculation are given in Appendix 4.1. Briefly, each 'good' result yields two points and each 'acceptable' result yields one point. For each participant, all analyte scores are added and normalized. Thus a participant reporting all 'good' results would score 100%. The proportion of participants achieving these goals is plotted, using year-end performance for each year between 2001 and 2007 (for 2007, performance observed for the second round

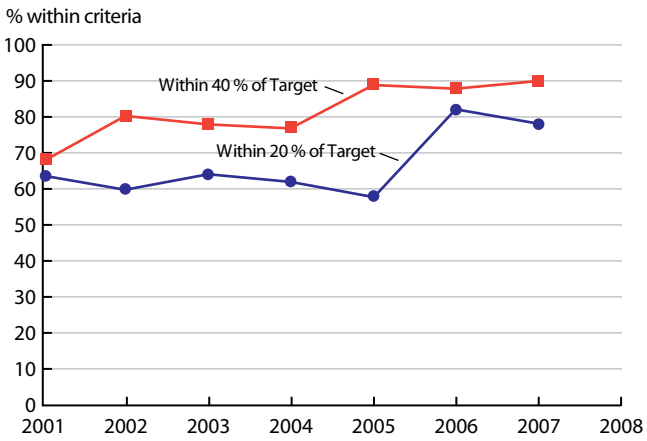


Figure 4·3. Performance trends for individual analytes: CB28. Data from all participants are plotted.

was used). Data from all participating laboratories was used, whether or not they were AMAP contributors.

For CB28, an example of a less-persistent PCB congener, the proportion of laboratories with acceptable and good results increased from 70% to 90%, and from 63% to 80%, between 2001 and 2007, respectively. For persistent PCB congeners, such as CB138 (Figure 4.4), the trend is even more pronounced. A similar trend is seen for most analytes, although year-to-year fluctuations may show surprising reversals (e.g., toxaphene).

4.2.2.4. **Individual performance**

A more relevant measure may be the performance of an individual laboratory contributing data to AMAP. It is particularly important to determine whether biases exist, that is, whether a laboratory consistently over- or underestimates their results over time, because this will affect the comparison of data from different laboratories (and thus, ultimately, countries). To measure bias, the RSZ was calculated for the different chemical families (PCBs, organochlorine pesticides, toxaphenes, and PBDEs, as well as for total serum lipids, this last parameter being used to normalize results with respect to individual fluctuations in lipid levels) for each laboratory. As an example, Figure 4.5 shows the individual RSZs for the 17 rounds between January 2002 and June 2007 for a participating laboratory with a good performance (one whose performance is better than the mean). To be acceptable, results must lie between −2 and +2, corresponding to a ± 40% difference from the target value. More importantly, the data should not lie consistently on the same side of the 0-ordinate as this would indicate systematic error, or bias over time. For PCBs, this representative laboratory generated data that were generally acceptable but were overestimated from 2004 to the beginning of 2005 (Figure 4.5). Data for organochlorine pesticides were almost always within the acceptable range. The PBDE and toxaphene data were very close to the target value and within the acceptable range of ± 2 z.

A more detailed appreciation of a laboratory's performance is achieved by examining the data for individual analytes. Figure 4.6 shows the performance of the example laboratory for nine PCB congeners. In this case, sequential sample numbers, rather than round numbers are plotted on the x-axis. Since each round comprised three samples, the number of data points plotted is correspondingly higher.

4.2.2.5. **Lipid measurements**

Levels of POPs in human serum are routinely reported on a lipid-adjusted basis, as a means of reducing intra- and inter-individual variations. The rationale for this adjustment is that POPs levels in circulating lipids are in equilibrium with those in stored body fat. This, however, necessitates the measurement of circulating lipids, with the potential for additional error. To determine whether participating laboratories were capable of reliably

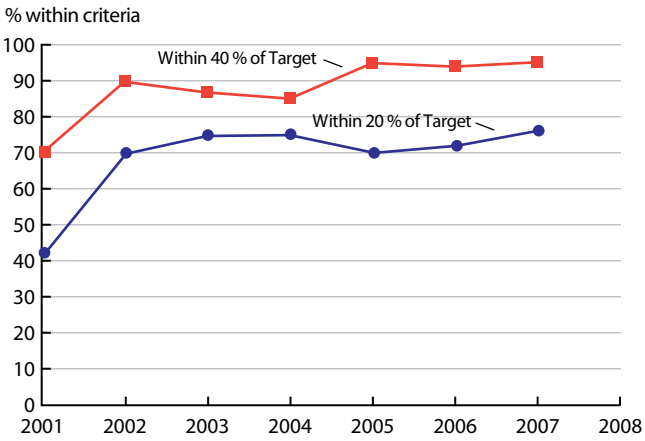


Figure 4.4. Performance trends for individual analytes: CB138. Data from all participants are plotted.

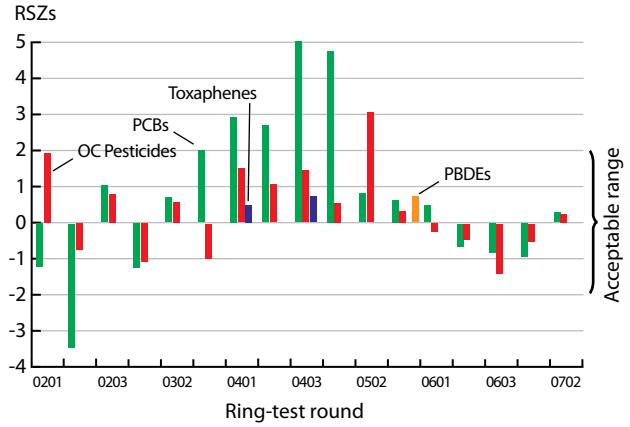


Figure 4.5. An individual participant's performance using RSZs.

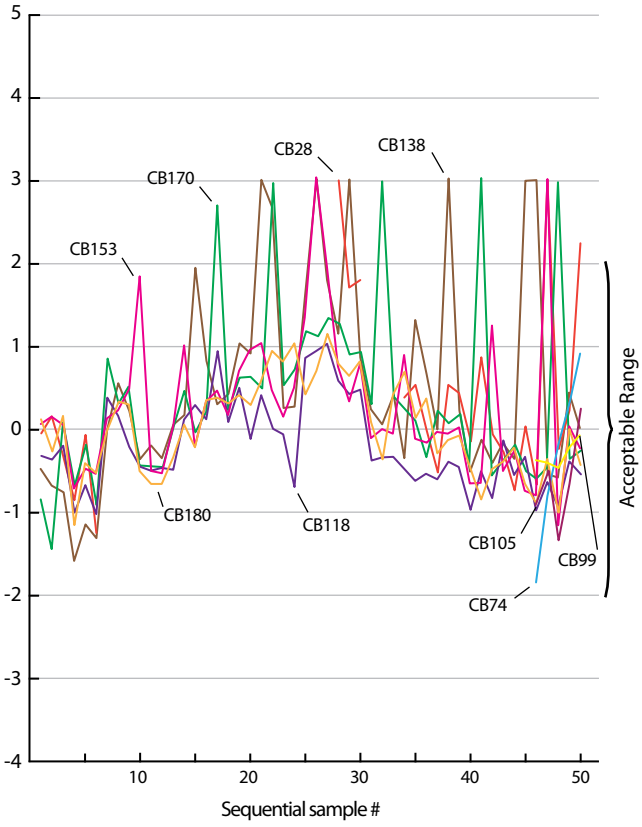


Figure 4.6. Individual PCB congener performance over time.

measuring lipids, this parameter was introduced into the Ring Test in 2004.

Lipids in blood are usually determined by gravimetric or enzymatic methods. The latter measures some or all of the individual lipid components which are then summed using various formulae. For gravimetric methods the lipids are extracted from the serum matrix, and the extract is then dried and weighed.

Overall performance for lipid determination improved between 2004 and 2007 (Figure 4.7). The performance criteria were the same as for POPs, that is, good (within 20% of target) and acceptable (within 40% of target).

However, overall performance is no predictor of individual bias. Figure 4.8 compares the lipid results from two laboratories between 2004 and 2007. It is clear that one laboratory had a tendency to overestimate lipid levels by 20% to 30% between 2004 and 2006, while the other underestimated lipid levels by 30% or more over this period. Both laboratories appear to have improved during 2007. These systematic differences are fraught with consequence, because even if the laboratories had generated identical POPs measurements, the lipid-adjusted results would be 50% higher for the laboratory underestimating lipid levels.

Gravimetric methods are most suited to matrices that are rich in lipids (e.g., fatty tissues, milk) and where sufficient sample volume is available for analysis. This is clearly not the case with blood serum or plasma, where the sample available for lipid determination is generally less than 0.5 mL. Extracting, drying, and weighing the lipids from such a tiny sample volume requires great technical proficiency and is thus very operator-dependent.

Enzymatic methods are performed on a routine basis by clinical laboratories all over the world to evaluate the health status of individuals based on their blood lipid status. Such methods require small quantities of plasma or serum (<0.1 mL). These routine measurements include two major categories of circulating lipids: total cholesterol and triglycerides. The other major category of circulating lipids, phospholipids, is less frequently analyzed, but is available from specialized clinical laboratories. This is also the case for free cholesterol. Clinical laboratories generally measure lipids using automated laboratory analyzers and proprietary technology available from clinical instrument manufacturers. These instruments have built-in quality control. Clinical laboratories in North America and Europe are also required to participate successfully in EQAS.

Lipid results submitted by participants in the AMAP Ring Test between 2004 and 2007 show that enzymatic methods generally yield higher results than gravimetric methods. This is illustrated in Figure 4.9 where the ratio:

$$(E/G) - 1 \qquad (4.1)$$

where E= mean enzymatic results and G = mean gravimetric results, has been plotted for 18 samples analyzed during 2006 and 2007. For 14 of the 18 samples, enzymatic results were significantly higher (10% to

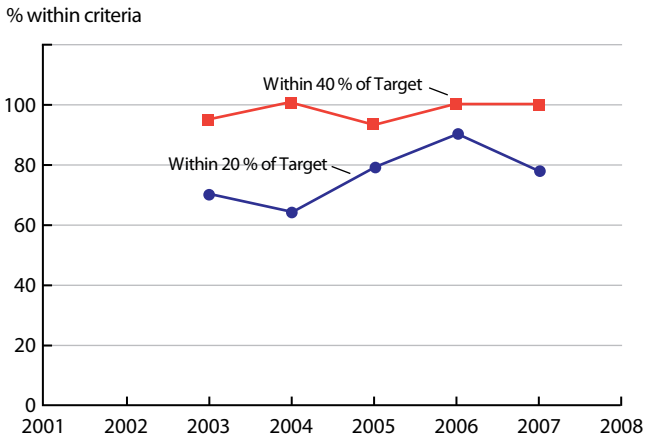


Figure 4·7. Lipid analysis performance over time. Data from all participants are plotted.

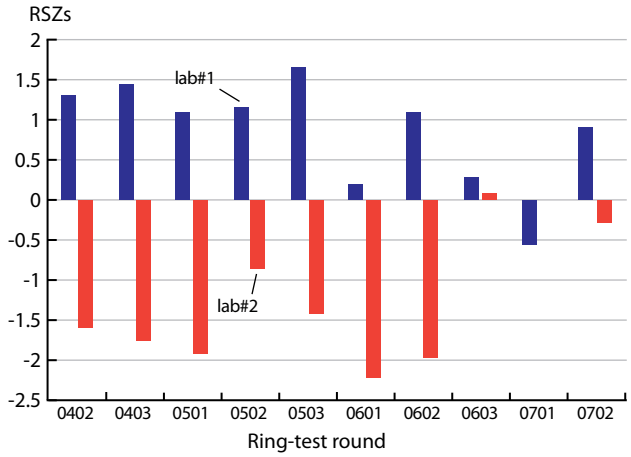


Figure 4·8. A comparison of lipid results for two laboratories.

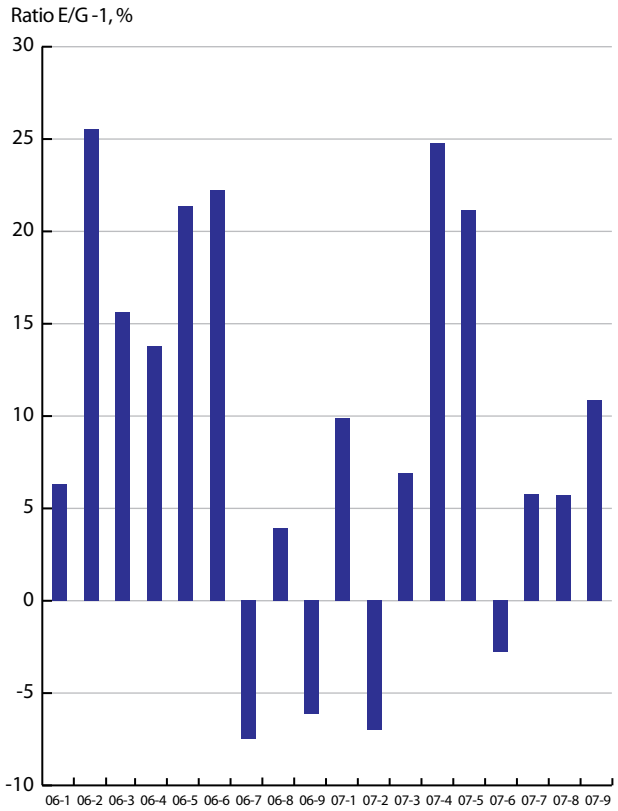


Figure 4·9. Comparison of total lipid results obtained from gravimetric and enzymatic methods.

25%) than the gravimetric results, whereas gravimetric results were higher (~ 7%) in the four remaining cases. The data also show that there is less variability among laboratories using enzymatic methods.

4.2.2.6. **Comparing enzymatic lipid results**

Total serum lipids are determined by summing the individual lipid components. When all four major lipid categories are measured the following equation can be used:

$$TL = 1.677 \times (TC - FC) + FC + TG + PL \text{ (Akins)} \quad (4.2)$$

where TL is total serum lipids, TC is total cholesterol, FC is free cholesterol, TG is triglycerides, and PL is phospholipids. This equation was derived at the American National Center for Environmental Health at the Centers for Disease Control and Prevention (Akins et al., 1989) after a comparison of gravimetric and enzymatic results for human blood pools. It yields results essentially identical to those from the gravimetric method and is used by at least two AMAP laboratories in evaluating lipid values.

Because phospholipid measurements are not always available, efforts have been made to evaluate alternative methods of obtaining total serum lipids, using only total cholesterol, free cholesterol, and triglyceride data.

Phillips et al. (1989) devised a 'short' formula for estimating total serum lipids using only total cholesterol and triglyceride measurements:

$$TL = 2.27 \times TC + TG + 0.623 \text{ (Phillips)} \quad (4.3)$$

Rylander et al. (2006) showed that 97.2% of the variation in total serum lipids could be explained by the sum of the triglyceride and cholesterol concentrations. They thus proposed to calculate total serum lipids from total cholesterol and triglycerides using the following equation:

$$TL = 0.9 + 1.3 \times (TC + TG) \text{ (Rylander)} \quad (4.4)$$

Covaci et al. (2006), using multiple linear regression on a large data set of lipid measurements from Belgium, arrived at another short formula using triglycerides and total cholesterol:

$$TL = 1.33 \times TG + 1.12 \times TC + 1.48 \text{ (Covaci)} \quad (4.5)$$

Bernert et al. (2007) measured the four lipid components on 899 stored blood samples and compared the performance of the preceding 'short' equations in predicting total lipids. They concluded that the Phillips equation (eqn. 4.3) provided results similar to those from the Akins method (eqn. 4.2), and that both the Rylander (eqn. 4.4) and the Covaci (eqn. 4.5) equations underestimated the total lipid concentration by 15% to 25%.

The same conclusion was obtained by The Canadian Centre de toxicologie of the Institut national de santé publique du Québec (LeBlanc, A., pers. comm., 2008) when comparing these equations on lipid data obtained from 212 human serum specimens. Figure 4.10 shows that the Phillips-calculated lipid data are well correlated with the Akins-calculated lipid data ($r^2 = 0.99$), with a slope close to 0.96, almost coincident with the diagonal. The other two equations are less well correlated and more importantly deviate significantly from the ideal slope.

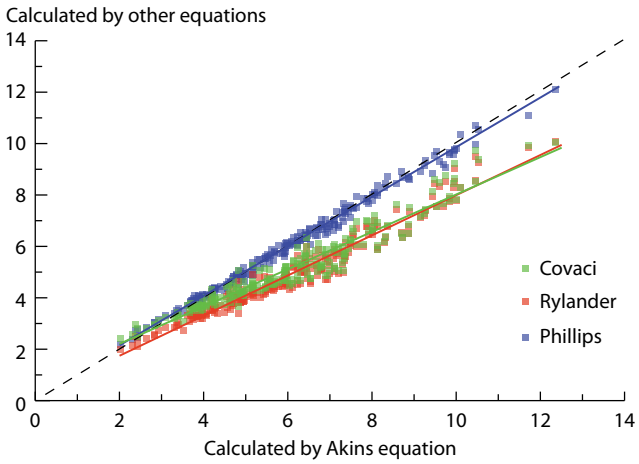


Figure 4.10. Calculation of total lipids in serum from enzymatic data.

4.2.3. **Overall discussion of the Ring Test**

The proficiency of participants in the AMAP Ring Test is determined from the proportion of laboratories within different scoring categories. To this end, participants were assigned to four performance categories: excellent (90% or above), good (70% to 90%), acceptable (60% to 70%), and need improvement (below 60%).

Changes in performance for the 14 rounds undertaken between 2002 and 2006 are shown in Table 4.1. Data for 2007 were not included in the table because the program was revised considerably at the start of 2007, with new analytes added, which makes a comparison of performance with previous years difficult. Although performance clearly fluctuates, there is a definite trend toward the proportion of laboratories showing excellent or good performance increasing slowly with time. This is illustrated in Figure 4.11, which shows a modest increase in performance over time, and with 80% of participating laboratories achieving good or excellent performance after the first two years of the Ring Test. However, this is a gross measure of overall performance which cannot address individual variations.

For the purpose of AMAP data comparability, it is more useful to examine the performance of individual participants, for each of the analytes. Fluctuations in performance are to be expected, both within and between laboratories. As long as there is no systematic over- or underestimation by a particular laboratory, or during a particular period, these fluctuations should have relatively little effect on the conclusions drawn from the composite data. However, if results from a laboratory are systematically under- or overestimated (i.e., biased), then the subject data will be correspondingly affected.

Table 4·1. Performance (%) over time in the AMAP Ring Test.

Round	Excellent, ≥90%	Good, 70-90%	Acceptable, 60-70%	Need improvement, <60%
2002-1	24	36	12	28
2002-2	21	49	14	16
2003-1	38	24	10	29
2003-2	32	32	14	23
2003-3	35	35	10	20
2004-1	43	43	0	14
2004-2	37	53	0	10
2004-3	37	26	5	32
2005-1	38	48	-	14
2005-2	38	38	24	-
2005-3	39	48	-	13
2006-1	54	21	4	21
2006-2	35	30	13	22
2006-3	33	50	-	17

To help determine whether bias is present and to what extent it may affect results, individual performance of selected laboratories (those known to be suppliers of data to researchers within the AMAP Human Health Assessment Group) was examined over the period 2002 to 2007. The following analytes were examined for bias or unusual fluctuations: PCB congeners 28, 118, 138, 153, 170 and 180; the organochlorine pesticides DDE, DDT, HCB, HCH, *trans*-nonachlor, oxychlordane, toxaphene congeners Parlar 26 and 50; and total serum lipids. The results, which are summarized in Table 4.2, should be useful to those whose task it is to compile and compare data from the various AMAP regions.

The AMAP Ring Test has been very useful in evaluating laboratory proficiency with respect to the measurement of PCBs and organochlorine pesticides in serum, over its first six years of operation. The program has clearly helped laboratories to improve their analytical quality and its continuation is encouraged, especially as no comparable program exists. It can be concluded that the laboratories that produce data for AMAP monitoring purposes generally do so with acceptable quality. However in some cases, biases were identified and these should be taken into account when comparing data between regions and over time.

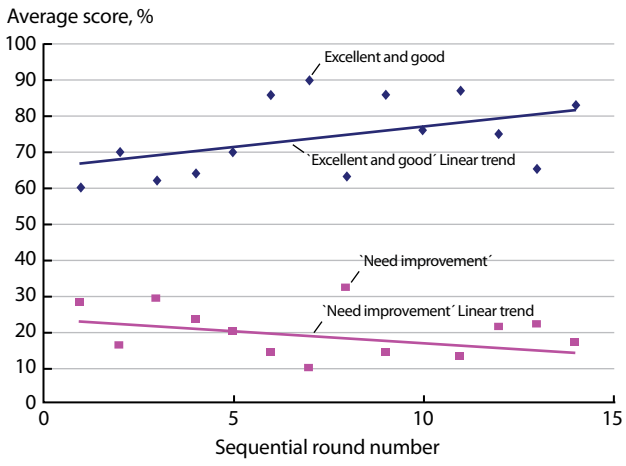


Figure 4·11. Performance trends for POPs 2002 to 2006.

For serum lipids, the program demonstrated convincingly that results were very method-dependent and that to accurately measure lipid levels in human serum requires the use of enzymatic methods. Gravimetric methods are difficult to apply to the very small sample volumes (typically 0.5 mL or less) available and often lead to underestimated levels. The 'gold standard' in serum lipid determination requires the measurement of four components: total cholesterol, free cholesterol, triglycerides, and phospholipids. Because phospholipids, and to a lesser extent free cholesterol measurements are not widely available, formulae linking total serum lipids to total cholesterol and triglycerides have been proposed by several authors. The Phillips formula (eqn. 4.3) best approximates results from the reference Akins formula (eqn. 4.2).

4.3. QA for metals

In contrast to the situation for POPs in human samples, several international EQAS exist for metals in biological fluids, as well as a number of national schemes (for which participation is usually restricted to within-country laboratories). International schemes include:

- The UK Trace Element Quality Assessment Scheme (University of Surrey, Guilford)
- The German External Quality Assessment Scheme (Institute and Out-Patient Clinic of Occupational, Social and Environmental Medicine of the University Erlangen-Nuremberg)
- The Interlaboratory Comparison Program for Metals in Biological Matrices (The Canadian Centre de toxicologie of the Institut national de santé publique du Québec)
- The Quebec Multielement External Quality Assessment Scheme (The Canadian Centre de toxicologie of the Institut national de santé publique du Québec)

National EQAS are operated within many countries, including France, Belgium, Spain, Italy, the UK and the United States. Most of these schemes have been operating for a decade or more, and so laboratories analyzing heavy metals in human biological fluids and tissues have had the opportunity to validate the quality of their results by participating in these schemes. It is accepted practice for laboratories working in this field to do so.

Performance criteria vary among schemes. Some criteria are embedded within national legislation whereas others are determined by clinical relevance and achievable performance. In an attempt to harmonize performance criteria, the Organizers of EQAS for Occupational and Environmental Laboratory Medicine, regrouping intercomparison programs from

Table 4-2. Observed bias and variability in AMAP Ring Test: 2002 to 2007.

Laboratory Code	PCB congeners		
	CB28	CB118	CB138
2003	Slight negative bias (<10%).	2003: −10%; 2004-5: −15%; 2006-7: −10%.	2002 to 2003: variable (+ or −) 2004 to 2007: −20%.
2004	OK	OK	2002-3: OK; 2004: many high values >40% over target, some >60%; 2005-7: generally OK, occasional very high values (>60%).
2008	OK	OK	OK
2014	Variable: many missing data points.	OK	OK (three high spikes, >60% over target).
2015	Many missing data points (all PCBs).	Generally OK	High spikes
2017	2002, 2004: five low values (−20–30%). 2006-7: +10–20%.	OK	OK
2019	Participated only in 2002: variable results for all analytes.	See CB28	See CB28
2023	OK, three high spikes and some variability.	OK	OK
2024	Participated only twice, first round each of 2002 and 2003: limited number of analytes: data not useable.	See CB28	See CB28
2028	Participated 2002 to 2005: very variable, some >06% over target, others <60% below.	Very variable, generally high (seven >60% above).	OK but some high spikes.

Laboratory Code	Organochlorine pesticides			
	DDE	DDT	HCB	HCH
2003	−20% but variable.	2002: very high (+60% and more); 2003-4: OK; 2005: −20%; 2006-7: very variable (+ and −); Data not useable for this analyte.	−15%.	OK
2004	OK	OK	OK	OK
2008	OK	2002-3: −10%; 2004-2005 (first round): OK; 2005(second round) to 2007: −20%.	OK	2002-2005 (first round): OK; 2005 (second round) to 2007: −20%.
2014	OK	OK	Insufficient data.	OK
2015	Many missing data points (all organochlorines). Generally OK	OK	OK	OK
2017	OK	OK but four high spikes 2002 – 2005. (>60%)	OK	OK
2019	See CB28	See CB28	See CB28	See CB28
2023	OK	2002: very variable; 2003: OK; 2004 (first two rounds): −20%; 2004 (last round) to 2005 (second round): +15%; 2005 (third) to 2006: +20–30%; 2007 (round two) ~ −10%.	~ −10%	OK
2024	See CB28	See CB28	See CB28	See CB28
2028	Variable	Variable 2002-4, generally high (+20–60% above) 2005-6: variable.	Few data points, high.	Variable

PCB congeners		
CB153	CB170	CB180
Variable but OK	2002 first two rounds: OK; 2002 last round to 2003 second round: −40%; 2003 third round to 2004 first round: OK; 2004 second round to end 2004: −30%; 2005 first two rounds: OK; 2005 third round to 2006 first round: −20%; 2006 second round to end 2006: OK; 2007: −40%.	Generally follows CB170 but with reduced amplitude.
OK	OK but several high values > 60% above target (5 in all over 6 years).	OK
OK	OK	OK
OK	Variable, generally close to target, five high spikes (>60% above).	2002 to mid-2006: OK; 2006 (two rounds): ~+40%; 2007: OK.
OK	OK	OK
OK	OK	OK
See CB28	See CB28	See CB28
OK	OK but four high spikes.	2002–2003: −20%; 2004: −10%; 2005–2007 : -20%.
See CB28	See CB28	See CB28
+10 %, some variability.	−20% but variable.	OK

Organochlorine pesticides		Toxaphenes	Lipid
trans-Nnonachlor	Oxychlordane	Parlars 26 and 50	
2002-2004 no data; 2005-2007: OK.	−25 to −30%.	OK	OK
OK	OK	Insufficient data.	2006-7 only: +10%.
OK	OK	OK	2004-2005: +20%; 2006-7: OK.
OK, but many missing data points.	2002: OK; 2003: low, −20%; 2004: high (+60%); 2004 (third round) to 2005: no data; 2006 (one round): >60% above target; 2007(round 2): OK.	Many missing data points. 2006-7: high by 20−30%.	No data
OK	OK	Extremely sparse data but OK.	No data
OK	OK	OK	No data
See CB28	See CB28	No data	No data
2005-7: −30 to −60%.	Some variability	2003-5: OK; 2006-7: −20%; (P26 OK for 2nd round 2007).	2004-2006 (round two) −20 to −25%; 2006 (third round) to 2007: OK.
See CB28	See CB28	No data	No data
No data	−20%, variable.	Few data points, variable.	OK (2004-5).

ten countries, has published guidelines for medical surveillance and laboratory measurement of lead in blood and air (Taylor et al., 2007; Arnaud et al., 2008). The group is examining performance for other metals of toxicological interest and will be issuing further guidelines.

4.4. Synthesis of QA/QC data for new Russian data

Four laboratories in Russia analyzed samples and supplied data for the AMAP assessment on persistent toxic substances, food security, and indigenous peoples of the Russian North (AMAP, 2004b). For POPs, three of the four laboratories participated in the AMAP Ring Test, and demonstrated acceptable performance. There has been no external quality control of results from the fourth laboratory.

The laboratories analyzed a different number of samples from each region. This complicated the statistics considerably because potential differences between laboratories could be interpreted as differences between regions. A significant challenge in combining these data into a single database concerned the differences in detection limits and how to replace values below detection limits. Two of the laboratories analyzed 2 mL samples only, whereas the other two analyzed samples of 2 mL to 6 mL and so had much larger variation in their detection limits. In addition to variations resulting from different plasma volumes, instrumental differences also influence detection limits. On the basis of work by Anda et al. (2007), a conservative approach was chosen for this assessment using the detection limits achieved when analyzing 2 mL samples. Values below the highest detection limit (LOD) were replaced by: $1/\sqrt{2}$ LOD values, for all compounds.

Although this conservative approach reduced the amount of information held in the dataset, it also reduced the chances of drawing erroneous conclusions. For some congeners, in particular those with low detection frequency, this could influence mean values. In accordance with accepted practices, statistical analysis can be performed on raw data (expressed here as mass of analyte per volume of serum, i.e., wet weight) for all congeners for which the detection frequency was above 70%. Care must be taken when stratifying the data that no single group or category has a frequency of more that 60% below the detection limit.

A comparison of wet weight values between laboratories and regions gives no indication of values that are unreliable and too high. There is thus no systematic error for any of the laboratories in overestimating levels. The majority of the wet weight data could therefore be merged and treated statistically when using the conservative detection limit approach.

It was however not possible to perform comparisons on lipid-adjusted data because of the variability in the measurement of lipids. Two laboratories determined lipids enzymatically, while the other two determined lipids gravimetrically. Analysis of the lipid weight data revealed that at least one of the laboratories was systematically underestimating lipids, relative to what is expected in human plasma samples. In fasting samples the lipid level is expected to be between 0.45% and 1.0%. Taking into account that the individuals were not fasting when the samples were obtained, the lipids would be expected to be higher than the reference values. However, 45% of the data from this particular laboratory had lipid values of below 0.3%. These data were not added to the lipid-adjusted database. Underestimation of lipids was confirmed by the AMAP Ring Test results, even though the Ring Test data were not from the same time period as the samples analyzed.

On this basis, it is advised that no statistics should be undertaken on the lipid-adjusted data. Alternatively, an arbitrary lipid value, such as the known mean lipid level in that population could be assigned to the individual results. This would enable comparisons with results from other countries. Regional comparisons can probably be made for some compounds. As for the wet weight data, statistics can be performed on compounds for which more than 70% of results are above the detection limit.

4.5. Compiling and synthesizing QA/QC data for emerging compounds

Most of the 'legacy' POPs have now been banned or their use severely curtailed. However, many new compounds are being developed, some of which are sufficiently persistent to accumulate in the environment. Monitoring the presence of these 'emerging' compounds in human tissues is important to allow policy makers to take appropriate measures and so avoid health risks in exposed populations.

Although there is still discussion about their relative importance or actual threat to human health, some of the emerging compounds of concern include:

- Brominated flame retardants, a generic class which includes the following: tetrabromobisphenol-A (TBBPA), hexabromocyclododecane (HBCD), polybrominated biphenyls (PBBs), and polybrominated diphenylethers (PBDEs). PBDEs are currently of greatest interest.
- Perfluorinated chemicals, including PFOS, PFOA, and perfluorohexanesulfonate (PFHS)
- Bisphenol-A (BPA)
- Alkylphenols
- Phthalates

This list is not exhaustive; as these compounds are identified and possibly phased out, other, substituent compounds could turn out to have a greater impact on health. The three latter groups of compounds are not lipophilic and are better investigated in urine.

Measuring these emerging chemicals poses challenges for analytical laboratories. Biological levels are mostly very low, thus straining the capability

of even sophisticated analytical instrumentation. Some compounds (e.g., PFOS) require measurement technology that is not currently available in many laboratories. Presently, only a few laboratories have sufficient experience in analyzing these compounds to produce reliable results. The paucity and cost of analytical standards and reference materials are significant obstacles to improving the situation.

There is clearly a need to monitor prospectively the performance of laboratories measuring these chemicals in human biological media. The AMAP Ring Test responded to the challenge by adding PBDEs and perfluorinated chemicals in 2007. However, consideration should be given to providing external quality assurance for a larger range of emerging compounds.

4.6. Conclusions and recommendations

Monitoring of population exposure to persistent environmental toxicants requires laboratory data of high quality. For the evaluation of spatial distribution and temporal trends, it is essential that data obtained over time, and by different laboratories be consistent and comparable. An EQAS is the only practical means of evaluating quality of data among laboratories. For POPs in human serum, the AMAP Ring Test, an EQAS which has operated since 2001, has allowed an evaluation of laboratory performance and has been instrumental in improving the quality of data generated by the laboratories.

Data from an EQAS can be used to identify systematic error or bias by examining the long-term performance of each participant. Analysis of the data submitted by participants in the AMAP Ring Test has not shown any significant bias between the laboratories for the measurement of POPs.

Accurate measurement of serum lipids is of paramount importance, because any error in evaluating this parameter will be reflected in the lipid-adjusted result. It is clear that gravimetric methods are not sufficiently reliable for this purpose. It is therefore recommended that AMAP-reporting laboratories determine serum lipids using enzymatic methodology (routinely available in most clinical laboratories). Ideally, the four principal lipid components should be measured, and the Akins formula applied to the results. If phospholipid determination is not available, applying the Phillips formula to the total cholesterol and triglyceride results should yield comparable results for total serum lipids.

Accurate determination of heavy metal levels in serum is achievable in qualified laboratories. To ensure quality of results, laboratories supplying analytical results to AMAP-related human health research, for heavy metals in blood, urine, hair, or other human biological tissues should participate in a recognized EQAS which offers an ongoing quality assessment for the analytes of interest. Several recognized EQAS exist in Europe and North America. Some restrict participation to laboratories within their own country; others are open to all comers. Organizers of open schemes include, among others, the Institute and Out-Patient Clinic for Occupational, Social and Environmental Medicine of the University Erlangen-Nuremberg (German External Quality Assessment Scheme for Analyses in Biological Materials, http://www.g-equas.de) and the Institut national de santé publique du Québec (PCI and QMEQAS, http://www.inspq.qc.ca/ctq/paqe). Information on other schemes can be found on the EPTIS website (http://www.eptis.bam.de) which contains a worldwide database of ISO-43 accredited EQAS. Laboratories should make available to their clients the periodic performance evaluations received from the EQAS organizers.

4.6.1. Striving for higher quality results

Since 2002, laboratories providing data to AMAP have been encouraged to participate in intercomparison programs, such as the AMAP Ring Test. Although this has had a beneficial effect on laboratory performance, there is no guarantee that all laboratories have generated accurate and bias-free results.

It is important that AMAP is able to demonstrate convincingly to its partners and clients (including the United Nations Environment Programme and the World Health Organization) that observed trends are real. It is therefore recommended that AMAP takes a more proactive role in ensuring that laboratories provide accurate data for all measured substances, including heavy metals, legacy POPs, and emerging contaminants. This will entail:

1. Promulgating acceptability criteria for laboratory measurements of contaminants in biological matrices, for AMAP trend monitoring purposes.
2. Enforcing these criteria by requiring laboratories to demonstrate their proficiency before accepting data for AMAP purposes.
3. Ensuring that an adequate EQAS for emerging POPs or other emerging contaminants of concern, persistent or not, is available to laboratories.

To implement item 1, it is recommended that the AMAP Human Health Assessment Group be tasked with establishing performance criteria for contaminants in human biological media, based on best available technology and currently achievable performance.

Implementation of Item 2 will need to be discussed: It will require that all AMAP countries agree to police their national laboratories, or to defer this task to a mandated body.

The AMAP Ring Test has financed its operation solely through the contribution of participating laboratories. Because there is only a limited number of participants, addition of new analytes is not economically feasible in the current situation. AMAP might find it a wise and profitable investment to contribute recurring financial aid to ensure the viability and continued development of the Ring Test.

Appendix 4.1

Preparation of Material, Assigned Values, and Performance Parameters for the AMAP Ring Test

A.1. Preparation of proficiency testing material

Proficiency test materials (PTMs) are prepared in-house from blood obtained from healthy, non-exposed volunteers. Analytes, as well as potential coeluants are added in appropriate amounts to the serum matrix. Individual aliquots of 5 mL of serum are then prepared and tested for homogeneity. PTMs are kept frozen at −20 °C until needed.

A.2. Determination of assigned values

The assigned value is usually determined using the median of the data reported by participants, after removing outliers, which are determined by calculating the median absolute deviation (MAD), a robust estimator of the dispersion of values, and applying Hampel's test (Bednarova et al., 2006). In exceptional cases, other means must be used to determine the assigned values. These cases include: (1) abnormal distribution of data (e.g., bimodal); (2) the use by participants of biased methods, or methods subject to interferences; (3) the inability of some participants to measure low levels of the analyte; and (4) the PTM being a duplicate. In this case, the assigned value determined in the initial round will be used.

For the other cases, the assigned value will be determined taking into account the following factors: (1) formulation (i.e., the known spiking concentration); and (2) results from participants with previous good performance or not affected by the presence of a coeluant. In these cases, the justification for not using the median as the assigned value will be indicated following the table below.

A.3. Performance criteria and calculations

Performance is evaluated using a zonal system (Taylor et al., 1986) by which results within ± 40% of the assigned value are attributed 1 point and those also within ± 20% are attributed another point, for a maximum of 2 points per result. These two levels were chosen as being indicative of good and acceptable performance respectively. The annual participant's score, expressed as a percentage is therefore calculated as:

$$Score(\%) = 100\left(\sum_{i=1}^{n} p_i\right)/2n$$

where p represents the participant's score (0,1, or 2) for each result submitted.

A.4. Combining z-scores to evaluate laboratory proficiency for a class of analytes

Individual z-scores for each laboratory are combined within a chemical class (e.g., PCBs, or organochlorine pesticides) yielding the two composite scores RSZ (rescaled sum of z scores) and SSZ (sum of squared z-scores), which are both indicators of the overall laboratory proficiency for the specified chemical class (SSC, 1995). The RSZ, calculated as:

$$RSZ = \sum_{i=1}^{n} Zi/\sqrt{n}$$

where n = number of scores being combined, uses the signs of the z-scores to detect bias in an analytical system. The SSZ, calculated as:

$$SSZ = \sum_{i=1}^{n} Zi^2$$

SSZ does not take into account the signs of the z-scores and detects abnormally high deviations from the assigned value, whether positive or negative.

The RSZ and SSZ are complementary scores and both must be acceptable for a laboratory to be considered proficient. The RSZ is interpreted using the same scale as for the individual z-scores. However, it must be noted that the RSZ will magnify trends. The SSZ has a chi-squared distribution and will be interpreted using a chi-squared distribution table at the 95% confidence limit with n degrees of freedom.

In order to avoid undue emphasis on an isolated poor result, z-scores greater than +3 or less than -3 are assigned values of +3 and -3 respectively.

RSZ* range	Rating
RSZ ≤ 2	Good
2 >RSZ≤ 3	Satisfactory
3 > RSZ ≤ 4	Questionable
RSZ ≥ 4	Unsatisfactory

* Absolute value of RSZ.

Chapter 5

Human Tissue Levels of Environmental Contaminants

Jay Van Oostdam and Shawn G. Donaldson

Summary

This assessment is the third AMAP assessment of human health in Arctic regions but is the first to contain initial trend data for some organochlorines and metals. The assessment also incorporates the first comparison of all Russian Arctic regions as part of a circumpolar human health assessment.

Concentrations of environmental contaminants that are linked to marine mammal consumption continue to be elevated in Inuit regions of Greenland and Canada compared to other populations in the circumpolar region. The new data for the Chukchi and Inuit peoples of the coastal Chukotka region in Arctic Russia indicate that concentrations of polychlorinated biphenyls (PCBs) and oxychlordane are similar to concentrations among Inuit from Greenland and Arctic Canada. New data from Arctic Russia also indicate that dichlorodiphenyldichloroethylene (DDE) and dichlorodiphenyltrichloroethane (DDT) are elevated in both indigenous and non-indigenous populations.

Initial data are available for Arctic Canada, Greenland, Iceland, Sweden, Finland and Russia to assess the change in contaminant concentrations over time. Many of these data indicate that concentrations of contaminants such as PCBs, oxychlordane, and mercury (Hg) are decreasing in a broad range of Arctic populations.

Guidelines are available for concentrations of PCBs, Hg, and lead (Pb) in blood. Inuit from the high Arctic that consume marine mammals continue to have higher proportions of the population that exceed these guideline values. In parallel with the decreases in the concentrations of PCBs and Hg in Arctic mothers, the proportion of mothers exceeding these guidelines is also decreasing.

In addition to the legacy POPs monitored in the Arctic, a growing number of compounds are being detected in humans from the Arctic regions of the world. Some of these compounds are fairly 'new' compounds whereas others have been around for decades but have only recently been detected due to advances in analytical techniques. The main compounds addressed in this chapter (see section 5.2) are the brominated flame retardants and the perfluorinated compounds, in particular the polybrominated diphenylethers (PBDEs), perflourooctane sulfonate (PFOS), and perflourooctanoic acid (PFOA). Until recently, there were few data available on human concentrations of these compounds.

5.1. Concentrations and trends of legacy contaminants

The data presented in this chapter were supplied by biomonitoring studies undertaken in different parts of the circumpolar region. The focus is on maternal blood concentrations of several legacy POPs and metals; although data for both men and women living in the Arctic are also provided.

Exposure to environmental contaminants from a traditional diet is a potential risk to human health, especially for the developing fetus and young children due to their physiological and anatomical immaturity and rapid development. The greater sensitivity of the developing fetus is one of the main reasons that many of the data presented in this assessment concern contaminant concentrations in mothers. Biomonitoring studies are an important part of the process involved in determining the extent of potential risks.

The studies describe three key aspects of human tissue concentrations of environmental contaminants. First, they provide an update on the spatial pattern of human exposure to environmental contaminants in the Arctic. Second, they provide data to assess trends in human exposure over time, indicating whether contaminant concentrations are decreasing, remaining the same, or increasing. Third, the data collected provide important information on dietary habits and offer important insights into the relationship between contaminant exposure, traditional food consumption, and other lifestyle factors. Comparison of the new data against those of the second AMAP assessment (AMAP, 2003) allows for a greater understanding of trends in human tissue concentrations of environmental contaminants and their ongoing causative factors.

Comparable methods were used in all studies to ensure that conclusions about spatial distributions or temporal trends were not just the result of methodological or analytical variability. The quality assurance/quality control (QA/QC) program in which the human health analytical laboratories participated is described in Chapter 4. The QA/QC program ensures that the data can be compared from one study to another and from one time period to another. Any analysis has a level of uncertainty and the usual analytical precision for contaminants in this assessment is plus or minus 20% to 25%. Differences between regions/countries or time periods that are smaller than 25% are not discussed. The data for persistent organic pollutants (POPs) are expressed on a lipid weight basis (μg/kg lipid in plasma) because POPs accumulate in lipids, and lipid levels in plasma increase throughout pregnancy and vary in response to meals. The data for metals, which do not accumulate in lipids, are expressed on a whole blood basis (μg/L in whole blood). For comparative purposes, the data for POPs are also presented on a wet weight basis (μg/L plasma) in Appendix 5.1.

This chapter focuses on trend analyses for several legacy POPs which are found at higher concentrations in some Arctic populations (e.g., DDE, a metabolite of DDT) and several other POPs for which people have often exceeded

tolerable daily intakes (e.g., the chlordane metabolite oxychlordane, toxaphene, and PCBs). Trend analyses are undertaken for metals, such as Hg and Pb, which are also found at higher concentrations in Arctic populations than non-Arctic populations (AMAP, 1998, 2003).

Initial data are available to assess changes in contaminant concentrations over time for several Arctic countries but the strength of these data varies considerably. Many of the data sets are only based on two population samples separated by five to ten years, in which case it is only possible to indicate increasing or decreasing concentrations rather than a trend. Nevertheless, it is very encouraging to see that the results are very similar to trends for mothers from Disko Bay (Greenland) and Nunavik (Canada) where more frequent sampling was available over a similar time period.

5.1.1. **Alaska, United States**

Regional tribal health system authorities have collected and archived blood samples from Alaska Native mothers for a number of years. Contaminant concentrations have been measured in some of these samples since the late 1990s. This assessment is the first to include a full set of organochlorine and metal data for Yupik mothers from the Yukon-Kuskokwim Delta and Iñupiat (Inuit) mothers from the north slope of Arctic Alaska. The data allow comparisons between contaminant concentrations in these two groups, and some initial data for the Yupik mothers enable a first examination of increases or decreases in contaminant concentrations.

5.1.1.1. **Organochlorines**

Table 5.1 presents the mean concentrations of organochlorines in maternal blood for Alaska Natives. The Iñupiat and the Yupik are indigenous groups that live in different regions of Alaska and so have different traditional diets and possibly different contaminant exposure patterns. Care must be taken when comparing contaminant concentrations between Iñupiat and Yupik mothers because the sampling timeframes do not always overlap. However, for the 1999 – 2003 period, data are available for both groups, although the contaminant patterns look quite different. Concentrations of many organochlorines, such as oxychlordane, DDE and CB153, are lower among Iñupiat mothers than Yupik mothers (21, 68, 8.6 μg/kg serum lipid, and 29, 135, 17 μg/kg serum lipid, respectively, Table 5.1). This is likely to be due to dietary differences between the two groups. The Iñupiat diet consists predominantly of land mammals, followed by whale, and then lesser amounts of fish (mostly freshwater species). The main marine mammal is the bowhead whale (*Balaena mysticetus*), which feeds at a low trophic level. In comparison, dietary surveys by participants indicate that the Yupik rely less on land mammals and more heavily on Pacific salmon (*Oncorhynchus* spp.), seals, and sea lions, which feed at higher levels of the food chain (Berner, J., pers. comm., 2008).

Fewer Iñupiat mothers were included in the study (Table 5.1) and the difference between two time points is less; therefore, comments on changes in contaminant concentration are limited to Yupik mothers. Among the

Table 5·1. Concentrations of POPs in maternal blood (μg/kg serum lipid) from Alaska, by region and ethnic group. Data show geometric mean (and range) for specified period of sampling.

	North Slope Arctic Coast		Yukon-Kuskokwim River Delta Region	
	Iñupiat 1997 25.5 [a] n = 20 [b]	Iñupiat 1999 – 2003 25 [a] n = 43 [b]	Yupik 1999 – 2003 26 [a] n = 106 [b]	Yupik 2004 – 2006 26.4 [a] n = 206 [b]
Oxychlordane	9.9	21	29	12 (1.5 – 234)
Trans-nonachlor	11	3.8	5.3	21 (1.75 – 310)
p,p'-DDT	3.7	5.2	6.4	3.4 (1.15 – 23)
p,p'-DDE	118	68	135	124 (3.1 – 777)
DDE:DDT	29	13	21	
HCB	28	6.7	14	22 (2.35 – 188)
β-HCH [d]	7.9	7.0	6.7	7.7 (1.1 – 138)
Mirex	1.5	8.8	24	3.3 (1.1 – 36)
Toxaphene				
Parlar 26	na	1.1 [c]	2.0 [c]	3.2 (1.1 – 27.4)
Parlar 50	na	0.8 [c]	1.4 [c]	2.7 (1.0 – 20.3)
PCBs				
CB118	na	na	na	5.6 (0.4 – 78)
CB138	12	13 [e]	35 [e]	14 (0.2 – 221) [e]
CB153	19	8.6	17	24 (0.75 – 416.5)
CB180	6.8	na	na	10 (0.35 – 192)

na: Not available.

[a] Average age of group sampled; [b] number of individuals sampled; [c] results performed on a total of 24 pooled specimens; 12 from the Arctic Coast and 12 from the Yukon-Kuskokwim River Delta; [d] information that was received as this assessment was about to go to press indicated that an error in the standard for β-HCH would cause these values to be approximately 35% higher than the actual value; [e] sum of CB138 + CB158.

Yupik mothers, the concentrations of oxychlordane, DDE, and CB138 decreased between 1999 – 2003 and 2004 – 2006, while concentrations of other contaminants, such as hexachlorobenzene (HCB), β-HCH, and toxaphene, increased. Yupik mothers also showed an unexpected inverse relationship between changes in oxychlordane and *trans*-nonachlor concentrations; both components of the pesticide chlordane, with one increasing and the other decreasing. Further data will be needed to see if this relationship continues. No statistical comparison of these two time points was available for this assessment.

5.1.1.2. **Metals**

Table 5.2 presents the mean concentrations of metals in maternal blood for Alaska Natives. Similar to the ethnic patterns for organochlorines, concentrations of Hg and Pb were lower among the Iñupiat mothers than the Yupik mothers in 1999 – 2003. Again, the lower concentrations among Iñupiat mothers is likely to be due to dietary differences (i.e., the predominant consumption of land mammals and Bowhead whale by the Iñupiat compared to the greater consumption of Pacific salmon, seals, and sea lions by the Yupik). Another possible factor is the seasonal timing of blood collection among Yupik mothers. Alaska Native peoples' consumption of fish and seal varies seasonally and this would affect Hg concentrations in blood; however, this factor has not yet been analyzed.

Only two time points for metals in maternal blood are available for Yupik mothers. The concentrations of Hg, Pb and cadmium (Cd) among Yupik mothers decreased between 1999 – 2003 and 2004 – 2006, from 5.0, 18, and 0.44 μg/L whole blood to 3.4, 17, and 0.39 μg/L whole blood, respectively, although the small changes in Pb and Cd concentrations are unlikely to be significant. Statistical analyses of these differences were not available for this assessment.

5.1.2. **Canada**

5.1.2.1. **Inuvik region, Northwest Territories**

5.1.2.1.1. *Exposure assessment in the Inuvik region*

This section presents the results of a biomonitoring study that took place in the Inuvik region of the Northwest Territories (NWT). This was a follow-up study to assess changing concentrations of human exposure to environmental contaminants using maternal blood and hair as biomarkers of exposure. The baseline study was completed in 1999 and the follow-up study was completed in 2006. People in the Inuvik region were included in the follow-up study because this region had the lowest concentrations of contaminants among Inuit regions in the baseline study. Follow-up within the Inuvik region provides a useful comparison to follow-up in regions which had higher contaminant concentrations, such as Baffin and Nunavik.

There were 89 participants enrolled in the study with 76 contributing blood samples for follow-up (52 Inuit women, 17 Métis/Dene women, and 7 Caucasian women). Samples were collected in the late third trimester or immediately after birth. The samples were analyzed for a similar range of POPs and metals as for the baseline study as well as vitamins and various nutrients. Dietary information for the mothers is also available and was presented in Chapter 3. A brief overview of some health effects of the traditional contaminants that are a priority for trend monitoring is given in Box 5.1.

Table 5·2. Concentrations of metals in maternal blood (μg/L whole blood) from Alaska by region and ethnic group. Data show geometric means for specified period of sampling. Source: Berner, J., pers. comm. (2008).

	North Slope Arctic Coast	Yukon-Kuskokwim River Delta Region	
	Iñupiat 1999 – 2003 Mean age = 25 [a] n = 43 [b]	Yupik 1999 – 2003 Mean age = 26 [a] n = 106 [b]	Yupik 2004 – 2006 Mean age = 25 n = 75 [b]
Total Hg	1.1	5.0	3.4
Pb	11	18	17
Cd	0.57	0.44	0.39

[a] Mean age of group sampled; [b] number of individuals sampled.

5.1.2.1.2. *Tissue concentrations of environmental contaminants by ethnic group in the Inuvik region*

Table 5.3 presents the concentrations of CB153 in maternal blood for each ethnic group. In the follow-up study (2005–2006), mean concentrations of CB153 were three- to four-fold higher in Inuit mothers than in Dene-Métis or Caucasian mothers (17, 5.9 and 4.3 μg/kg lipid in plasma, respectively). A similar pattern occurs for CB138 and CB180 as well as for the total PCBs measured as Aroclor 1260 (data not displayed). It is useful to summarize the data as Aroclor 1260 because this allows comparisons with data from older studies where PCBs were quantified by packed column techniques and also allows comparisons with the only PCB blood guidelines, which are expressed on an Aroclor basis.

Toxaphene Parlars 26 and 50 were measured in the follow-up study (2005–2006) and the results for Parlar 50 are shown in Table 5.3. The mean concentration of Parlar 50 in maternal blood was six- and eight-fold higher in Inuit mothers than in Dene-Métis and Caucasian mothers (2.9 *vs* 0.46 and 0.36 μg/kg lipid in plasma, respectively).

The mean concentration of oxychlordane in maternal blood among Inuit mothers was five- to six-fold higher than in Dene-Métis and Caucasian mothers (8.7 vs 1.6 and 1.3 μg/kg lipid, respectively (Table 5.3). A similar pattern is seen for *trans*-nonachlor although the concentrations are higher (data not presented).

The concentrations of DDE are the highest of all the POPs shown in Table 5.3. The mean concentration during the follow-up study (2005 – 2006) was highest in the Inuit mothers and almost two-fold higher than in the Dene-Métis and Caucasian mothers (76 *vs* 35 or 38 μg/kg lipid in plasma, respectively).

Box 5·1. Background information on environmental contaminants

Metals

Metals are elements that occur naturally in rock or soils, but may also be released into the environment through industrial activities. Some metals are essential for life processes, but excessive exposure to other metals can produce harmful effects.

Lead occurs naturally in the environment. However, anthropogenic activities such as mining and smelting increase the release of Pb. The use of leaded fuels was the primary source of Pb in the air. The concentration of Pb in the air has declined significantly since the introduction of unleaded gasoline in 1975. Previous work has shown that indigenous mothers may have higher exposures to Pb through the use of lead shot in hunting game birds (Dewailly et al., 2000b), although exposures are decreasing with the declining use of lead shot.

Mercury is present in air, water, and soil from both natural sources and as a result of human activity. Hg is naturally higher in the Canadian Shield and is emitted from power generation facilities and municipal/industrial incineration, and is also found in the manufacture of electrical transformers and historically in heavy duty paints. Hg can occur locally from discharges associated with the gold extraction process or waste dumps.

Persistent Organic Pollutants

Most POPs are manufactured chemicals and do not occur naturally. POPs do not easily degrade and accumulate in the fatty tissue of animals.

Polychlorinated biphenyls (PCBs) are a group of man-made, industrial organochlorine chemicals (there are 209 structurally similar compounds which only differ in the number and placement of the chlorine atoms). Because they do not conduct electricity, PCBs were used from the 1930s in electrical transformers as insulators and for a variety of industrial and consumer applications. They do not break down easily in the environment. Use of PCBs was banned in Canada in the 1970s.

Toxaphene is an organochlorine that is a complex mixture of chlorinated camphenes and was used as a pesticide in the past. It has never been licensed for use in Canada (minor non-licensed usage noted) but was used extensively in the southern United States on cotton, and was banned in the United States in 1982.

Chlordane is a mixture of over 120 structurally-related organochlorine compounds, and was introduced as a broad spectrum insecticide in the 1940s and widely used in North America. Although chlordane is no longer registered in either Canada or the United States, various chlordane-related contaminants, distinct from the original mixture, persist in the environment (U.S. EPA, 1999).

Together, ***trans*-nonachlor** and **oxychlordane** made up 76% to 78% of chlordane-related residues in ringed seal (*Phoca hispida*) blubber samples collected from the NWT in 1991, and 83% of chlordane-related residues in walrus (*Odobenus rosmarus*) blubber samples collected from Greenland in 1989 (Addison and Smith, 1998; Muir et al., 2000). The pattern of chlordane-related residue accumulation in humans parallels that seen in the highest levels of the Arctic marine food chain. *Trans*-nonachlor and oxychlordane make up more than 90% of the total chlordane contaminants measured in breast milk from both northern and southern Canadians, with combined residues in the late 1990s more than four-fold higher in the Arctic samples (Newsome and Ryan, 1999).

DDE is the principle metabolite of **DDT**, which is an insecticide that has been heavily used worldwide for agricultural and disease vector control purposes. DDT was banned in Canada for most uses during the 1970s, and Canada has been working for a global restriction on its use through the Stockholm Convention.

Total Hg concentrations in maternal blood during the most recent sampling period (2005 – 2006) ranged from 0.10 to 14 μg/L. Mean Hg concentrations in Inuit mothers were more than four-fold higher, and in Dene-Métis mothers almost three-fold higher, than in Caucasian mothers (1.1, 0.7 and 0.22 μg/L, respectively) (Table 5.3).

Maternal blood Pb concentrations during the most recent sampling period (2005 – 2006) ranged from 4.4 to 56 μg/L. Mean blood Pb concentrations in Inuit and Dene-Métis mothers were similar (13 μg/L) and almost twice as high as for Caucasian mothers (Table 5.3).

5.1.2.1.3. *Dietary exposure to contaminants in the Inuvik region*

The dietary survey undertaken with this monitoring study is described in Chapter 3. Based on the amount of food consumed and the concentration of each contaminant in a food item, estimated intake levels for selected contaminants were calculated for all foods and expressed in micrograms per person per day. In general, the dietary studies indicate that the participants increased their country food consumption, although the amount and type of food varied considerably by community and population. These intake levels were then correlated with maternal blood concentrations of contaminants. The results are shown in Table 5.4 for Inuit and Dene-Métis mothers. Caucasian mothers were not included because too few enrolled in the study and most did not eat much country food. There were moderate to strong correlations (all of which were significant) between food intake and contaminant concentrations measured in the blood for a broad range of contaminants, including

Table 5·3. Contaminant concentrations (μg/kg plasma lipids for POPs, μg/L whole blood for metals) in Dene-Métis, Inuit and Caucasian mothers from the Inuvik region, NWT, Canada. Data show geometric mean (and range) for specified period of sampling. Source: baseline study (Tofflemire, 2000), follow-up study (Armstrong et al., 2007).

	Dene- Métis		Significant difference, $p < 0.05$	Inuit		Significant difference, $p < 0.05$	Caucasian		Significant difference, $p < 0.05$
	Baseline study 1998 – 1999	Follow-up study 2005 – 2006		Baseline study 1998	Follow-up study 2005		Baseline study 1998	Follow-up study 2005	
	24 (18 – 35) [a]	24 (16 – 36) [a]		23 (15 – 37) [a]	26 (17 – 38) [a]		31 (19 – 45) [a]	3 (23 – 40) [a]	
	n = 42 [b, c] n = 41 [b, d]	n = 17 [b, c] n = 18 [b, d]		n = 31 [b]	n = 52 [b]		n = 21 [b]	n = 6 [b]	
Oxychlordane	4.4 (1.0 – 25)	1.6 (0.29 – 5.0)	SD [g]	18 (2.4 – 108)	8.7 (0.29 – 117)	SD [f]	4.1 (1.9 – 8.7)	1.3 (0.59 – 3.4)	SD [f]
p,p'-DDE	64 (23 – 222)	35 (13 – 141)	SD [e]	125 (44 – 491)	76 (5.3 – 867)	SD [f]	64 (26 – 189)	38 (18 – 111)	ns [h]
Toxaphene, parlar 50	1.7 (0.96 – 7.9)	0.46 (0.29 – 2.2)	SD [g]	6.8 (0.77 – 53)	2.9 (0.29 – 75)	SD [f]	1.1 (0.83 – 1.4)	0.36 (0.29 – 1.1)	SD [f]
CB153	16 (3.2 – 130)	5.9 (0.59 – 34)	SD [f]	30 (6.5 – 105)	17 (0.59 – 152)	SD [f]	12 (3.5 – 32)	4.3 (2.0 – 9.0)	SD [f]
Total Hg	1.1 (0.1 – 6.0)	0.7 (0.1 – 4.4)	ns [h]	2.1 (0.6 – 24)	1.1 (0.1 – 14)	SD [f]	0.65 (0.1 – 2.3)	0.22 (0.1 – 0.9)	SD [e]
Pb	35 (5.0 – 112)	13 (4.8 – 35)	SD [g]	19 (2.1 – 101)	13 (4.4 – 56)	ns [h]	13 (2.1 – 37)	6.9 (4.6 – 10)	SD [f]

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.; [c] organochlorines; [d] metals; [e] SD (p = < 0.05 – 0.01); [f] SD (p = <0.01 – 0.001); [g] SD (p = 0.001 – <0.0001); [h] not significant ($p > 0.05$).

PCBs, DDE, toxaphenes, HCHs, chlordanes, Pb and Hg. Only for Cd was the correlation between dietary intake and maternal contaminant concentration low and non-significant. This indicates that diet is not a significant source of Cd in this study. Other studies in Arctic Canada have indicated that cigarette smoking is a much more significant source of Cd (Butler Walker et al., 2006).

Separate analyses indicated that dietary sources of Pb were mostly from terrestrial mammal meat and bird meat. The main food sources for exposure to Hg, based on this survey, were fish and marine mammal fat. As would be expected it was marine mammal fat that supplied the greatest amount of exposure to contaminants such as PCBs (Armstrong et al., 2007).

5.1.2.1.4. *Comparisons between the baseline study and the follow-up study*

Great care must be taken when comparing contaminant concentrations measured during the baseline study (1998 – 1999) and the follow-up study (2005 – 2006). These are not random population samples and due to the limited birth rate in the north, any mother from a region could volunteer to be included. Chapter 3 provides the basic demographic information. The age of the mothers and parity are similar for the two studies but the different ethnic proportions in the two studies indicate that results can only be interpreted on an ethnic-specific basis. The proportion of mothers from each community also varied between the studies but could not be adjusted for due to small numbers. It should also be noted that the number of women who smoked increased over the seven years (52% to 67%) (Armstrong et al., 2007).

5.1.2.1.5. *Changes in dietary exposure to contaminants*

Initial dietary analyses were provided by Armstrong et al. (2007) and allow some general comments on exposure in this assessment, but Armstrong and co-workers recommended that more detailed analyses should be

Table 5·4. Dietary intake versus body burden for Inuit and Dene-Métis mothers in the Inuvik region, Canada. Spearman correlation coefficients (p values).

Estimated dietary exposure	n	Measured body burden
Chlordane	73	0.49 (0.000)
HCB	75	0.46 (0.000)
Mirex	75	0.41 (0.000)
PCBs	75	0.45 (0.000)
Toxaphenes	75	0.57 (0.000)
Dichlorodiphenyltrichloroethane	75	0.27 (0.02)
HCHs	75	0.55 (0.000)
Hg	74	0.55 (0.000)
Cd	75	0.03 (ns)
Pb	76	0.30 (0.008)
As	76	0.35 (0.002)
Hg blood:hair	74	0.763 (0.000)

n: Number of individuals sampled.

undertaken. Estimated exposure concentrations for selected contaminants were expressed in micrograms per person per day for the two ethnic groups in relation to specific foods. This made it possible to approximate the daily exposure to certain contaminants from different foods. The analyses indicated that Cd intake from the diet was very similar in the two studies. Lead consumption was actually higher in the follow-up study due to an increase in the consumption of birds. Mercury intake was higher in the follow-up study in both Inuit and Dene-Métis populations, primarily due to the increase in fish consumption. In contrast, the intake of various POPs was similar in the two studies for the Dene-Métis, while the Inuit had a marked decrease in POPs intake mostly related to a decreased consumption of marine mammal fat (Armstrong et al., 2007).

It is important not to over-interpret these data because the concentrations of contaminants were not actually measured in the dietary survey, and average values from other regions were often used. Also, it was not possible to perfectly match the communities in the two studies.

5.1.2.1.6. *Changes in contaminant concentrations in the Inuvik region and dietary implications*

Data on concentrations of several contaminants in maternal blood for the baseline study (1998 – 1999) and follow-up study (2005 – 2006) are shown in Table 5.3. Trend analyses and significant differences ($p < 0.05$) are also presented.

Among the organochlorines it is clear that the mean concentrations of all contaminants decreased significantly in all ethnic groups over this period (1998 to 2006). Inuit mothers showed the greatest absolute decrease for pesticides such as *p,p'*-DDE and oxychlordane (125 to 76 μg/kg lipid and 18 to 8.7 μg/kg lipid, respectively). The absolute change in concentrations of contaminants such as *p,p'*-DDE was less among Dene-Métis and Caucasian mothers (64 to 35 μg/kg lipid and 64 to 38 μg/kg lipid, respectively). PCB concentrations also decreased significantly especially among Inuit mothers, with the most marked decrease in CB138 and CB153.

Among the metals, Pb showed the greatest change in concentration over the period 1998 to 2006 and the greatest decrease was seen among Dene-Métis mothers (35 to 13 μg/L whole blood). In regions where hunting of traditional foods is common, researchers were able to use Pb isotope signatures to link a decline in maternal body burdens to reduced use of lead shot (Dewailly et al., 2000b). Although this decrease in maternal blood concentrations in the Inuvik region may be related to less use of Pb shot in the hunting of game birds and waterfowl, there are no data to validate this conclusion for this region. Mercury concentrations also decreased significantly over this period among all ethnic groups, with the greatest magnitude of change in Inuit mothers (2.1 to 1.1 μg/L whole blood).

The decrease in maternal blood concentrations of various organochlorines is supported by dietary information which indicates that fewer marine mammals are being consumed by Inuit mothers while greater quantities of other less-contaminated foods such as fish and caribou/moose, are being consumed. This is encouraging because much of the risk communication information, released after the previous AMAP assessment in 2003, indicated that mothers should continue to eat their traditional foods, but should consume traditional foods with lower contaminant concentrations if they were concerned about contaminants. For other contaminants, the trend data in maternal blood is not fully supported by the dietary contaminant exposure information from the region. The dietary exposure information indicates that exposure to Hg and Pb has increased while the contaminant concentrations in these mothers have significantly decreased. Armstrong et al. (2007) indicated that this may be due to relying on regional averages for contaminant concentrations in various species and not having actually measured the contaminant concentrations in the diets as consumed. This is a challenge that all dietary/contaminant studies face: limited budgets, a large number of contaminants, and a wide range of food items.

5.1.2.2. **Nunavik**

5.1.2.2.1. *Temporal trends in maternal concentrations of POPs and metals*

Over the past fifteen years, several studies in Nunavik have monitored the exposure of Inuit mothers to POPs and heavy metals. The aims of the studies were to compare current exposure concentrations to POPs with past concentrations and to assess exposure to emerging POPs. Maternal blood concentrations of contaminants have been studied due to concern about possible effects on infant and newborn development.

A series of nine studies have focused on contaminants in mothers from Nunavik. These studies included pregnant women in the 1992 Quebec Inuit Health Survey, Infant Development Studies led by Muckle and colleagues between 1996 and 2001, plus more recent surveys that focused on trend monitoring in Nunavik mothers (2004 – 2007). Eleven to 53 mothers were recruited each year and the average age ranged was from 24 to 27 years (Table 5.5). Measurements of the legacy POPs, emerging POPs, and heavy metals (which include 14 PCB congeners, 11 chlorinated pesticides, total and methyl mercury, Pb, and selenium) were carried out on all samples. Exposure assessment data from past and present studies were integrated into a functional database for this assessment. Dietary data were not available for this assessment.

Table 5.5 and Figure 5.1 summarize the time trend data for the legacy POPs and the metals. A temporal trend analysis of plasma concentrations of organochlorines in pregnant women was performed using multiple regression modeling with the contaminant concentrations (log) as dependant variables, and year of sampling as the main independent variable. The data were adjusted for age and region of sampling (Hudson

Table 5·5. Trends in contaminant concentrations (µg/kg plasma lipids for POPs, µg/L whole blood for metals) in pregnant Inuit women from Nunavik, Québec, Canada. Data show geometric mean (and range) for specified period of sampling. Source: 1992 (Santé Québec, 1994), 1996 – 2001 (Dallaire et al., 2003), 2004 (Dewailly et al., 2007a,b), 2007 (Pereg et al., 2008).

	1992 24 [a] (18 – 35) [a] n = 11 [b]	1996 24 [a] (17 – 34) [a] n = 25 [b]	1997 25 [a] (15 – 41) [a] n = 53 [b]	1998 25 [a] 15 – 37) [a] n = 46 [b, c] n = 27 [b, d]	1999 26 [a] (17 – 36) [a] n = 26 [b, c] n = 16 [b, d]	2000 26 [a] (17 – 39) [a] n = 36 [b, c] n = 29 [b, d]	2001 27 [a] (17 – 39) [a] n =20 [b, c] n 19 [b, d]	2004 27 [a] (18 – 42) [a] n = 29 [b, c] n = 31 [b, d]	2007 24 [a] (18 – 37) [a] n = na n = 42 [b, d]	Significant difference, $p <$ 0.05 [e, f]
Oxychlordane	77 (32 – 244)	41 (6.1 – 177)	48 (8.6 – 390)	34 (7.0 – 342)	47 (15 – 138)	40 (7.5 – 207)	36 (8.2 – 130)	35 (7.1 – 230)	22 (< DL – 182)	0.004
p,p'-DDE	636 (292 – 1567)	287 (71 – 1022)	369 (59 – 1444)	266 (67 – 2269)	287 (142 – 901)	274 (64 – 1328)	226 (54 – 1685)	231 (55 – 933)	150 (30 – 718)	< 0.0001
CB153	172 (71 – 287)	105 (19 – 409)	125 (23 – 612)	83 (27 – 709)	115 (29 – 473)	97 (15 – 499)	82 (16 – 417)	72 (16 – 253)	40 (4.5 – 218)	< 0.0001
Total Hg	12 (3.6 – 33)	13 (4.2 – 29)	11 (3.8 – 44)	7.2 (3.2 – 27)	8.5 (2.6 – 31)	9.0 (1.8 – 38)	9.9 (1.6 – 33)	7.6 (1.2 – 30)	4.0 (0.7 – 24)	< 0.0001
Pb	41 (8.3 – 172)	48 (17 – 141)	56 (10 – 259)	54 (27 – 131)	53 (19 – 112)	44 (10 – 137)	33 (5.2 – 129)	19 (5.8 – 85)	16 (6.6 – 77)	< 0.0001

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] organochlorines; [d] metals; [e] special analysis, Pereg, D. pers. comm. (2007); [f] using anova adjusted for age and region (Hudson or Ungava), regression adjusted for age and region (Hudson or Ungava) and smoking status (smoker, ex-smoker, non-smoker).

vs. Ungava) because there were significant effects of these two parameters. All three models explained between 16% and 30% of the variance observed in contaminant concentrations (Pereg, D., pers. comm., 2007).

The concentrations of PCBs decreased significantly in maternal blood in Nunavik over the period 1992 to 2007 with CB153 the congener showing the greatest change (172 to 40 µg/kg plasma lipid). The chlordane derivative oxychlordane also decreased significantly over this period. *p,p'*-DDE had the highest concentration of all the POPs (636 µg/kg plasma lipids in 1992) and decreased to 150 µg/kg plasma lipids in 2007.

The concentration of Pb in maternal blood in Nunavik decreased over the period 1992 to 2007 from 41 to 16 µg/L whole blood. This decrease was statistically significant even though the maximum concentration of 56 µg/L whole blood occurred in 1997. The concentration of total Hg also decreased significantly over this period, from 12 µg/L whole blood in 1992 to 4.0 µg/L whole blood in 2007.

5.1.2.2.2. *Concentrations of legacy POPs and metals in adults from Nunavik in 1992 and 2004*

In 1992, a major health survey was undertaken in Nunavik to assess the health of the population. A wide range of health measures were assessed, blood samples taken, and dietary questionnaires given (Santé Québec, 1994). Some of the major endpoints of this survey included that: two-thirds of Inuit smoked daily; traditional foods remained 'good' for consumption despite the presence of PCBs; and that the most frequent health problems reported were ear infections, lung disease, and mental illness. Some of the environmental contaminant and dietary data were reported in the first and second CACAR reports (Jensen

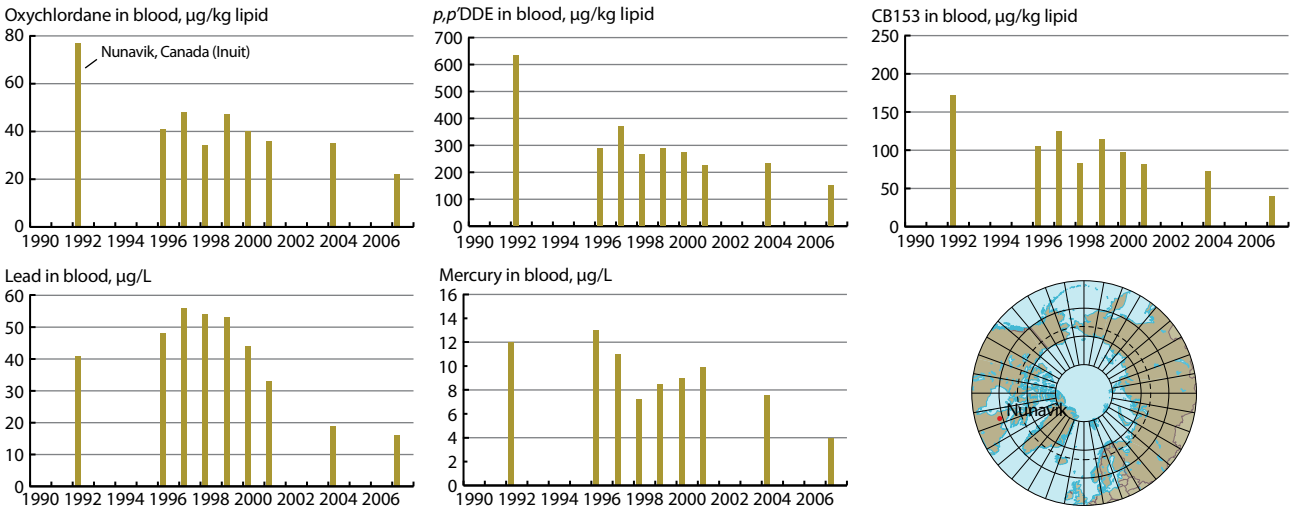


Figure 5·1. Temporal trends of POPs and metals in maternal blood samples from Nunavik, Canada.

et al., 1997; Van Oostdam et al., 2003). A major follow-up health survey was undertaken in Nunavik in 2004 to reassess health status and identify risk factors of chronic disease. Concentrations of contaminants in blood were measured and levels of country food consumption were established for the population. Initial results for legacy and emerging POPs and metals were reported by Dewailly et al. (2007a,b) but detailed dietary analyses were not available for this assessment.

Contaminants were analyzed at the Laboratoire de toxicology of the Institut national de santé publique du Québec utilizing a new method known as Automated Solid Phase Extraction (ASPE). This method allows measurement of 86 contaminants in a single analysis. Thus, all legacy POPs as well as a wide range of emerging POPs could be measured in a single sample. This section reports on legacy POPs only, data on emerging POPs are reported in section 5.2. In 2004, blood samples were obtained from 917 men and women 18 years of age and older with a participation rate of 69% (Dewailly et al., 2007a,b). Special analyses were undertaken for this assessment (Dewailly et al., 2007a) and the results are shown in Table 5.6. 498 women and 408 men agreed to contribute blood samples for the 2004 follow-up study. It is very encouraging to see the similar age ranges in both sampling periods (18 to 73 or 74 years) and the similar mean ages (35, 36, or 37 years) in all four groups. In-depth analyses of the data show the expected age-dependent increase in POPs concentrations in both men and women (Dewailly et al., 2007a,b).

Concentrations of POPs in Inuvik adults have declined significantly (Table 5.6). Previous monitoring in the Arctic and elsewhere found that CBs 138, 153, and 180 were the most abundant congeners in blood. CB153 concentrations declined significantly in men and women in Nunavik between 1992 and 2004 (340 to 189 μg/kg plasma lipids and 263 to 158 μg/kg plasma lipids, respectively). Concentrations of *p,p'*-DDE showed the greatest absolute decrease, from 1195 to 461 μg/kg plasma lipids for men and 1001 to 467 μg/kg plasma lipids for women. Concentrations of the chlordane component oxychlordane also declined significantly in women and men.

It is interesting to note that in adults from Nunavik, concentrations of legacy POPs were much higher (10% to 20%) in men than women in 1992. This changed in 2004 with concentrations of oxychlordane, *p,p'*-DDE and CB138 similar between men and women and only CBs 153 and 180 still 10% to 20% higher in men (data not presented, see Dewailly et al., 2007a,b).

Concentrations of all metals declined in Nunavik adults over the period 1992 to 2004. The greatest change was seen for Pb where concentrations decreased from 96 to 46 μg/L whole blood for men and from 78 to 34 μg/L whole blood for women. Concentrations of Hg also declined significantly in both men and women but at a slower rate than for Pb.

5.1.2.3. **Qikiqtaaluk (Baffin) region of the Nunavut Territory**

5.1.2.3.1. *Monitoring temporal trends in environmental contaminants*

The Qikiqtaaluk (Baffin) region in Nunavut Territory recently completed a multi-year study which assessed temporal trends in human exposure to selected environmental contaminants using maternal blood and hair as biomarkers. The study was conducted as a follow-up to a previous study which took place in 1997. The region was identified as a monitoring priority due to the historically high concentrations of many contaminants compared to other regions of Arctic Canada that conducted baseline assessments during 1994 to 1999.

The current project in the Baffin region aims: (1) to update spatial patterns of maternal exposure; (2) to provide data to assess trends in maternal exposure over time, whether concentrations of different classes of contaminants are increasing, decreasing, or remain

Table 5·6. Contaminant concentrations (μg/kg plasma lipids for POPs, μg/L whole blood for metals) in Inuit women and men from Nunavik, Quebec, Canada. Data show geometric mean (and range) for specified period of sampling. Source: 1992 (Santé Québec, 1994), 1994 (Dewailly et al., 2007a,b).

	Inuit women 1992 35 [a] (18 – 73) [a] n = 282 [b]	Inuit women 2004 37 [a] (18 – 74) [a] n = 498 [b]	Significant difference, $p < 0.05$ [c]	Inuit men 1992 36 [a] (18 – 74) [a] n = 210 [b]	Inuit men 2004 37 [a] (18 – 74) [a] n = 408 [b]	Significant difference, $p < 0.05$ [c]
Oxychlordane	115 (5.0 – 1957)	66 (2.3 – 2692)	$p < 0.0001$	138 (1.9 – 2849)	66 (0.93 – 1608)	$p < 0.0001$
p,p'-DDE	1001 (97 – 14597)	467 (27 – 8306)	$p < 0.0001$	1195 (115 – 11330)	461 (13 – 8306)	$p < 0.0001$
CB153	263 (27 – 2452)	158 (5.7 – 5805)	$p < 0.0001$	340 (14 – 2865)	189 (6.3 – 3428)	$p < 0.0001$
Total Hg	16 (2.0 – 112)	12 (0.20 – 164)	$p < 0.0001$			
Pb	78 (8.3 – 472)	34 (5.8 – 311)	na	14 (0.8 – 97)	9.2 (0.08 – 241)	$p < 0.0001$

na: Not available.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] Dewailly et al. (2007a).

Table 5-7. Contaminant concentrations (µg/kg plasma lipids for POPs, µg/L whole blood for metals) in Inuit mothers from the Baffin Region, Nunavut Territory, Canada. Data show geometric mean (and range) for specified period of sampling. Source: baseline study (Butler-Walker et al., 2003, 2006), follow-up study (Potyrala, M., unpubl., 2008).

	Baseline study 1997 24 (15 – 39) [a] n = 30 [b]	Follow-up study 2005 – 2007 24 (15 – 39) [a] n = 99 [b]	Significant difference, $p < 0.05$
Oxychlordane	69 (12 – 264)	26 (4.8 – 216)	< 0.0001
p,p'-DDE	248 (70 – 719)	128 (17 – 672)	< 0.0001
Toxaphene, parlar 50	15 (3.9 – 73)	8.6 (0.93 – 97)	0.0008
CB153	121 (33 – 355)	42 (6.2 – 276)	< 0.0001
Total Hg	6.7 (0.10 – 34)	4.0 (0.52 – 28)	0.0152
Pb	42 (5.0 – 120)	14 (4.1 – 71)	< 0.0001

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

unchanged; and (3) to collect information on maternal dietary habits and to describe relationships between contaminant exposure, frequency of consumption of country foods, and selected lifestyle factors. Inuit women in their ninth month of pregnancy were invited to participate and were asked a series of dietary and lifestyle questions. Blood and hair samples were collected and analyzed.

The study population consisted of 100 pregnant Inuit women recruited between December 2005 and January 2007. Blood samples were collected in the late third trimester and concentrations were evaluated for legacy POPs, polybrominated diphenylethers (PBDEs), metals, vitamins, and nutrients (selenium and fatty acids). Hg exposure per trimester was measured from hair samples. Information on country food consumption patterns, and demographic and lifestyle characteristics were also collected. Only the initial demographic and contaminant concentrations dataset were available for this assessment (Table 5.7) and more in-depth analyses must await the availability of the full dataset and dietary data. It is encouraging to see that the mean age and range of the mothers at the two time points are very similar.

As for the mothers from the Inuvik region, the concentrations of all organochlorines decreased significantly between 1997 and 2007 for Inuit mothers from the Baffin region of Nunavut (Table 5.7). The greatest decrease in organochlorine pesticide concentrations is seen for *p,p'*-DDE and oxychlordane (248 to 128 and 69 to 26 µg/kg lipid). PCB concentrations also decreased significantly over this period with the greatest decrease in CB153.

Among the metals (Table 5.7), blood concentrations of Hg and Pb decreased markedly between 1997 and 2007. The greatest absolute change was for Pb which decreased from a mean of 42 to 14 µg/L whole blood. Total Hg decreased from a mean of 6.7 to 4.0 µg/L whole blood.

5.1.3. Greenland

5.1.3.1. Maternal blood – trend monitoring

Deutch and Hansen collected samples from pregnant women during 1994 to 2006 in the Disko Bay area of Greenland as part of the ongoing circumpolar mother infant health study. A total of 223 mother/infant pairs were included in the study with only live born and single birth babies included in the study population. Lifestyle, anthropometric factors, and dietary survey data were analyzed along with blood and plasma concentrations of lipids, fatty acid profiles, heavy metals, and organochlorine compounds (Deutch and Hansen, 2000).

Concentrations of all organochlorines declined signifi-cantly in pregnant women from the Disko Bay area between 1994 and 2006 (Table 5.8, Figure 5.2). For

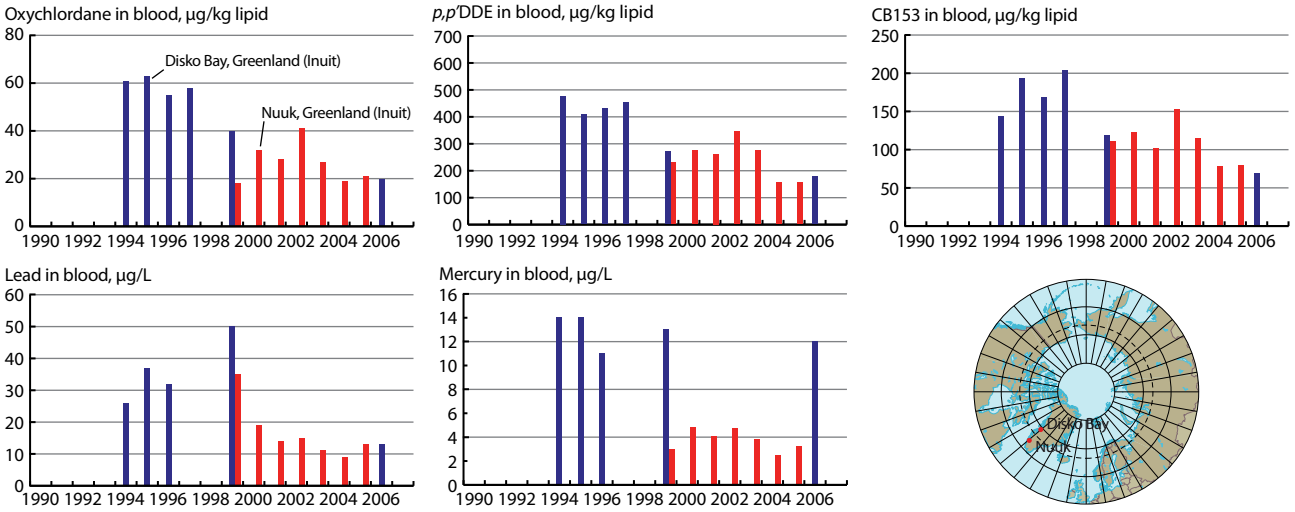


Figure 5-2. Temporal trends of POPs and metals in maternal blood samples from Nuuk and Disko Bay, Greenland.

Table 5·8. Trends in contaminant concentrations (μg/kg plasma lipids for POPs, μg/L whole blood for metals) in pregnant Inuit women from Disko Bay, Greenland. Data show geometric mean (and range) for specified period of sampling. The statistical analysis was a linear regression using log variables adjusted for age. Source: Deutch and Hansen (2000), Deutch et al. (2007a), Deutch unpubl. data.

	1994 25 [a] (20 – 35) [a] n = 10 [b]	1995 27 [a] (20 – 35) [a] n = 94 [b]	1996 27 [a] (20 – 35) [a] n = 63 [b]	1997 25 [a] (20 – 35) [a] n = 12 [b]	1999 26 [a] (22 – 34) [a] n = 21 [b]	2006 27 [a] (20 – 35) [a] n = 20 [b]	Significant difference, $p < 0.05$
Oxychlordane	61 (8.0 – 289)	63 (2.7 – 417)	55 (2.0 – 241)	58 (4.0 – 190)	40 (1.9 – 148)	20 (3.8 – 67)	$p < 0.0001$
p,p'-DDE	477 (63 – 2217)	408 (61 – 2023)	431 (61 – 1246)	453 (142 – 2023)	269 (75 – 692)	178 (34 – 481)	$p < 0.0001$
CB153	143 (36 – 918)	193 (40 – 596)	169 (40 – 563)	204 (72 – 596)	118 (43 – 372)	69 (22 – 224)	$p < 0.0001$
Total Hg	14 (1.9 – 76)	14 (2.0 – 75)	11 (5.0 – 29)	na	13 (2.0 – 58)	12 (3.5 – 33)	ns
Pb	26 (8.9 – 389)	37 (15 – 389)	32 (9.0 – 98)	na	50 (25 – 135)	13 (2.8 – 48)	$p < 0.0001$

na: Not available, ns: not significant.
[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

example, oxychlordane and CB 153 concentrations decreased from 61 to 20 μg/kg lipids and 143 to 69 μg/kg plasma lipids, respectively, over this period. Concentrations of Hg in this population did not decrease over this period, although there was a significant decrease in Pb concentrations. Because there are regional differences in traditional food consumption (Deutch et al., 2007a) the decrease in contaminant concentrations in pregnant women from the Disko Bay area may be due, in part, to an increase in the consumption of traditional food from the marine ecosystem that contains lower concentrations of some environmental contaminants (Deutch et al., 2007a).

A second trend assessment for contaminants in maternal blood is available for Inuit mothers from the Nuuk region of Greenland (1999 – 2005) (Figure 5.2). Concentrations of all contaminants are markedly lower in mothers from Nuuk (Table 5.9) than in mothers from the Disko Bay area (Table 5.8) as exemplified by oxychlordane concentrations in 1999 (18 and 40 μg/kg plasma lipid, respectively) (Bjerregaard et al., 2007). As well as having lower concentrations of organochlorines, there are only small and variable annual changes resulting in no significant decreases for Nuuk mothers. One reason for the lower concentrations of organochlorines in the capital Nuuk is likely to be a higher consumption of marine mammals in the more remote region of Disko Bay. Concentrations of Pb show a declining trend in both Nuuk and Disko Bay.

Table 5·9. Trends in contaminant concentrations (μg/kg plasma lipids for POPs, μg/L whole blood for metals) in pregnant Inuit women from Nuuk, Greenland. Data show geometric mean (and range) for specified period of sampling. Trend analysis based on linear regression analysis with adjustment for age. Trends and statistics calculated from log transformed concentrations. Source: based on Bjerregaard, P., pers. com. (2007).

	1999 28 [a] (19 – 45) [a] n = 20 [d]	2000 27 [a, b] (16 – 36) [a, b] 27 [a, c] (17 – 35) [a, c] n = 38 [d, b] n =24 [d, c]	2001 27 [a] (15 – 43) [a] n = 50 [d, b] n = 46 [d, c]	2002 29 [a, b] (18 – 42) [a, b] 30 [a, c] (18 – 42) [a, c] n = 37 [d, b] n = 36 [d, c]	2003 28 [a] (19 – 44) [a] n = 28 [d, b] n = 31 [d, c]	2004 26 [a] (18 – 37) [a] n = 24 [d, b] n = 28 [d, c]	2005 27 [a] (19 – 36) [a] n = 10	Significant difference, $p < 0.05$
Oxychlordane	18 (1.9 – 98)	32 (1.3 – 234)	28 (1.8 – 305)	41 (2.1 – 294)	27 (2.7 – 500)	19 (2.8 – 77)	21 (3.3 – 120)	ns
p,p'-DDE	228 (59 – 1023)	275 (32 – 1206)	261 (59 – 1913)	346 (45 – 2300)	274 (59 – 2700)	156 (40 – 740)	156 (43 – 690)	ns
CB153	111 (29 – 425)	122 (19 – 595)	101 (29 – 792)	152 (29 – 910)	115 (30 – 1200)	78 (23 – 270)	79 (25 – 400)	ns
Total Hg	3.0 (0.5 – 14)	4.8 (0.5 – 13)	4.1 (0.8 – 18)	4.7 (0.4 – 22)	3.8 (0.9 – 14)	2.5 (0.2 – 11)	3.2 (0.7 – 20)	ns
Pb	35 (25 – 57)	19 (5.2 – 77)	14 (5.2 – 52)	15 (5.9 – 81)	11 (4.5 – 25)	9.0 (3.9 – 18)	13 (5.9 – 57)	$p < 0.001$

ns: Not significant.
[a] Arithmetic mean age and range of group sampled; [b] organochlorines; [c] metals; [d] number of individuals sampled.

Table 5·10. Concentrations of POPs (μg/kg plasma lipids) in Inuit men from Greenland. Data show geometric mean (and range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch, B., pers. comm. (2007).

	Sisimiut 2002 – 2003 30.5 [b] (20 – 50) [b] n = 51 [c]	Qaanaaq 2003 33.7 [b] (20 – 50) [b] n = 41 [c]	Nuuk 2005 44.1 [b] (30 – 50) [b] n = 19 [c]	Quegertarsuaq 2006 35.3 [b] (20 – 50) [b] n = 35 [c]	Narsaq 2006 38.5 [b] (20 – 50) [b] n = 28 [c]	All Greenland [a] 1999 – 2006 34.6 [b] (19 – 50) [b] n = 314 [c]
Oxychlordane	57 (3.0 – 344)	397 (90 – 3089)	178 (25 – 573)	107 (13 – 446)	98 (13 – 492)	198 (3.0 – 3089)
Trans-nonachlor	128 (9.0 – 946)	621 (101 – 4470)	406 (69 – 1221)	238 (33 – 892)	213 (34 – 881)	334 (9.0 – 4490)
p,p'-DDT	5.2 (1.0 – 70)	34 (1.4 – 359)	17 (1.4 – 72)	12 (2.4 – 74)	11 (3.0 – 38)	16 (1.0 – 359)
p,p'-DDE	404 (85 – 2496)	970 (243 – 7197)	898 (232 – 2352)	720 (159 – 2285)	774 (118 – 2812)	NA
DDE:DDT	78 (16 – 360)	28 (6.2 – 277)	51 (19 – 170)	60 (23 – 260)	71 (26 – 375)	47 (6.2 – 375)
HCB	81 (23 – 364)	234 (50 – 1690)	201 (40 – 647)	164 (29 – 646)	113 (27 – 403)	169 (23 – 1690)
β-HCH	10 (1.5 – 68)	51 (11 – 265)	23 (1.4 – 65)	13 (1.4 – 43)	12 (3.5 – 41)	27 (1.4 – 384)
Mirex	10 (1.7 – 62)	37 (78 – 274)	30 (7.0 – 121)	14 (3.1 – 62)	18 (3.0 – 88)	30 (1.7 – 338)
Total Toxaphene	52 (8.0 – 470)	208 (24 – 1723)	200 (31 – 560)	108 (9.6 – 444)	89 (14 – 375)	131 (4.1 – 1724)
parlar 26	16 (1.6 – 204)	79 (8.1 – 742)	41 (6.2 – 119)	40 (3.7 – 152)	34 (4.6 – 156)	50 (1.6 – 742)
parlar 50	26 (1.6 – 280)	120 (12 – 977)	79 (13 – 221)	68 (5.9 – 292)	55 (10 – 219)	75 (1.6 – 977)
PCBs						
Aroclor 1260	1651 (339 – 8848)	5867 (1875 – 20438)	4093 (1315 – 12083)	2296 (571 – 6153)	3006 (772 – 10164)	4385 (339 – 59958)
CB118	23 (1.9 – 250)	88 (14 – 520)	73 (13 – 221)	47 (8.4 – 140)	35 (5.0 – 130)	65 (1.9 – 541)
CB138	89 (19 – 509)	292 (92 – 866)	226 (68 – 680)	127 (8.5 – 415)	185 (52 – 574)	260 (8.5 – 2635)
CB153	226 (45 – 1249)	832 (269 – 3169)	562 (178 – 16669)	300 (71 – 738)	391 (98 – 1360)	574 (45 – 16669)
CB180	102 (25 – 479)	388 (106 – 1512)	305 (107 – 875)	162 (34 – 500)	197 (41 – 754)	307 (25 – 8257)
Σ14 PCBs	597 (132 – 3311)	2152 (617 – 7452)	1531 (490 – 4360)	880 (201 – 2115)	1070 (256 – 3613)	1635 (132 – 26558)

[a] The eight regions in Greenland were Ittoqqortoormiit 1999, Uummannaq 1999, Tassiilaq 2000, Sisimiut 2002 – 2003, Qaannaq 2003, Nuuk 2005, Quegertarsuaq 2006 and Narsaq 2006; [b] arithmetic mean age and range of group sampled; [c] number of individuals sampled.

5.1.3.2. **Men and women of reproductive age blood monitoring**

Deutch and Hansen also collected samples from men and women of reproductive age (20 to 50 years). These individuals had a much higher participation rate than the maternal groups previously discussed and the sample could be drawn from a broader range of communities. This allowed a group of approximately 600 men and women of reproductive age to be collected between 1999 and 2006 from eight Greenland districts. The five districts presented here were not included in the 2003 AMAP assessment (Deutch and Hansen, 2000).

Concentrations of various organochlorine compounds in blood for men and women from five regions of Greenland are presented in Tables 5.10 and 5.11. A few general observations can be made in relation to this large amount of data. Geometric mean concentrations of *p,p'*-DDE are the highest of all the POPs measured, ranging from 404 to 970 μg/kg plasma lipids in men and 250 to 596 μg/kg plasma lipids in women. The PCB congener CB153 was found at concentrations approaching those for DDE and was followed by CBs 180 and 138 and the chlordane metabolite, *trans*-nonachlor. Concentrations of almost all contaminants are higher in men and women from Qaanaaq than all other communities and this is probably due to the higher intake of traditional food there (Deutch et al., 2007a). In comparing the results for all eight districts for men and women (see the final column in Tables 5.10 and 5.11) it is clear that men have higher concentrations of contaminants (*trans*-nonachlor, HCB, mirex, toxaphene and all four PCB congeners). The small difference in

Table 5·11. Concentrations of POPs (μg/kg plasma lipids) in Inuit women of reproductive age from Greenland. Data show geometric mean (and range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch, B., pers. comm. (2007).

	Sisimiut 2002 – 2003 33 (20 – 50) [b] n = 42 [c]	Qaanaaq 2003 33 (20 – 50) [b] n = 34 [c]	Nuuk 2005 36 (30 – 50) [b] n = 45 [c]	Quegertarsuaq 2006 34 (20 – 50) [b] n = 44 [c]	Narsaq 2006 35 (20 – 50) [b] n = 42 [c]	All Greenland [a] 1999 – 2006 33 (18 – 50) [b] n = 299 [c]
Oxychlordane	35 (2.0 – 290)	164 (5.4 – 1249)	25 (4.0 – 250)	45 (3.8 – 403)	69 (7.0 – 670)	82 (20 – 2132)
Trans-nonachlor	77 (7.7 – 564)	278 (19 – 1530)	62 (9.3 – 471)	100 (11 – 687)	144 (18 – 1158)	149 (7.7 – 1530)
p,p′-DDT	3.8 (1.3 – 56)	21 (1.7 – 131)	4.3 (1.1 – 24)	7.2 (2.7 – 48)	12 (3.0 – 143)	13 (1.1 – 359)
p,p′-DDE	250 (37 – 1453)	581 (28 – 3296)	283 (51 – 1617)	364 (34 – 2388)	596 (54 – 3148)	553 (28 – 3296)
DDE:DDT	65 (13 – 270)	28 (8.5 – 120)	66 (9.5 – 280)	51 (10 – 270)	50 (5.2 – 410)	42 (5.2 – 410)
HCB	68 (11 – 308)	152 (13 – 639)	52 (22 – 265)	99 (12 – 984)	95 (19 – 342)	102 (11 – 984)
β-HCH	7.1 (1.4 – 33)	29 (1.8 – 139)	4.1 (1.1 – 38)	7.1 (1.0 – 66)	10 (1.7 – 42)	14 (0.8 – 291)
Mirex	5.6 (1.4 – 24)	18 (1.8 – 99)	4.7 (1.0 – 49)	5.9 (1.0 – 63)	12 (1.0 – 77)	12 (0.8 – 234)
Total Toxaphene	40 (6.8 – 218)	110 (9.2 – 614)	41 (5.5 – 200)	55 (5.3 – 391)	70 (5.0 – 707)	76 (5.0 – 941)
parlar 26	13 (1.4 – 87)	40 (1.8 – 247)	8.9 (1.3 – 40)	20 (2.0 – 137)	27 (2.0 – 280)	26 (1.3 – 373)
parlar 50	18 (1.4 – 126)	61 (1.8 – 362)	16 (1.8 – 81)	35 (3.3 – 254)	43 (3.0 – 427)	40 (1.4 – 528)
PCBs						
Aroclor 1260	950 (168 – 3824)	2819 (222 – 15858)	970 (272 – 6764)	1117 (184 – 10609)	2259 (253 – 10609)	2213 (168 – 36380)
CB118	21 (3.1 – 114)	58 (3.0 – 263)	20 (2.2 – 119)	28 (3.0 – 258)	36 (5.7 – 204)	43 (2.2 – 575)
CB138	54 (11 – 277)	155 (13 – 700)	59 (20 – 350)	69 (9.0 – 417)	146 (18 – 204)	139 (9.5 – 2125)
CB153	128 (20 – 354)	385 (30 – 2350)	126 (33 – 926)	144 (22 – 896)	286 (31 – 1463)	283 (20 – 4870)
CB180	54 (8.4 – 201)	171 (21 – 1268)	63 (13 – 500)	73 (8.0 – 583)	132 (15 – 605)	140 (8.0 – 3594)
Σ14 PCBs	353 (67 – 1384)	1043 (99 – 5980)	358 (97 – 2427)	430 (58 – 2500)	807 (93 – 3571)	825 (58 – 13242)

[a] The eight regions in Greenland were Ittoqqortoormiit 1999, Uummannaq 1999, Tassiilaq 2000, Sisimiut 2002 – 2003, Qaannaq 2003, Nuuk 2005, Quegertarsuaq 2006 and Narsaq 2006; [b] arithmetic mean age and range of group sampled; [c] number of individuals sampled.

average age between the men and women sampled is unlikely to explain the higher concentrations in men. It is more likely that the ability of women to lose these contaminants through pregnancy and breast feeding, as well as dietary differences, are the major explanatory factors.

By comparing organochlorine concentrations in men by age class (Table 5.12) it is apparent that the concentrations of these contaminants increase two- to three-fold with each age class (35-38, 42-50, 51-77 years), which indicates age-related bioaccumulation of organochlorine compounds. Further data analysis showed that age, gender, and district or n-3 fatty acid intake (a surrogate for marine mammal intake) are the strongest predictors for higher human body burdens of organochlorines or heavy metals. Smoking has also been found to correlate with contaminant concentrations (Deutch and Hansen, 2000; Deutch et al., 2007a).

A summary of total Hg, Se, Pb, and Cd concentrations in blood for women and men in various Greenland communities (Tables 5.13 and 5.14) shows markedly higher concentrations of Hg in men and women from Qaanaaq, which is thought to be due to the higher intake of traditional food there and possibly the higher concentrations of Hg in marine mammals from northwestern Greenland (Deutch et al., 2007a). On average, concentrations of total Hg in men exceed those in women (20 *vs* 13 μg/L whole blood – all eight regions). Lead is also higher among men than women (43 *vs* 27 μg/L whole blood – all eight regions), although Nuuk and Qaanaaq both have higher concentrations.

Table 5·12. Concentrations of POPs (µg/kg plasma lipids) in Inuit men from Nuuk, Greenland by age class. Data show geometric range mean (and range) for 2005. Source: Deutch et al. (2007a), Deutch, B., pers. comm. (2007).

	Age class			All ages
	36 (35 – 38) [a] n = 3 [b]	46 (42 – 50) [a] n = 16 [b]	61 (51 – 77) [a] n = 31 [b]	55 (35 – 77) [a] n = 50 [b]
Oxychlordane	98 (85 – 111)	193 (25 – 575)	446 (125 – 1724)	302 (25 – 1724)
Trans-nonachlor	199 (171 – 231)	449 (69 – 1220)	934 (338 – 3793)	657 (68 – 3793)
p,p'-DDT	14 (13 – 16)	18 (1.4 – 72)	31 (10 – 106)	25 (1.4 – 106)
p,p'-DDE	760 (442 – 1304)	919 (232 – 2352)	1818 (437 – 10344)	1351 (232 – 10344)
DDE:DDT	55 (28 – 104)	51 (19 – 170)	58 (28 – 101)	55 (19 – 170)
HCB	114 (81 – 159)	218 (40 – 647)	405 (146 – 1149)	302 (40 – 1149)
β-HCH	12 (9.7 – 16)	25 (1.4 – 65)	49 (22 – 149)	36 (1.4 – 149)
Mirex	20 (13 – 30)	32 (7.0 – 120)	88 (19 – 321)	56 (7.0 – 321)
Total Toxaphene	103 (100 – 106)	219 (31 – 560)	347 (134 – 1413)	274 (31 – 1413)
parlar 26	21 (20 – 22)	46 (6.2 – 119)	77 (31 – 310)	59 (6.2 – 310)
parlar 50	41 (40 – 42)	87 (13 – 220)	135 (50 – 551)	107 (13 – 551)
PCBs				
Aroclor 1260	3083 (2429 – 3983)	4262 (1315 – 12083)	9163 (3728 – 27586)	6527 (1315 – 27586)
CB118	57 (34 – 94)	76 (13 – 220)	170 (63 – 540)	119 (12 – 540)
CB138	177 (135 – 232)	234 (68 – 680)	463 (203 – 1264)	342 (68 – 1264)
CB153	422 (342 – 521)	585 (178 – 1666)	1290 (491 – 4022)	909 (178 – 4022)
CB180	208 (157 – 275)	322 (106 – 875)	823 (260 – 2643)	542 (106 – 2644)
Σ14 PCBs	1123 (875 – 1442)	1600 (490 – 4361)	3594 (1396 – 11112)	2509 (490 – 11112)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table 5·13. Concentrations of metals (µg/L whole blood) in Inuit women of reproductive age, Greenland. Data show geometric mean (and range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch, B., pers. comm. (2007).

	Sisimiut 2002 – 2003 32 (20 – 50) [b] n = 42 [c]	Qaanaaq 2003 32 (20 – 50) [b] n = 36 [c]	Nuuk 2005 36 (20 – 50) [b] n = 45 [c]	Quegertarsuaq 2006 34 (20 – 50) [b] n = 44 [c]	Narsaq 2006 35 (20 – 50) [b] n = 42 [c]	All Greenland [a] 1999 – 2006 33 (18 – 50) [b] n = 299 [c]
Total Hg	8.2 (1.2 – 33)	50 (5.7 – 164)	2.2 (0.5 – 10)	18 (3.5 – 65)	13 (4.1 – 60)	13 (0.5 – 164)
Se	158 (69 – 363)	502 (120 – 1910)	124 (58 – 428)	213 (86 – 798)	140 (85 – 409)	196 (58 – 1910)
Pb	30.2 (8.0 – 118)	41 (18 – 164)	16 (5.0 – 101)	16 (2.8 – 84)	18 (2.0 – 404)	26.8 (2.1 – 404)
Cd	0.8 (0 – 5.3)	1.7 (0 – 11)	0.8 (0 – 2.5)	0.8 (0 – 2)	1.1 (0 – 6.4)	1.1 (0 – 11)

[a] The eight regions in Greenland were Ittoqqortoormiit 1999, Uummannaq 1999, Tassiilaq 2000, Sisimiut 2002 – 2003, Qaannaq 2003, Nuuk 2005, Quegertarsuaq 2006 and Narsaq 2006; [b] arithmetic mean age and range of group sampled; [c] number of individuals sampled.

Table 5·14. Concentrations of metals (µg/L whole blood) in Inuit men, Greenland. Data show geometric mean (and range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch, B., pers. comm. (2007).

	Sisimiut 2002 – 2003 31 (20 – 50) [b] n = 52 [c]	Qaanaaq 2003 34 (20 – 50) [b] n = 43 [c]	Nuuk 2005 44 (20 – 50) [b] n = 19 [c]	Quegertarsuaq 2006 35 (20 – 50) [b] n = 35 [c]	Narsaq 2006 39 (20 – 50) [b] n = 29 [c]	All Greenland [a] 1999 – 2006 35 (18 – 50) [b] n = 314 [c]
Total Hg	6.5 (1.4 – 23)	54 (2.3 – 240)	16 (3.0 – 52)	22 (3.5 – 79)	10 (3.0 – 25)	20 (1.4 – 240)
Se	141 (59 – 1457)	468 (73 – 1379)	274 (95 – 1241)	255 (86 – 2258)	132 (72 – 397)	219 (59 – 2258)
Pb	39 (12 – 267)	50 (14 – 231)	52 (16 – 127)	23 (9.3 – 102)	20 (3.6 – 20)	43 (3.6 – 380)
Cd	1.2 (0 – 7.6)	1.4 (0 – 7.5)	1.4 (0.4 – 6.2)	0.7 (0 – 3.5)	0.8 (0 – 5.4)	1.4 (0 – 7.6)

[a] The eight regions in Greenland were Ittoqqortoormiit 1999, Uummannaq 1999, Tassiilaq 2000, Sisimiut 2002 – 2003, Qaannaq 2003, Nuuk 2005, Quegertarsuaq 2006 and Narsaq 2006; [b] arithmetic mean age and range of group sampled; [c] number of individuals sampled.

5.1.4. **Iceland**

Concentrations of POPs in maternal plasma from Iceland have been monitored in three studies (1995, 1999, and 2004). Results from the first two studies were reported in earlier AMAP assessments (AMAP, 1998, 2003). A similar suite of contaminants were measured in all three studies and all samples were collected from pregnant women during their third trimester (Olafsdottir, K., pers. comm., 2007). The mean age of the mothers and the parity did not change significantly over this period. In 1995, all sampling was conducted in Reykjavik. In the follow-up studies, sampling was conducted in other areas, especially coastal villages where seafood consumption was likely to be above average. Concentrations of metals in these maternal blood samples are not available.

For mothers from all regions of Iceland the concentrations of *p,p'*-DDE and CB153 decreased significantly between 1995 and 2004 (Table 5.15). The concentration of oxychlordane is low and has not changed significantly.

Breaking down the data for 2004 by the city of the mothers' residence, there does not appear to be any one city for which concentrations are consistently higher than in any other (Table 5.16). The trend assessment in Table 5.15 was also carried out only for Reykjavik, the only city sampled in 1995, and a similar temporal trend was found for this city alone (data not shown). A recent food intake survey from 2002 revealed a reduction in fish consumption (about 30%) between 1990 and 2002 (Steingrímsdóttir et al., 2003). This was especially evident among young adults, and seems to be the most likely

Table 5·15. Concentrations of POPs (µg/kg plasma lipids) in Icelandic mothers. Data show geometric mean (and range) for specified period of sampling. Lipid normalization of data based on average lipid concentrations from 1995. Source: Olafsdottir, K., pers. comm. (2007).

	Reykjavik 1995 30 (18 – 41) [a] n = 40 [b], p = 1.9 [c]	All Iceland 1999 28.7 (20 – 42) [a] n = 39 [b], p = 1.9 [c]	All Iceland 2004 30.3 (20 – 40) [a] n = 40 [b], p = 1.8 [c]	SD [d]
Oxychlordane	6.7 (2.6 – 30)	4.7 (1.3 – 22)	6.5 (1.3 – 22)	ns
p,p'-DDE	113 (42 – 514)	100 (33 – 306)	54 (19 – 226)	$p < 0.0001$
CB153	68 (26 – 158)	60 (24 – 143)	40 (19 – 98)	$p < 0.0001$

ns: Not significant.
[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] parity; [d] significant differences using Kruskal-Wallis Test (Nonparametric ANOVA) between 1995 and 2004.

Table 5·16. Concentrations of POPs (µg/kg plasma lipids) in maternal blood from Icelandic mothers, by region. Lipid normalization of data based on average lipid concentrations from 1995. Data show geometric mean for 2004. Source: Olafsdottir, K., pers. comm. (2007).

	Reykjavik 2004 31 (20 – 40) [a] n = 20 [b], p = 1.5 [c]	Akureyri 2004 31 (22 – 39) [a] n = 10 [b], p = 2.4 [c]	Vestmannaeyjar 2004 29 (22 – 39) [a] n = 10 [b], p = 1.8 [c]	All regions 2004 30 (20 – 40) [a] n = 40 [b], p = 1.8 [c]
Oxychlordane	5.6	11	5.1	6.4
Trans-nonachlor	7.2	8.9	6.9	7.6
p,p'-DDT	2.7	4.0	2.6	3.0
p,p'-DDE	59	53	51	56
DDE:DDT	22	13	33	20
HCB	28	26	29	28
β-HCH	9.1	12	5.3	8.7
Toxaphene				
parlar 26	1.4	2.0	1.7	1.6
parlar 50	2.3	3.7	3.8	2.8
PCBs				
Aroclor 1260	330	328	347	333
CB118	10	12	9.9	11
CB138	23	24	24	23
CB153	41	40	43	41
CB180	22	25	24	23
Σ14 PCBs	127	135	132	130

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] parity.

explanation for the lower contaminant concentrations in the mothers. Older women were more likely to eat more fish meals per week than the younger women, and women from Vestmannaeyjar had a higher consumption of fish and seabirds than women from the mainland; however, this was not significantly reflected in plasma concentrations of organochlorines.

5.1.5. **Norway**

Concentrations of POPs measured in maternal plasma from northern Norway (Kirkenes and Bodø) in 1996 and 2004 suggest that contaminant concentrations in maternal blood are relatively low and declining (Table 5.17). The people in both communities have a similar exposure to organochlorines due to similarities in their diet (Odland, J., pers. comm., 2008). Researchers found that a comparable amount of store-bought food and ocean and river run fish is consumed in both communities.

Owing to only two sampling points, possible community differences, and a limited recent sample size it is not possible to draw firm conclusions concerning trends, however, a large maternal blood contaminant monitoring program is underway in northern Norway that will soon allow better conclusions on changes in the concentrations of these contaminants over time.

Table 5·17. Concentrations of POPs (μg/kg plasma lipids) in maternal plasma from northern Norway. Data show geometric mean (and range) for specified period of sampling. Source: Kirkenes (AMAP, 1998), Bodø (SPFO, 2005).

	Kirkenes 1996 29 (19 – 44) [a] n = 66 [b]	Bodø 2004 30 (20 – 35) [a] n = 10 [b]
Oxychlordane	3.9 (1.6 – 11)	2.6 (1.0 – 6.1)
p,p'-DDE	79 (19 – 436)	67 (26 – 175)
CB153	52 (25 – 130)	23 (10 – 50)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

5.1.6. **Sweden**

Studies examining the concentrations of contaminants in maternal blood were undertaken in the Kiruna region of Arctic Sweden in 1996 and 2007. The samples consisted of consecutive pregnant women coming for a prenatal visit to the maternity ward in Kiruna. The pregnancy was their first, they were aged between 22 and 33 years, and they had lived in the Kiruna area for more than 20 years. The mothers were of Sami and Swedish ethnicity. Because there are no dietary or other social or environmental differences between these two groups, ethnicity has no impact on environmental contaminant exposure in the Kiruna region (Messner, T., pers. comm., 2008).

Contaminant concentrations were mostly low to moderate in 1996 and CB153, DDE, Pb and total Hg decreased significantly between 1996 and 2007 (Table 5.18), for example concentrations of DDE and Hg decreased from 84 to 34 μg/kg plasma lipids and 1.3 to 0.7 μg/L whole blood, respectively. Other studies in Sweden have also found decreasing concentrations of various POPs in breast milk and have indicated that this may be due to dietary advice to women indicating that they should limit their consumption of various fish species (FSB, 2007).

Table 5·18. Contaminant concentrations (μg/kg plasma lipids for POPs, μg/L whole blood for metals) in pregnant women from the Kiruna region in northern Sweden. Data show geometric mean (and range) for specified period of sampling. Source: POPs 1996 (Van Oostdam et al., 2004), metals 1996 (Dewailly, E., pers. comm., 2007), POPs and metals 2007 (Messner, T., pers. comm., 2008).

	Sweden 1996 29 (22 – 33) [a] n = 40 [b] n=23 [c]	Sweden 2007 27 (22 – 33) [a] n = 25 [b] n=23 [c]	Significant difference, $p < 0.05$
Oxychlordane	1.9 (0.83 – 4.0)	nd	
p,p'-DDE	84 (34 – 444)	34 (11 – 119)	$p < 0.001$
CB153	69 (29 – 161)	27 (11 – 62)	$p < 0.001$
Total Hg	1.3 (0.60 – 6.2)	0.7 (0.2 – 3.4)	$p = 0.003$
Pb	18 (10 – 35)	8.0 (5 – 35)	$p < 0.001$

nd: Not detected.
[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled for organochlorines; [c] number of individuals sampled for metals.

5.1.7. **Finland**

New data for maternal blood concentrations of organochlorine pesticides and metals are not available for Finland. Instead, this section presents the concentrations of organochlorine pesticides in breast milk from primipara (first-time) mothers from southern (non-Arctic), central (non-Arctic), and northern (Arctic) Finland. The breast milk studies took place between 1987 and 2005, making trend analyses and regional comparisons possible. Analyses for dioxins, furans and PCBs were undertaken on the earlier samples, and analyses of the more recent samples also included DDT and DDE.

The concentration of CB153 in breast milk from primipara mothers from both southern and central Finland decreased markedly between 1987 and 2005 (Table 5.19). In southern Finland, there was about a three-fold decrease in CB153 (from 113 μg/kg lipids to 30 μg/kg lipids) and in central Finland about a four-fold decrease (from 93 μg/kg lipids to 21 μg/kg lipids). A statistical analysis of the trend was not possible because the more recent data (2000 and 2005) were only available as a single analysis of pooled samples. Because the mothers were all primipara and similar in age, these factors should not affect the trend. It can also be seen that concentrations of CB153 are slightly higher in southern Finland than in central Finland.

Table 5-19. Trends in CB153 concentrations (μg/kg lipids) in breast milk from primipara mothers in southern (non-Arctic) and (non-Arctic) central Finland. Data show arithmetic mean (and range) for specified period of sampling. Source: 1987 (Vartiainen et al., 1997), 1993 – 1994, 2000, 2005 (Kiviranta, H., pers. comm., 2007).

	Southern Finland				Central Finland			
	1987 26.9 (20-37) [a] n = 47 [b]	1993-1994 27.9 (19-36) [a] n = 14 [b]	2000 29 (22-35) [a] n = 23 [b]	2005 28.7 (20-39) [a] n = 35 [b]	1987 25.4 (19-34) [a] n = 37 [b]	1993-1994 27 (18-39) [a] n = 28 [b]	2000 29.5 (22-36) [a] n = 12 [b]	2005 27.3 (19-40) [a] n = 31 [b]
CB153	113 (48-373)	85 (24-148)	40 [c]	30 [c]	93 (39-209)	52 (18-110)	34 [c]	21 [c]

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] pooled samples.

In 2005, data for DDT, DDE, other organochlorines, and PCBs in breast milk of primipara mothers from southern, central, and northern (Arctic) Finland became available (Table 5.20). Concentrations of organochlorine pesticides in breast milk were consistently higher in women from southern Finland (non-Arctic) relative to those from central Finland (non-Arctic) and northern Finland (Arctic). The analyses were on a composite basis so only mean concentrations were available. The highest concentrations of DDT, DDE, and PCBs were seen in southern Finland and lower and more similar concentrations were seen in central and northern Finland.

Table 5-20. Concentrations of POPs (μg/kg lipids) in pooled breast milks from primipara mothers in southern (non-Arctic), central (non-Arctic), and northern (Arctic) Finland. Data show geometric mean for 2005. Source: Kiviranta, H., pers. comm. (2007).

	Southern Finland 2005 28.7 (20 – 39) [a] n = 35 [b]	Central Finland 2005 27.3 (19 – 40) [a] n = 31 [b]	Northern Finland 2005 26.3 (21 – 41) [a] n = 11 [b]
Oxychlordane	1.5	0.5	1.1
Trans-nonachlor	3.3	2.2	2.8
p,p'-DDT	3.1	1.7	2.4
p,p'-DDE	56	40	36
DDE:DDT	18	18	15
HCB	2.8	2.4	2.9
β-HCH	5.4	2.8	3.9
Mirex	< 0.5	< 0.5	< 0.5
Toxaphene			
parlar 26	1.1	< 0.5	< 0.5
parlar 50	2.3	1.0	1.3
PCBs			
Aroclor 1260 [c]	240	173	165
CB118	6.7	3.6	3.1
CB138	16	12	11
CB153	30	21	20
CB180	14	11	11
Σ14 PCBs	88	63	60

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] Aroclor 1260 quantified as 5.2 (CB138 + CB153), CB28, CB52, CB99, CB101, CB105, CB118, CB128, CB138, CB153, CB156, CB170, CB180, CB183, and CB187.

There was no clear explanation for the differences observed in organochlorine pesticide concentrations in breast milk between the southern and the central and northern parts of Finland (Kiviranta, H., pers. comm., 2007). The difference may be related to higher contaminant concentrations in the fish consumed by the women. People living in southern Finland commonly consume Baltic Sea fish that have higher concentrations of organochlorine pesticides than the inland lake fish and ocean fish consumed in central and northern Finland (Kiviranta, H., pers. comm., 2007). Also, the mothers from the southern parts of Finland are slightly older than those in the central and northern parts of Finland.

5.1.8. **Russia**

The Russian Federation undertook a research project entitled the Persistent Toxic Substance, Food Security and Indigenous Peoples of the Russian North, 2001 – 2004 (AMAP, 2004b). This project was only possible due to the support of the North-West Public Health Research Centre (NWPHRC), AMAP, the Global Environment Facility (GEF), and the Russian Arctic Indigenous Peoples Organization (RAIPON). Data published in the first report on this project (AMAP, 2004b) were mainly blood data from one of the four participating laboratories and so represented only a section of the populations investigated. Additional data from four main Arctic regions, and from Kamchatka and the Commander Islands, were available for the present assessment. The first report (AMAP, 2004b) included data for 220 pregnant women and 240 other adults (men and women) whereas this assessment presents data for 346 pregnant women and 360 other adults. Additional samples came from archived samples collected during 2001 to 2003 by the same sampling program.

The five regions covered in this assessment include the Kola Peninsula (Murmansk Oblast), the Pechora River Basin (Nenetskiy Autonomous Okrug), the Taymir Peninsula (Taymyrskiy AO), the Chukotka Peninsula (Chukotskiy AO), the Kamchatka Peninsula, and the Commander Islands (Kamchatskaya Oblast). There are more than 120 settlements of indigenous peoples within the study area. Ethnic groups within these settlements (containing a relatively small overall number of residents) represent almost two-thirds of the overall ethnic composition of indigenous peoples of the Russian Arctic. Blood samples were collected for contaminant analyses and all participants answered dietary and lifestyle questionnaires.

5.1.8.1. **Organochlorines**

Concentrations of organochlorines in blood for pregnant women from the Chukotka Peninsula coastal region were higher than in the other regions (Table 5.21). For example, concentrations of oxychlordane were more than 30-fold higher, concentrations of HCB three- to eight-fold higher, and concentrations of β-HCH two- to six-fold higher. The highest concentrations of PCBs were also found in pregnant women from the Chukotka Peninsula coastal region.

Table 5.21 also shows that the concentrations of DDT (48 μg/kg plasma lipids) and DDE (452 μg/kg plasma lipids) in pregnant ethnic Russian women from the Norilsk area were elevated relative to those in pregnant women from other areas. However, concentrations of DDE are generally high in all communities. High concentrations of the parent compound DDT is often associated with recent use of this pesticide. In Russia, household/environmental use of insecticides, second-hand use of waste technical containers and barrels for souring plants and vegetables, home-made alcohol fermentation, and water storage are possible sources for a number of these contaminants. Additional information about the contamination of food during processing in the household environment is given in Chapter 3.

Concentrations of organochlorines in the blood of the general indigenous northern population of women (Table 5.22) show a very similar pattern to that for pregnant women (Table 5.21). The highest concentrations of contaminants were commonly found in women and men from the Chukotka Peninsula coastal area (Tables 5.22 and 5.23), with concentrations greatest in Chukchi and Inuit men. This 'Chukotka Peninsula pattern' of contaminants in all groups studied (pregnant women, and women and men from the general population) is likely to be due to marine mammal consumption, but also to the widespread practices in Chukotka of home-producing alcohol in waste barrels, specific methods of food conservation (ground pits – due to soil/ground water contamination), and retail accessibility to Chinese-produced insecticides (Dudarev, A., pers. comm., 2008).

Men often have higher concentrations of bioaccumulative-lipophilic contaminants as they may consume more contaminated foods, and do not have the

Table 5·21. Concentrations of POPs (μg/kg plasma lipids) in pregnant women by area and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007), Anda, E., pers. comm. (2008), Sandanger et al. (2003), Dudarev et al. (2003), Konoplev et al. (2005, 2006), Dudarev and Chashchin (2006).

	Chukotka Peninsula		Kola Peninsula	Pechora River Basin	Taymir Peninsula	Norilsk	Kamchatka
	Coastal	Inland					
	Chukchi & Inuit	Chukchi	Saami, Nenets & Komi	Nenets	Dolgan	Ethnic Russian	Koryak & Even
	26 (15 – 41) [a] n = 68 [b]	25 (18 – 40) [a] n = 58 [b]	22 (18 – 32) [a] n = 16 [b]	23 (16 – 38) [a] n = 38 [b]	27 (16 – 42) [a] n = 69 [b]	27 (16 – 37) [a] n = 59 [b]	21 (15 – 39) [a] n = 8 [b]
Oxychlordane	41 (0.98 – 550)	1.8 (0.98 – 24)	1.3 (0.98 – 4.6)	1.6 (0.95 – 8.4)	2.0 (0.98 – 15)	1.1 (0.98 – 7.2)	3.7 (0.98 – 11)
Trans-nonachlor	64 (7.1 – 531)	6.5 (2.1 – 37)	4.1 (2.1 – 18)	4.7 (2.1 – 44)	12 (2.1 – 63)	3.4 (2.1 – 15)	16 (4.6 – 75)
p,p'-DDT	32 (8.6 – 171)	30 (8.6 – 146)	35 (8.6 – 114)	38 (8.6 – 264)	30 (8.6 – 121)	48 (12 – 895)	16 (8.6 – 48)
p,p'-DDE	323 (106 – 997)	202 (10 – 907)	294 (110 – 937)	227 (8.6 – 777)	214 (30 – 1093)	452 (113 – 2806)	249 (147 – 350)
HCB	183 (46 – 863)	74 (20 – 389)	49 (21 – 233)	81 (21 – 297)	82 (10 – 300)	37 (11 – 176)	41 (27 – 78)
β-HCH	237 (47 – 1086)	95 (13 – 354)	23 (2.9 – 246)	47 (2.9 – 161)	93 (2.9 – 433)	149 (2.9 – 816)	69 (43 – 150)
PCBs							
Aroclor 1260	1092 (217 – 4271)	239 (63 – 1209)	357 (63 – 776)	459 (63 – 2191)	451 (111 – 1746)	334 (63 – 1472)	293 (125 – 464)
CB99	40 (9.0 – 125)	11 (4.3 – 104)	13 (4.3 – 29)	11 (4.3 – 33)	18 (4.3 – 51)	20 (4.3 – 70)	11 (4.3 – 27)
CB118	50 (10 – 213)	24 (4.3 – 200)	25 (4.3 – 86)	17 (4.3 – 43)	32 (4.3 – 122)	31 (8.6 – 194)	23 (8.7 – 36)
CB138	49 (13 – 168)	16 (7.1 – 103)	31 (7.1 – 81)	22 (7.1 – 80)	29 (7.1 – 106)	23 (7.1 – 83)	15 (7.1 – 28)
CB153	159 (27 – 687)	29 (5.0 – 140)	37 (5.0 – 71)	64 (5.0 – 341)	57 (14 – 230)	40 (5.0 – 200)	41 (17 – 74)
CB180	33 (8.0 – 148)	8.9 (2.9 – 42)	13 (2.9 – 40)	25 (3.0 – 186)	20 (2.9 – 80)	11 (2.9 – 51)	12 (6.7 – 17)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table 5-22. Concentrations of POPs (μg/kg plasma lipids) in women (general population) by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007), Anda, E., pers. comm. (2008), Sandanger et al. (2003), Dudarev et al. (2003), Konoplev et al., 2005, 2006), Dudarev and Chashchin (2006).

	Chukotka Peninsula		Kola Peninsula		Pechora River Basin	Taymir Peninsula	Commander Islands
	Coastal	Inland	Lovosero	Krasnoschelye			
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Saami, Nenets and Komi	Nenets	Dolgan	Aleuts
	38 (21 – 69) [a] n = 26 [b]	37 (19 – 81) [a] n = 28 [b]	47 (26 – 76) [a] n = 17 [b]	44 (18 – 78) [a] n = 47 [b]	37 (18 – 65) [a] n = 31 [b]	44 (20 – 72) [a] n = 40 [b]	34 (18 – 46) [a] n = 49 [b]
Oxychlordane	35 (3.0 – 305)	4.3 (0.8 – 71)	1.7 (0.8 – 7.6)	– [c]	1.6 (0.8 – 9.9)	5.1 (0.8 – 33)	2.0 (0.8 – 27)
Trans-nonachlor	145 (18 – 965)	19 (2.5 – 244)	15 (6.8 – 44)	6.2 (2.5 – 103)	7.2 (2.5 – 46)	15 (2.5 – 138)	27 (5.7 – 241)
p,p'-DDT	29 (10 – 116)	18 (10 – 80)	60 (25 – 169)	71 (19 – 682)	66 (10 – 530)	34 (10 – 93)	34 (10 – 217)
p,p'-DDE	350 (77 – 1128)	187 (50 – 415)	484 (62 – 1517)	411 (14 – 7547)	349 (39 – 1969)	200 (11 – 763)	389 (8.3 – 4805)
HCB	115 (14 – 570)	125 (41 – 429)	126 (65 – 193)	94 (8.7 – 290)	134 (44 – 376)	215 (8.5 – 593)	70 (27 – 718)
β-HCH [d]	285 (36 – 1363)	29 (3.3 – 259)	163 (15 – 693)	125 (3.3 – 636)	96 (24 – 612)	176 (21 – 649)	103 (29 – 454)
PCBs							
Aroclor 1260	790 (144 – 4709)	106 (40 – 495)	230 (106 – 620)	240 (32 – 777)	197 (27 – 1757)	176 (36 – 558)	251 (81 – 1602)
CB99	53 (7.7 – 207)	11 (5.0 – 46)	17 (5.0 – 32)	43 (5.0 – 665)	22 (5.0 – 1468)	13 (5.0 – 86)	25 (5.0 – 193)
CB118	73 (12 – 306)	25 (5.0 – 93)	44 (19 – 118)	49 (5.0 – 222)	32 (5.0 – 933)	28 (5.0 – 138)	37 (5.0 – 298)
CB138	122 (23 – 697)	18 (8.3 – 64)	41 (17 – 137)	52 (8.3 – 171)	37 (8.3 – 475)	34 (8.3 – 121)	48 (13 – 301)
CB153	300 (52 – 1819)	38 (13 – 201)	80 (31 – 194)	74 (8.5 – 286)	66 (5.8 – 464)	59 (11 – 208)	85 (27 – 555)
CB180	77 (12 – 625)	12 (3.3 – 56)	38 (20 – 107)	23 (3.3 – 117)	18 (3.3 – 185)	16 (3.3 – 81)	28 (3.3 – 175)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] thirty samples were missing from Krasnoschelye; [d] ten samples for β-HCH were missing from one lab, all in the same area (Kanchalan), thus will give an artificially low estimate.

ability to excrete contaminants through lipid transfer during pregnancy or breast feeding of infants. DDE concentrations are much higher in men, as expected, and a number of regions also have high concentrations of DDE (Chukotka Inland, Kola Peninsula, Taymir Peninsula). Markedly higher concentrations of DDE were also found in the Aleuts from the Commander Islands.

5.1.8.2. **Metals**

Table 5.24 presents the concentrations of Hg, Pb and Cd in maternal blood by region in Russia. The highest concentration of Hg in blood for pregnant women was seen among the Dolgani from the Taymir Peninsula and the lowest concentration was seen in ethnic Russians from Norilsk (1.8 *vs* 0.8 μg/L whole blood). The highest concentration of Pb was seen in pregnant women from the Taymir Peninsula and the lowest seen in ethnic Russians from Norilsk (49 *vs* 20 μg/L whole blood). For Cd, the highest concentrations are among coastal Chukchi and Inuit (1.0 μg/L whole blood) and the lowest in Saami/Komi from the Kola Peninsula (0.3 μg/L whole blood). Nevertheless, the overall results (Table 5.24) indicate that concentrations of Hg, Pb, and Cd in pregnant women from Russia are relatively low.

Table 5.25, which shows the concentrations of Hg, Pb and Cd in the blood of women by region in Russia, indicates that contaminant concentrations are higher in women's blood from the Chukotka Peninsula than in maternal blood samples from this region. The table shows that the concentrations of Hg, Pb and Cd were higher among people from the coastal part of the Chukotka Peninsula (7.7, 85 and 2.4 μg/L whole blood, respectivlely) were higher than from the inland part (5.7, 46, and 0.82 μg/L whole blood, respectively). Higher exposure to Hg in coastal Chukotka is likely to result from the higher marine mammal consumption in this region. Also, the concentrations of Hg, Pb and Cd are higher among women from the Chukotka Peninsula and Lovosero regions than among women from the

Table 5-23. Concentrations of POPs (μg/kg plasma lipids) in men (general population), by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007), Anda, E., pers. comm. (2008), Sandanger et al. (2003), Dudarev et al. (2003), Konoplev et al. (2005, 2006), Dudarev and Chashchin (2006).

	Chukotka Peninsula		Kola Peninsula		Pechora River Basin	Taymir Peninsula	Commander Islands
	Coastal	Inland	Lovosero	Krasnoschelye			
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Saami, Nenets and Komi	Nenets	Dolgan	Aleuts
	35 (19 – 68) [a] n = 24 [b]	32 (19 – 54) [a] n = 14 [b]	44 (18 – 77) [a] n = 4 [b]	44 (18 – 77) [a] n = 15 [b]	25 (18 – 62) [a] n = 13 [b]	39 (18 – 69) [a] n = 12 [b]	39 (18 – 58) [a] n = 40 [b]
Oxychlordane	91 (0.77 – 534)	3.8 (0.77 – 22)	1.9 (0.77 – 7.7)	1.5 (0.77 – 6.8)	2.1 (0.77 – 24)	3.3 (0.77 – 67)	NA [c]
Trans-nonachlor	321 (2.7 – 1267)	23 (8.0 – 10)	29 (15 – 47)	15 (2.7 – 51)	14 (2.7 – 61)	25 (2.7 – 66)	36 (2.7 – 228)
p,p'-DDT	36 (11 – 133)	25 (11 – 43)	105 (50 – 340)	47 (25 – 106)	53 (11 – 114)	32 (11 – 92)	37 (11 – 1265)
p,p'-DDE	637 (243 – 1516)	299 (192 – 580)	872 (345 – 3047)	37 (77 – 1272)	302 (19 – 1871)	322 (165 – 755)	533 (121 – 1807)
HCB	170 (3.6 – 610)	112 (63 – 259)	176 (113 – 231)	122 (36 – 362)	151 (61 – 424)	260 (104 – 1094)	44 (3.6 – 132)
β-HCH	392 (3.6 – 1162)	81 (3.6 – 875)	164 (74 – 297)	122 (49 – 292)	89 (48 – 224)	181 (86 – 340)	25 (3.6 – 359)
PCBs							
Aroclor 1260	1751 (337 – 6014)	147 (101 – 229)	569 (472 – 725)	300 (103 – 787)	220 (58 – 865)	265 (135 – 603)	176 (24 – 915)
CB99	113 (30 – 247)	22 (13 – 34)	32 (24 – 36)	19 (5.5 – 55)	21 (5.5 – 227)	18 (5.5 – 43)	6.3 (5.5 – 91)
CB118	136 (25 – 298)	44 (17 – 82)	77 (31 – 135)	36 (13 – 80)	23 (11 – 60)	35 (11 – 113)	8.0 (5.5 – 73)
CB138	304 (65 – 960)	32 (24 – 49)	107 (82 – 155)	61 (23 – 219)	45 (9.1 – 185)	57 (32 – 119)	47 (9.1 – 249)
CB153	807 (149 – 2863)	61 (37 – 107)	251 (219 – 360)	127 (39 – 310)	93 (28 – 365)	111 (54 – 264)	54 (6.4 – 397)
CB180	237 (47 – 934)	19 (8.9 – 48)	116 (85 – 191)	69 (15 – 182)	40 (9.1 – 270)	42 (12 – 122)	27 (3.6 – 379)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] not available.

Table 5-24. Concentrations of metals (μg/L whole blood) in pregnant women by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007; 2008).

	Chukotka Peninsula		Kola Peninsula	Pechora River Basin	Taymir Peninsula	Norilsk	Kamchatka
	Coastal	Inland					
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Nenets	Dolgan	Ethnic Russians	Koryak & Even
	26 (15 – 41) [a] n = 68 [b]	25 (18 – 40) [a] n = 58 [b]	20 (18 – 23) [a] n = 7 [b]	23 (16 – 38) [a] n = 38 [b]	27 (16 – 42) [a] n = 69 [b]	27 (19 – 35) [a] n = 10 [b]	21 (15 – 39) [a] n = 89 [b]
Total Hg	1.3 (0.50 – 6.2)	1.4 (0.50 – 7.7)	0.89 (0.50 – 2.4)	0.93 (0.50 – 5.6)	1.8 (0.50 – 20)	0.83 (0.50 – 3.0)	1.1 (1.0 – 2.8)
Pb	47 (18 – 227)	33 (13 – 92)	28 (17 – 52)	32 (2.5 – 92)	49 (14 – 224)	20 (10 – 37)	25 (11 – 53)
Cd	1.0 (0.19 – 4.7)	0.72 (0.10 – 2.5)	0.27 (0.05 – 1.3)	0.41 (0.05 – 2.8)	0.69 (0.05 – 2.9)	0.60 (0.21 – 1.2)	0.78 (0.43 – 1.3)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table 5.25. Concentrations of metals (µg/L whole blood) in women's blood by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007).

	Chukotka Peninsula		Kola Peninsula		Pechora River Basin	Taymir Peninsula	Commander Islands
	Coastal	Inland	Lovosero	Krasnoschelye			
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Saami, Nenets and Komi	Nenets	Dolgan	Aleuts
	38 (21 – 69) [a] n = 26 [b]	36 (19 – 81) [a] n = 18 [b]	42 (26 – 69) [a] n = 11 [b]	44 (18 – 78) [a] n = 47 [b]	32 (18 – 65) [a] n = 23 [b]	41 (20 – 72) [a] n = 28 [b]	34 (18 – 46) [a] n = 49 [b]
Total Hg	7.7 (2.4 – 23)	5.7 (1.0 – 29)	7.3 (1.3 – 29)	3.3 (1.0 – 8.2)	1.7 (0.52 – 4.6)	2.2 (0.53 – 6.1)	1.3 (1.0 – 8.7)
Pb	85 (41 – 166)	46 (16 – 81)	31 (14 – 165)	38 (12 – 343)	45 (17 – 184)	64 (22 – 123)	42 (16 – 158)
Cd	2.4 (0.67 – 9.2)	0.82 (0.18 – 2.1)	0.49 (0.11 – 1.2)	1.0 (0.05 – 4.9)	0.78 (0.05 – 3.0)	0.55 (0.04 – 2.4)	0.62 (0.10 – 6.3)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Kola Peninsula, the Pechora River Basin, the Taymir Peninsula, and the Commander Island regions. The higher concentrations of metals in older women from the coastal Chukotka region are in contrast to the lower concentrations seen in the Chukotka mothers (Table 5.24), possibly indicating a greater traditional food consumption by older women.

Concentrations of metals in men's blood from the same regions (Table 5.26) show a similar regional pattern to that for women, with concentrations highest in the Chukotka region. It is also apparent that concentrations of Hg, and Pb in men from the coastal part of the Chukotka region (10 and 129 µg/L whole blood, respectively) are slightly higher than in women from this region (7.7 and 85 µg/L whole blood, respectively).

5.1.8.3. **Breast milk**

Table 5.27 presents the concentrations of various organochlorine contaminants in the breast milk of mothers from the Arkhangelsk, Murmansk, and Chukotka regions of Russia. Concentrations of breast milk contaminants in the Arctic Russian regions of Arkhangelsk and Murmansk are available for two periods separated by five to nine years. The Chukotka data are only available for the period 2001 to 2002. Care must be taken in interpreting these data because sample size is limited in some regions.

Concentrations of oxychlordane in breast milk samples (Figure 5.3) were about eight-fold higher in indigenous (Inuit and Chukchi) Chukotka mothers (41 µg/kg lipids) than ethnic Russian mothers in the Arkhangelsk (4.9 µg/kg lipids) or Murmansk (5.2 µg/kg lipids) regions. Although concentrations were lower in the Arkhangelsk and Murmansk regions they declined significantly over this period. Concentrations of *p,p'*-DDE (Figure 5.4) show a different pattern with higher concentrations seen in the ethnic Russian mothers (710 and 748 µg/kg lipids) than in the indigenous mothers from Chukotka (225 µg/kg lipids). This pattern of higher oxychlordane concentrations in Chukotka mothers and higher *p,p'*-DDE concentrations in ethnic Russians is also seen in the maternal blood data (Table 5.21). As was the case for the maternal blood data, consumption of marine mammals is likely to be the source of oxychlordane, and commercial foods or local pesticide use may be the

Table 5.26. Concentrations of metals (µg/L whole blood) in men's blood by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007).

	Chukotka Peninsula		Kola Peninsula		Pechora River Basin	Taymir Peninsula	Commander Islands
	Coastal	Inland	Lovosero	Krasnoschelye			
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Saami, Nenets and Komi	Nenets	Dolgan	Aleuts
	35 (19 – 68) [a] n = 24 [b]	29 (19 – 42) [a] n = 12 [b]	40 (24 – 53) [a] n = 9 [b]	55 (45 – 77) [a] n = 4 [b]	33 (18 – 62) [a] n = 9 [b]	39 (18 – 69) [a] n = 12 [b]	39 (18 – 58) [a] n = 40 [b]
Total Hg	10 (3.6 – 26)	6.5 (0.50 – 15)	6.6 (0.50 – 22)	5.4 (3.0 – 12)	2.4 (1.0 – 4.4)	2.9 (1.0 – 7.5)	0.72 (0.01 – 226)
Pb	129 (73 – 332)	97 (32 – 196)	58 (21 – 117)	72 (42 – 102)	53 (29 – 85)	80 (27 – 189)	47 (13 – 121)
Cd	2.6 (1.4 – 6.2)	1.5 (0.05 – 4.6)	0.60 (0.18 – 1.2)	0.89 (0.38 – 1.7)	0.67 (0.32 – 1.6)	0.65 (0.05 – 2.7)	1.6 (0.01 – 8.6)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table 5-27. Regional variation and trends in contaminant concentrations (µg/kg lipid) in human breast milk from mothers in Chukotka, Arkhangelsk and Murmansk, Russia. Data show geometric mean (and range) for specified period of sampling. Source: Arkhangelsk 1996 (Polder et al., 2003), Arkhangelsk 2000 – 2002 (Polder et al., 2008), Murmansk 1993 (Polder et al., 1998), Murmansk 2000 – 2002 (Polder et al., 2008), Chukotka 2001 – 2002 (Anda et al., 2007b).

	Arkhangelsk Ethnic Russian			Murmansk Ethnic Russian			Chukotka Indigenous
	1996 22 (17 – 30) [a] n = 40 [b]	2000 – 2002 22 (17 – 27) [a] n = 23 [b]	SD [e]	1993 23 (18 – 30) [a] n = 8 [b]	2000 – 2002 21 (17 – 32) [a] n = 14 [b]	SD [e]	2001 – 2002 24 (21 – 30) [a] n = 48 [c]
Oxychlordane	6.3 (nd – 19)	4.9 (2 – 10)	$p < 0.001$	17 [d] (na – na)	5.2 (na – na)	$p < 0.0001$	41 (2 – 1070)
p,p'-DDE	1114 (352 – 3824)	710 (216 – 1735)	$p < 0.05$	1251 (817 – 2816)	748 (428 – 1473)	$p < 0.002$	225 (62 – 812)
CB153	72 (28 – 213)	49 (20 – 112)	ns	116 (66 – 318)	82 (49 – 183)	$p < 0.001$	82 (15 – 1252)
Toxaphene parlar 50	na	5.0 (5.0 – 22)	na	na	7.3 (na – na)	na	9.0 (> 0.5 – 112)

na: Not available; nd: not detected; ns: not significant.
[a] Arithmetic mean age and range of group sampled; [b] number of primipara mothers sampled; [c] number of primipara and multipara mothers sampled; [d] n = 3 in 1993 for oxychlordane; [e] significant difference.

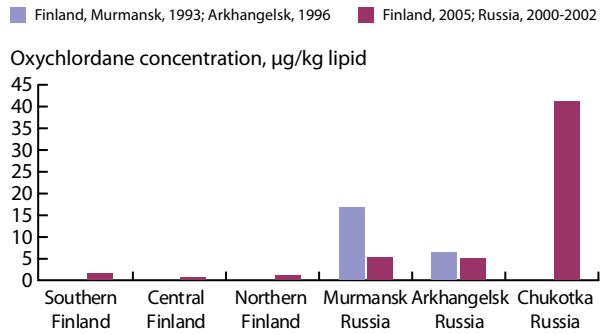


Figure 5-3. Oxychlordane concentrations in breast milk from various regions of Finland and northern Russia.

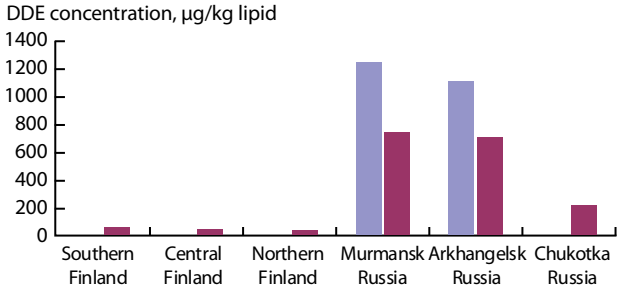


Figure 5-4. DDE concentrations in breast milk from various regions of Finland and northern Russia.

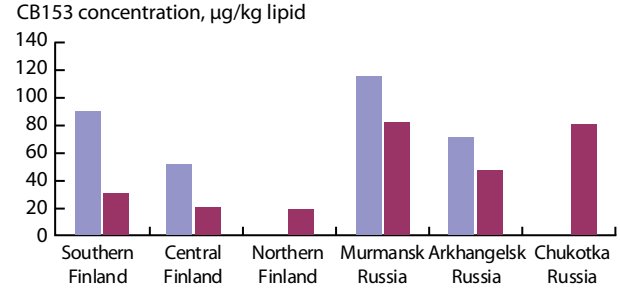


Figure 5-5. PCB (CB153) concentrations in breast milk from various regions of Finland and northern Russia.

reason for the increased *p,p'*-DDE concentrations. The decline in *p,p'*-DDE and oxychlordane concentrations may indicate that commercial foodstuffs in Russia have lower concentrations of these contaminants or that there is less use of these compounds for local pest control.

The concentration of CB153 in the breast milk of Russian mothers (Figure 5.5) does not follow the pattern seen in maternal blood or for oxychlordane in breast milk, where higher concentrations were seen in coastal Chukotka mothers. Significant declines in CB153 were seen in both Arkhangelsk (72 to 49 µg/kg lipids) and Murmansk (116 to 82 µg/kg lipids) in maternal breast milk and Chukotka mothers had similar concentrations to those in Murmansk. However, the sample size is limited so the data should not be over-interpreted as they may simply represent the range of variability in small sub-samples of a population.

5.1.9. Inter-country comparisons and temporal trends in the Arctic

The sampling of human tissue (blood and breast milk) for contaminants has taken place in a number of circumpolar countries since the early 1990s (see Figure 5.6). These data sets provide an opportunity to assess temporal trends and additional inter-country comparisons of organochlorines and heavy metals in pregnant women and in some cases, in adults (both men and women).

This analysis is based on the various population samples available for each country. The population sampled and the time periods covered for each country differ, but overall comparisons can be made. Some countries have two sampling time points, while others have several. The pattern of declining concentrations in countries that have two data points are similar to trends seen among mothers from parts of Arctic Canada and Greenland where more frequent population sampling took place over a similar period.

The similar patterns strengthen the overall findings presented in this section.

5.1.9.1. **Maternal blood and breast milk comparisons**

AMAP has generally used blood as the medium of choice for evaluating human exposure, although in some cases breast milk has been used where maternal blood data were not available.

The United Nations Environment Programme, in developing a global POPs monitoring program to support the effectiveness evaluation of the Stockholm Convention, identified blood, milk, and adipose tissue as essential indicators for human exposure evaluation (UNEP, 2003).

Although breast milk is useful in specific instances, notably when evaluating perinatal health risks, it suffers from several limitations which make it less than ideal for population exposure monitoring. Because concentrations in breast milk can only be determined after the birth, *in utero* exposure is not addressed. Also, because not all environmental contaminants are found in breast milk, child exposure from other sources may go unnoticed. In some cultures, women are unwilling to provide breast milk, but will provide blood samples.

Blood monitoring has a number of advantages over breast milk in evaluating population exposure. Blood is universally available from all members of a population; men, women and children all of whom are exposed to contaminants through diet (during and after breast-feeding in the case of infants and children) or from their immediate environment. Blood is easy to collect using standard techniques known to local health care workers (little training required) and cross contamination is rare. Blood concentrations accurately reflect the body burden of most contaminants, whether lipophilic, protein-bound, or ionic. For weakly lipophilic compounds, concentrations are much higher in blood than in milk. As an example, perfluorooctane sulfonate (PFOS) serum concentrations were found to be 100-fold greater than breast milk concentrations in paired maternal-newborn samples (Karrman et al., 2007a). For lipophilic compounds, which include most POPs, blood concentrations expressed on a lipid basis are well-correlated with concentrations in other compartments such as stored fat and breast milk. Blood concentrations obtained from pregnant women enable public health action, if required, during the pregnancy when the fetus is very susceptible to damage. Occupational and environmental exposure guidelines based on blood concentrations exist for many compounds.

Concerns that have been expressed regarding transmission of infectious diseases through handling of blood are not warranted. Blood samples are drawn and processed safely by thousands of health workers daily. Issues related to blood handling have been addressed by health practitioners worldwide through the use of universal precautions and appropriate transportation and storage protocols. Measurement of contaminant concentrations in blood can be performed with accuracy and adequate sensitivity. Previous studies have shown a very high correlation between maternal blood concentrations of organochlorines and breast milk concentrations in individual mothers, but these are separate population samples and it is very encouraging that they lead to very similar conclusions on regional concentrations and trends (Ayotte et al., 2003; Anda et al., 2007b).

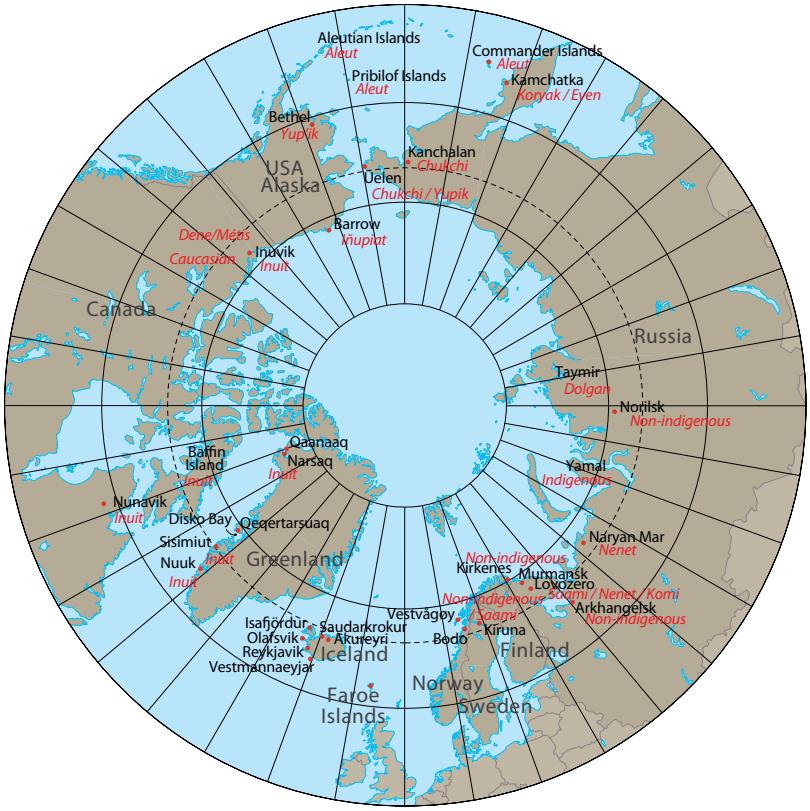
In conclusion, blood and breast milk are both useful and complementary media for monitoring environmental contaminants. With regard to blood, the focus on QA/QC related to the AMAP human health monitoring has been highly successful and has made inter-regional and time-trend evaluations meaningful for Arctic residents, scientists, and policy makers and as a component of the Stockholm Convention efforts to evaluate effectiveness.

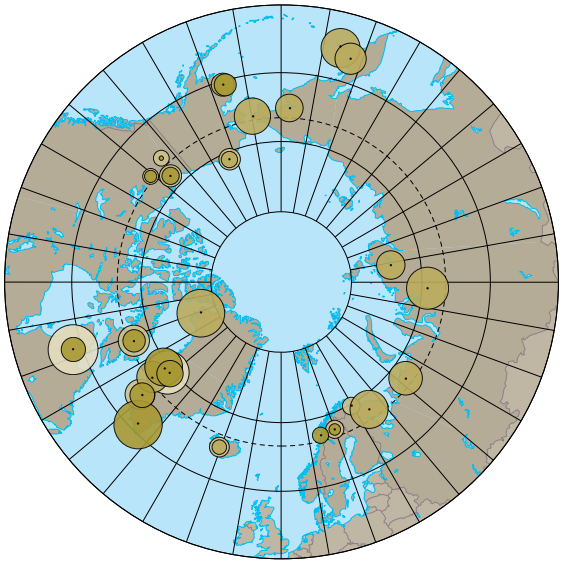
5.1.9.1.1. *Persistent organic pollutants*

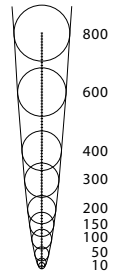
The results of recent biomonitoring studies reported in this chapter suggest that the concentrations of certain POPs (e.g., oxychlordane, DDE) are two- to ten-fold higher among Inuit living in eastern parts of the Canadian Arctic (Baffin and Nunavik) and Greenland compared to other populations in the Arctic (Norway, Sweden, Iceland, Dene-Métis from Inuvik Canada, see Figures 5.7 to 5.10), as was seen in previous assessments (AMAP, 1998, 2003). There are several cases where various organochlorines are similarly elevated in specific regions of Russia. For oxychlordane and CB153, the highest concentrations were found in maternal blood of Inuit and Chukchi living in the Chukotka Peninsula coastal region. These concentrations were slightly higher than the more recent concentrations among Inuit mothers from Arctic Canada and Greenland but not as high as some of those seen in the 1990s from these regions. Data for organochlorines in Inuit men are also available for Canada, Greenland, and Russia (Tables 5.7, 5.10, 5.23). The highest concentrations of oxychlordane and CB153 were seen in Qaanaaq, Greenland. These varying inter-country comparisons indicate the need for further time trend and regional monitoring. In Russia, the DDE concentrations in maternal blood were elevated in non-indigenous (ethnic Russian) and indigenous populations. The highest DDE concentration (452 μg/kg plasma lipids) was found among pregnant ethnic Russian women in the Norilsk area (Figure 5.7). This elevation of DDE in the Russian population is likely to be due to the use of DDT in the commercial Russian food supply or its use for residential or environmental pest control.

As shown in Figures 5.7 to 5.10, the data sets suggest that concentrations of legacy POPs have decreased in many populations compared to the data presented in the two previous AMAP assessments (AMAP, 1998, 2003). Notable decreases occurred in concentrations of oxychlordane, DDE and CB153 in maternal blood of Inuit living in parts of the eastern Canadian Arctic (Baffin and Nunavik) and Disko Bay in Greenland.

Figure 5·6. Locations and ethnicity of populations included in AMAP human health studies.







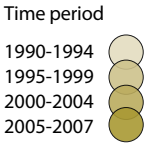
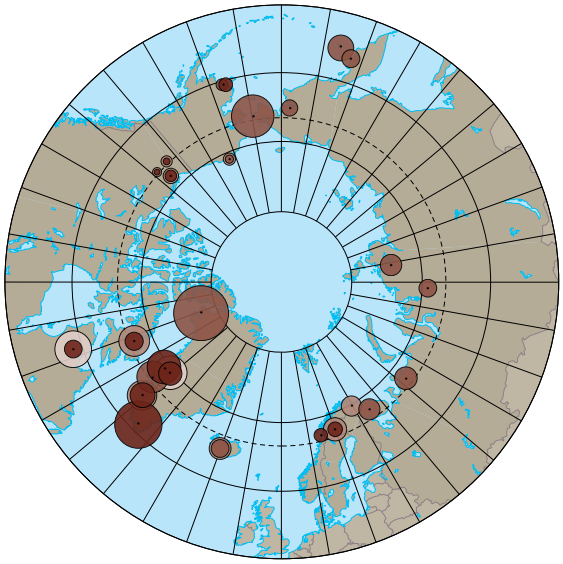
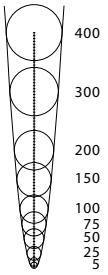


Figure 5·7. DDE (*p,p′*-DDE) concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.





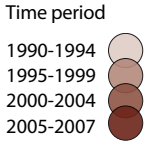


Figure 5·8. PCB (CB153) concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

There are exceptions to the overall decreases in POPs concentrations in maternal blood samples in the circumpolar region. In Nuuk, Greenland, where only intermediate concentrations of contaminants were found in mothers during the 1990s, due to lower marine mammal consumption, annual changes are variable and there has been no significant decline in the concentrations of oxychlordane, DDE, and CB153. People living in Nuuk have always had greater access to store-bought food and may not have changed their marine food consumption as much as other communities where people relied more heavily on traditional marine foods.

Dietary studies help to interpret trends in POPs concentrations in human populations. Unfortunately, dietary studies were not carried out in parallel with many of the contaminant trend assessments. Initial dietary trend analyses have been assessed in the Inuvik region of Canada and Disko Bay in Greenland and provide support for the changes in maternal contaminant concentrations. In the Inuvik region, Inuit mothers were eating more fish (which have lower concentrations of contaminants, see sections 5.1.2 and 3.1.4 for further details) and less marine mammal fats (which have higher concentrations of contaminants). In Greenland, mothers are also eating smaller amounts of the more highly contaminated marine mammals, which supports the declining trends observed in maternal contaminant concentrations (see section 5.1.3 for further details).

The more moderate decrease in organochlorine concentrations in Norway, Sweden, Iceland, and Finland is likely to be due to the banning and/or restriction of many of these compounds in these regions during the 1970s, and the resulting decline in the concentrations of these contaminants in the commercial/store-bought food chain. In Russia, the results of this assessment suggest that exposure to several organochlorines could be associated with household or environmental use of insecticides, possible use in the commercial food supply, or contamination during food processing.

The breast milk studies carried out in Finland and Russia complement the data in the maternal blood

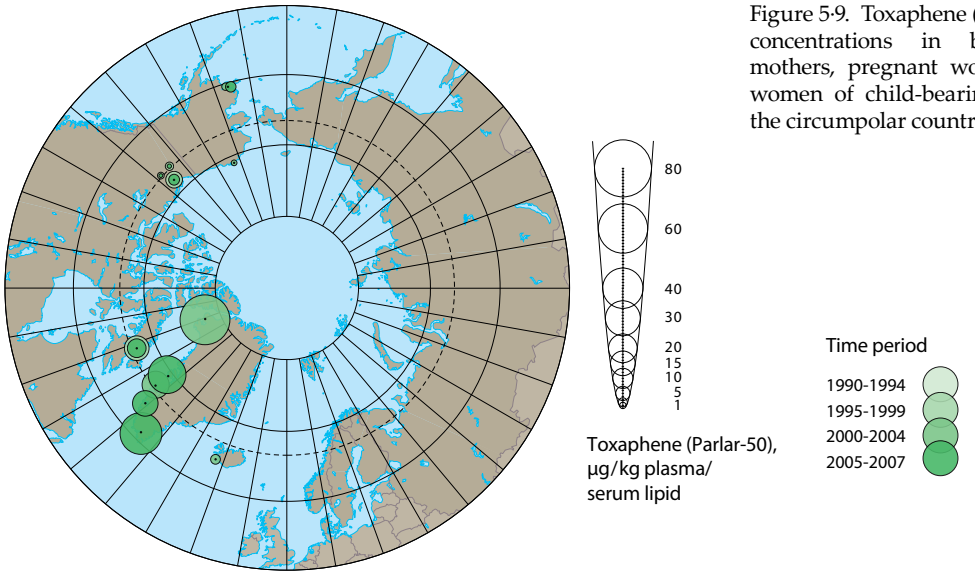


Figure 5-9. Toxaphene (parlar-50) concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

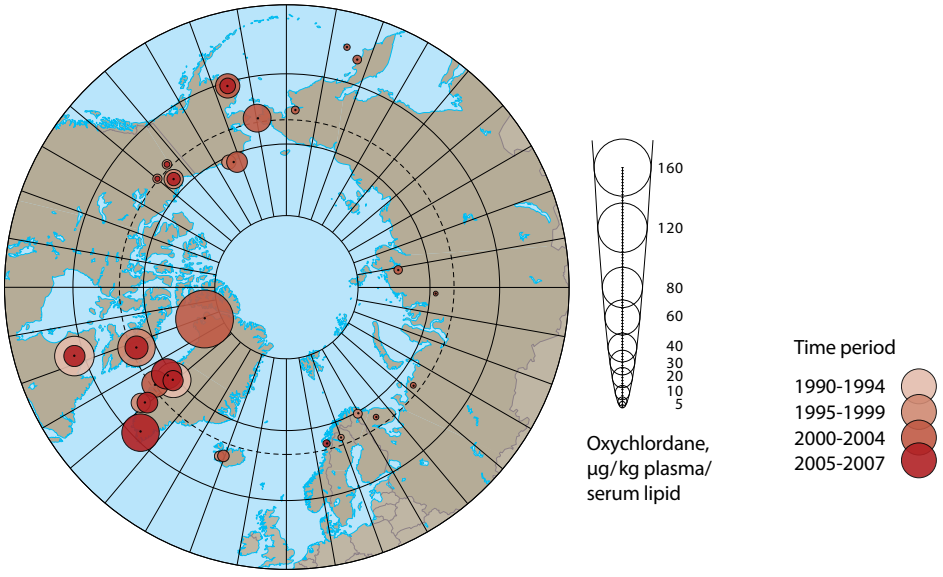


Figure 5-10. Oxychlordane concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

studies (see sections 5.1.7 and 5.1.8 for details). Breast milk studies are available for southern and central Finland and the Murmansk, Arkhangelsk, and Chukotka regions in Russia. As shown in Figures 5.3 to 5.5, for the cases where two time points were available in Finland and Russia, there was a decrease in concentrations of oxychlordane, DDE, and CB153 as was seen elsewhere in the Arctic in maternal blood. Also, the highest concentrations of DDE and oxychlordane occur in Russian mothers as was seen in the maternal blood comparisons.

5.1.9.1.2. *Metals*

The highest concentrations of total Hg tend to be among Inuit mothers living in the Baffin and Nunavik regions of Arctic Canada and Greenland (Figure 5.11). These concentrations are linked to their high consumption of marine mammals. As was seen in previous assessments, Inuit women of child bearing age that consume marine mammals have Hg concentrations that are three- to ten-fold higher than in other populations in the Arctic that consume market foods (AMAP, 1998, 2003). The significant decline in maternal Hg concentrations in these populations with the highest exposure concentrations is encouraging. Also, it is interesting that the Russian populations with elevated concentrations of various organochlorines do not show elevated concentrations of Hg. This indicates the need for follow-up monitoring studies closely linked with dietary studies to examine these differences in exposure to contaminants.

Concentrations of Pb in indigenous Arctic populations tend to be slightly elevated, but are declining in most populations (Figure 5.12). This change was noted in the previous AMAP assessments (AMAP, 1998, 2003). However, recent monitoring of maternal blood in Russia has found moderately elevated concentrations of Pb (Figure 5.12), although the source is not known. Continued use of lead shot for hunting among indigenous peoples remains a significant source of Pb exposure in Arctic Canada and may be a significant source in other circumpolar countries.

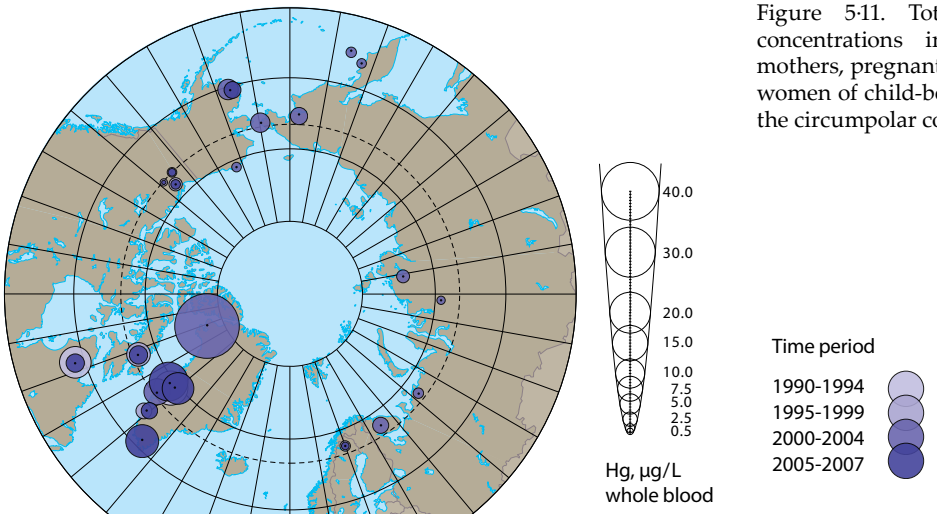


Figure 5·11. Total mercury concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

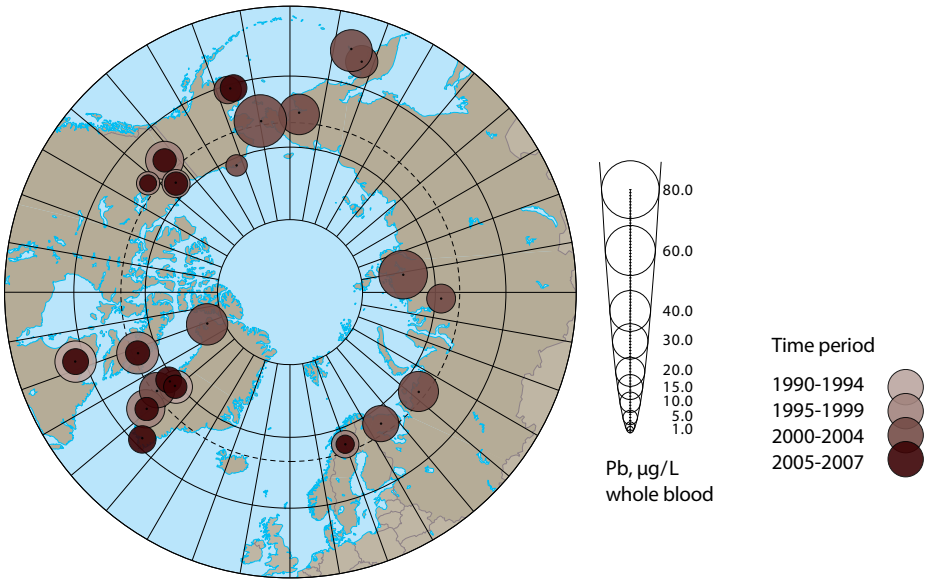


Figure 5·12. Lead concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

5.1.10. Contaminant tissue concentrations and guidelines

This section compares tissue concentrations of PCBs (as Aroclor 1260), Hg, and Pb within different regions of the Arctic against the established guidelines shown in Table 5.28. Background information on how these guidelines were developed is available in the previous AMAP assessment (AMAP, 2003). The percentage of mothers and women of reproductive age exceeding the blood guidelines in regions of Canada, Greenland, Iceland, and Russia is summarized in Table 5.29.

5.1.10.1. PCB tissue concentrations and guidelines

Few biological guidelines have been developed for PCBs (AMAP, 2003). The Health Canada (1986) PCB guideline suggests that the Level of Concern (LoC) is reached when concentrations are greater than 5 µg/L (as Aroclor 1260) in maternal blood. The Level of Action (LoA) occurs at concentrations greater than 100 µg/L in human blood.

Blood guideline exceedances for PCBs (as Aroclor 1260) (see Figure 5.13) are summarized for mothers from the Inuvik region (NWT), Nunavut, and the Nunavik region (northern Quebec) in Canada (Table 5.29). The recent results of biomonitoring studies (i.e., since 2003) conducted in the Inuvik region indicate that 7% of the Inuit mothers' blood samples exceeded the 5 µg/L LoC while none of those from Dene-Métis and Caucasian mothers exceeded this value. In Nunavut, 24% of the Inuit mothers' blood samples exceeded the 5 µg/L LoC, and in Nunavik this increased to 52%. None of the blood samples exceeded the 100 µg/L LoA in any

Table 5.28. Guidelines for selected contaminants, women of childbearing age.

	Level of Concern	Level of Action	Source
PCBs (as Aroclor 1260)	5 µg/L	100 µg/L	Health Canada, 1986
Hg (blood) based on US EPA evaluation	5.8 µg/L		No formal guideline developed in the United States. Based on NRC (2000) re-evaluation of Hg. Benchmark dose level of 58 µg/L and 10-fold safety factor
Hg (blood) health	20 µg/ L (increasing risk range)	100 µg/L (at risk range)	Health Canada, 1984
Pb	Not available	100 µg/L (level of intervention)	Health Canada, 1994

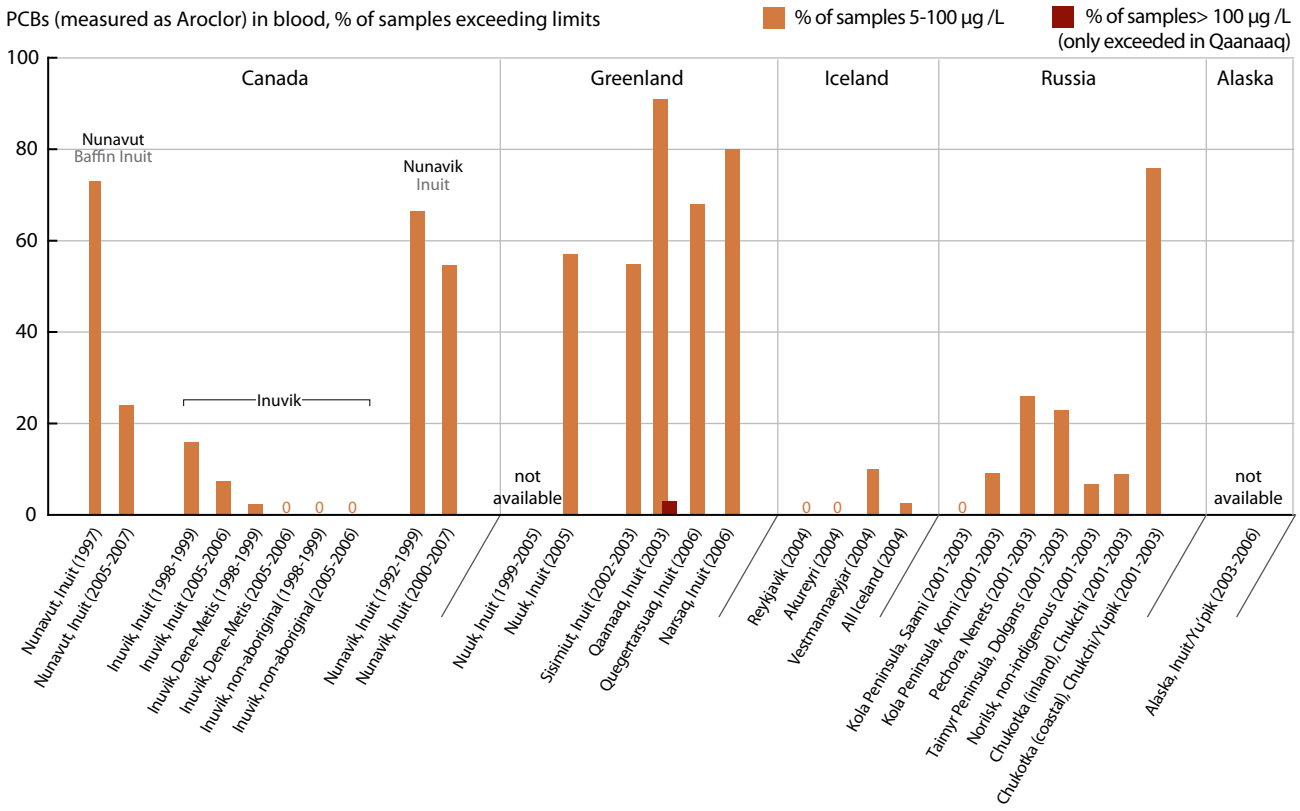


Figure 5.13. Exceedance of blood guideline values for PCB (measured as Aroclor) in mothers and women of child-bearing age in different populations around the Arctic (comparable data were not available from Norway, Sweden and Finland).

Table 5-29. Blood Guideline Exceedance (percentage of samples from mothers and women of reproductive age).

Country Region/ Ethnicity	n	Year	Mercury (total)		Lead	PCBs as Aroclor 1260	
			% of samples exceeding 5.8 µg/L	% of samples exceeding 20 µg/L	% of samples exceeding 100 µg/L	% of samples exceeding >5 µg/L	% of samples exceeding 100 µg/L
Alaska, USA							
Inuit-Yupik	75	2003 – 2006	19	na	na	na	na
Canada[a]							
Nunavut/ Baffin Inuit	31	1997	68	9.7	9.7	73	0
	100	2005 – 2007	32	2.0	0	24	0
NWT Inuvik/ Inuit	31	1998 – 1999	16	3.2	3.2	16	0
	52	2005 – 2006	5.6	0	0	7.4	0
Inuvik/ Dene/Metis	42	1998 – 1999	2.4	0	4.8	2.4	0
	17	2005 – 2006	0	0	0	0	0
Inuvik/ Non-Aboriginal	21	1998 – 1999	0	0	0	0	0
	6	2005 – 2006	0	0	0	0	0
Nunavik/ Inuit	11	1992	55	36	9.1	91	0
	25	1996	76	20	8	68	0
	53	1997	72	19	13	72	0
	27	1998	52	3.7	19	44	0
	16	1999	56	13	13	58	0
	29	2000	59	17	10	57	0
	19	2001	47	26	5.3	55	0
	31	2004	61	7	0	52	0
	42	2007	31	2.4	0	na	na
Greenland[b]							
Sisimiut/ Inuit	42	2002-2003	64	12	2.4	55	0
Qaanaaq/ Inuit	34[c]	2003	97	94	3.2	91	3
Nuuk/ Inuit	44, 45	2005	20	0	2.2	57	0
Quegertarsuaq/ Inuit	44, 45	2006	98	43	0	68	0
Narsaq/ Inuit	42	2006	86	19	2.4	80	0
All 8 regions	297[d]	1999 – 2006	76	35.3	3.3	72	7.7
Nuuk/ Inuit	195	1999 – 2005	30	1	0	na	na
Iceland[b]							
Reykjavik	20	2004	na	na	na	0	0
Akureyri	10	2004	na	na	na	0	0
Vestmannaeyjar	10	2004	na	na	na	10	0
All Iceland	40	2004	na	na	na	2.5	0
Norway			na	na	na	na	na
Sweden			na	na	na	na	na
Finland			na	na	na	na	na
Russia[a]							
Chuktoka Peninsula coastal/ Chukchi and Inuit	68	2001 – 2003	1.5	0	7.4	76	0
Chuktoka Peninsula inland/ Chukchi	58	2001 – 2003	6.9	0	0	9	0
Kola Peninsula / Saami	2	2001 – 2003	0	0	0	0	0
Kola Peninsula / Komi	5	2001 – 2003	0	0	0	9.1	0
Pechora River Basin/ Nenets	38	2001 – 2003	0	0	0	26	0
Taymir Peninsula / Dolgan	69	2001 – 2003	12	0	13	23	0
Norilsk-Ethnic Russians	10	2001 – 2003	0	0	0	6.8	0

na = not available; [a] mothers; [b] women of reproductive age; [c] in Qaanaaq n = 34 for PCB exceedance, n = 36 for mercury exceedance and n = 31 for lead exceedance; [d] for all eight Greenland regions n = 297 for PCB exceedance, n =300 for mercury exceedance and n =295 for lead exceedance.

of the Canadian mothers. The percentages of Inuit from Nunavut and Nunavik that exceeded the 5 μg/L PCB guideline are the highest of all the groups, which corresponds to the elevated concentrations of PCBs in these two populations.

By comparing the concentrations of PCBs from the recent biomonitoring studies to those of the older biomonitoring studies, insight into changes in contaminant concentrations can be gained. Table 5.29 indicates that the percentage of samples exceeding the LoC for PCBs is markedly higher in Inuit populations of the Inuvik, Baffin, and Nunavik regions and decreased markedly between the 1990s and 2006. Overall, these results indicate that there is a decreasing proportion of mothers exceeding the 5 μg/L LoC for PCBs and the results support the overall decreasing concentrations of PCBs among these mothers (see section 5.1.2 for more details).

In Greenland, Inuit women of reproductive age in Sisimuit, Qaanaaq, Nuuk, Quegertarsuaq, and Narsaq exceeded the 5 μg/L LoC for PCBs by 55%, 91%, 57%, 68%, and 80%, respectively. Data compiled from eight Greenlandic regions studied between 1999 and 2005, indicated that 72% of women exceeded the 5 μg/L guideline. Despite the high proportion of the populations exceeding the LoC, only 3% of women in Qaanaaq had blood PCB concentrations exceeding the 100 μg/L guideline and 8% overall in the eight Greenlandic regions studied. PCB exceedances in Greenland are most closely comparable to exceedance levels found in Inuit mothers in Nunavik, Canada (Table 5.29).

Results from a recent Icelandic study indicate that only 10% of women (of reproductive age) in Vestmanaeyjar exceeded the 5 μg/L LoC for PCBs, and none exceeded this level in the other regions. None of the women sampled exceeded the 100 μg/L LoA. In the previous AMAP assessment (AMAP, 2003), the percentage exceedance of the 5 μg/L LoC ranged from 22% to 50% in the four Icelandic regions of Reykjavik, Vestmannaeyjar, Olafsvik and Saudarkrokur (AMAP, 2003, section 9.3.2). The lower proportion of samples from the 2004 biomonitoring study which exceeded the PCB 5 μg/L guideline supports the trend for decreasing concentrations of PCBs in Iceland (section 5.1.4).

In Russia, all regions except that of the Saami on the Kola Peninsula had a proportion of the women with PCB concentrations above the 5 μg/L LoC. Of these, the percentage of mothers exceeding the 5 μg/L guideline in Russia was lowest for ethnic Russians in Norilsk at 7%, followed closely by Chukchi living inland on the Chukotka Peninsula at 9% and Komi from the Kola Peninsula also at 9%. The Nentsi from the Pechora River Basin region and the Dolgani from the Taymir Peninsula were similar at 26% and 23% of mothers exceeding the LoC, respectively. The highest percentage exceedance among all mothers in Russia was found to be for Chukchi and Inuit mothers from the coastal Chukotka region at 76%, which is the group with the highest concentrations of PCBs. None of the women in Russia exceeded the 100 μg/L LoA.

5.1.10.2. **Metal tissue concentrations and guidelines**

This section compares blood guideline exceedance for Hg (total) and Pb in women of reproductive age. Data from Canada, Greenland, and Russia show that the proportion of women exceeding LoCs for metals are generally lower than the percentage exceedance of the PCB LoC. Regional comparisons between countries and between indigenous and non-indigenous groups are limited because recent data for metals were not available for Iceland, Norway, and Finland.

5.1.10.2.1. *Mercury*

The blood guideline established by Health Canada for Hg considers concentrations below 20 μg/L in human blood to be within an acceptable range (Health Canada, 1984). Mercury concentrations between 20 and 100 μg/L have been determined by health officials to be at 'increasing risk', and Hg concentrations that exceed 100 μg/L in blood are considered to be 'at risk'. The U.S. National Research Council re-evaluated the Hg risk assessment (NRC, 2000). The NRC report developed a Bench Mark Dose level of 58 μg/L for Hg and suggested that a ten-fold uncertainty factor be applied in the development of a Tolerable Daily Intake (NRC, 2000). Based on this evaluation an informal blood guideline value for Hg of 5.8 μg/L in blood has been developed (see AMAP, 2003, section 9.3.1 for further details about Hg guidelines). Information on exceedance of the guidelines for maternal blood in the Arctic region is presented in Figure 5.14.

The recent contaminant monitoring among mothers from the Inuvik region, Nunavut, and Nunavik, indicates that only 2% of Inuit mothers from Nunavut and Nunavik were in the Health Canada 'increasing risk range' of 20 to 100 μg/L (Table 5.29). None of the Inuit, Dene-Métis or Caucasian mothers from the Inuvik region exceeded the 100 μg/L at risk guideline. The percentage of mothers that exceeded the 5.8 μg/L guideline value for Hg was 6% for Inuit from the Inuvik region, 32% for Inuit from Nunavut, and 31% for Inuit from Nunavik. In parallel with the decrease in Hg concentrations in maternal blood in many Arctic populations, the proportion of Inuit mothers from the recent biomonitoring studies that exceeded the Health Canada 20 μg/L 'increasing risk' guideline and the 5.8 μg/L value has decreased markedly relative to earlier biomonitoring studies reported by AMAP (2003).

In Greenland, a high proportion of women of reproductive age exceeded the Hg blood guidelines. In particular, women sampled in 2003 in Qaanaaq had a high level of exceedance, with 97% exceeding the 5.8 μg/L guideline, and 94% exceeding the 20 μg/L guideline. In comparison, 64% of women in Sisimiut exceeded 5.8 μg/ L and 12% exceeded 20 μg/L. In 2006, 98% of women in Quegertarsuaq exceeded 5.8 μg/L and 43% exceeded 20 μg/L, while 86% and 19% of women in Narsaq exceeded the 5.8 μg/L and 20 μg/L guidelines, respectively. For all eight Greenlandic regions, the guideline of 5.8 μg/L was exceeded by 76% of women

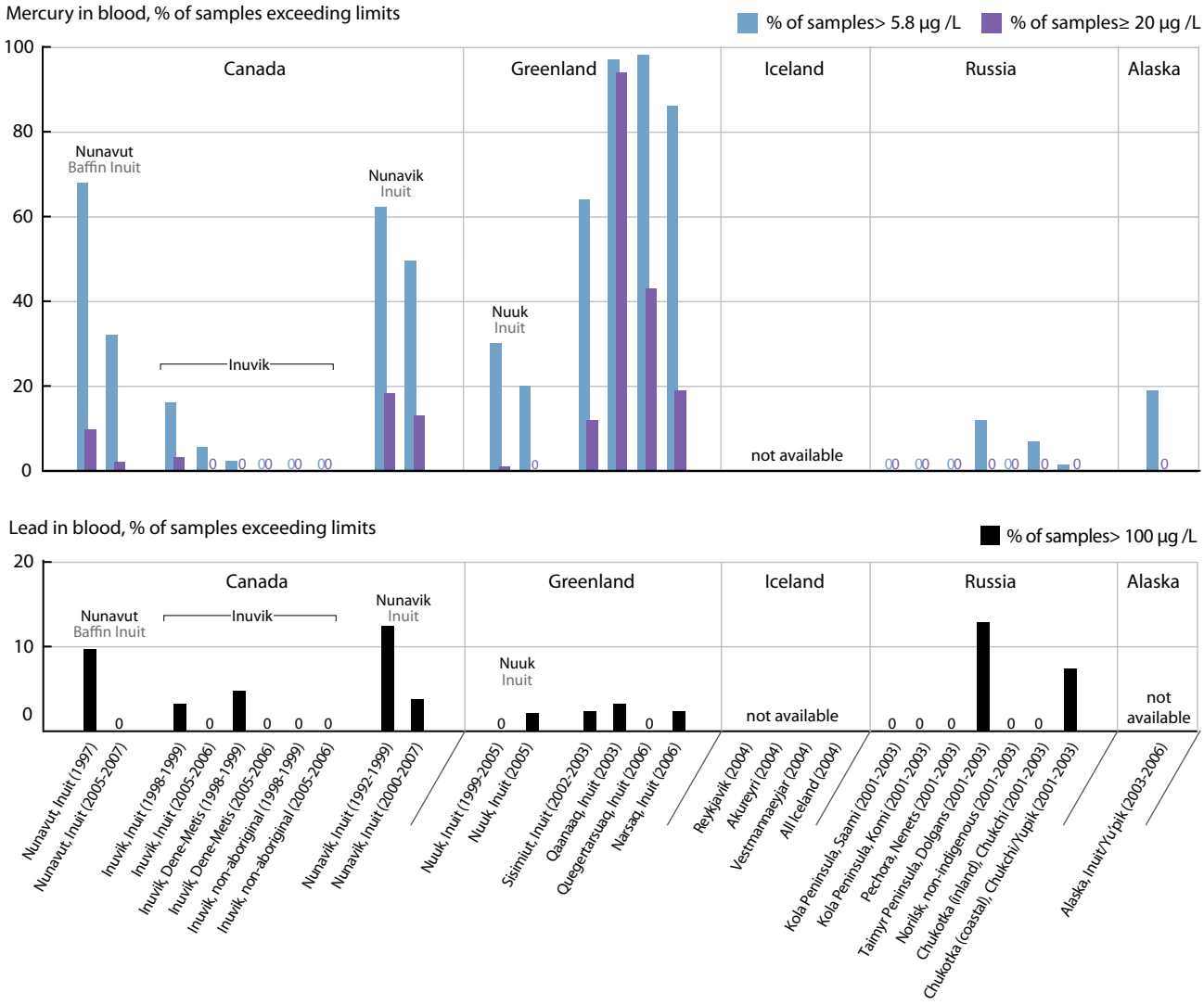


Figure 5-14. Exceedance of blood guideline values for (total) mercury and lead in mothers and women of child-bearing age in different populations around the Arctic (comparable data were not available from Norway, Sweden and Finland).

and the Health Canada guideline of 20 µg/L was exceeded by 35% of all women. Women in Nuuk in 2005 exhibited the lowest level of exceedance with only 20% exceeding the lower guideline and none exceeding the upper guideline. In a separate study which pooled data for the years 1999 to 2005 for Nuuk, comparable results found that 30% and 1% of women were above the 5.8 µg/L and 20 µg/L guidelines, respectively.

In Russia, none of the mothers exceeded the 20 µg/L guideline for Hg. The region with the highest exceedance of the 5.8 µg/L guideline was the Taymir Peninsula, yet only 12% of the Dolgani mothers exceeded this guideline. Chukchi and Inuit mothers on the Chuktoka Peninsula coastal and inland regions exceeded the 5.8 µg/L guideline by 2% and 7%, respectively. As Russian mothers had lower concentrations of Hg, the proportion exceeding various guidelines is lower. The Inuvik region of Canada, which also had lower concentrations of Hg, is the only area where the population's Hg exceedances are similar to those of Russia.

5.1.10.2.2. *Lead*

For Pb, the Canadian and U.S. blood Level of Intervention is 100 µg/L (Health Canada, 1994). In Canada, none of the mothers from the Inuvik region, Nunavut, or Nunavik exceeded the 100 µg/L guideline (Table 5.29). When comparing these results to previous biomonitoring studies reported by AMAP (AMAP, 2003), a large proportion of the population did not exceed this guideline (88% to 97%) in the 1990s, but there is a consistent decline in all populations studied in Arctic Canada. Information on exceedance of the guidelines for maternal blood in the Arctic region is presented in Figure 5.14.

A small proportion of women in all regions of Greenland exceeded this guideline concentration for Pb. The percentage exceedances of the 100 µg/L LoA in Sisimiut, Qaanaaq, Nuuk, and Narsaq were 2.4%, 3.2%, 2.2% and 2.4%, respectively. In Quegertarsuaq, none of the women had concentrations above the

guideline. None of the women sampled in Nuuk exceeded the guideline.

The percentage of Russian mothers exceeding the 100 μg/L LoC on the Chuktoka Peninsula coastal region and the Taymir Peninsula at 7% and 13%, respectively, were relatively high compared to those of Greenland and Canada. However, none of the mothers in the other Russian regions exceeded the guideline.

5.1.11. Conclusions

Several important conclusions can be drawn from the information that has been presented in this section on the concentrations of organochlorine chemicals and certain metals in pregnant women and mothers, as well as in adults (both men and women) living in the circumpolar region.

Inuit populations of Greenland, Canada, and the United States continue to have higher concentrations of legacy contaminants, similar to what was seen in the previous assessments (AMAP, 1998, 2003). These concentrations are linked to the consumption of marine mammals. In addition, this assessment incorporates new regional sampling from Russia, and again the Inuit or coastal populations that consume marine mammals have the highest concentrations of contaminants. Also, the patterns of DDT and DDE concentrations in some parts of Russia (with greater proportions of DDT) suggest that human exposures to pesticides are associated with local sources of contamination (e.g., soil contamination during food processing) and use of pesticides on the commercial food supply (see AMAP, 2003).

A series of biomonitoring studies have taken place in the Arctic which allow an initial assessment of changes in contaminant concentrations. The recent data presented in this assessment suggest that concentrations of contaminants such as DDE, PCBs, oxychlordane, Hg, and Pb are decreasing in many Arctic populations. The decrease may be related to lower concentrations of organochlorine chemicals in the environment as well as to dietary changes. Limited dietary data from Arctic Canada and Greenland suggest that changes are taking place in the traditional diet of Inuit mothers. Consumption of traditional food species that have higher concentrations of contaminants (e.g., marine mammals) is decreasing, while consumption of other species with lower concentrations of contaminants (e.g., fish and caribou) is increasing. This would result in an overall decrease in dietary exposure to contaminants. However, decreasing consumption of these traditional foods is not a positive indicator for human health as there are positive cardiovascular and neurobehavioral benefits to the consumption of these foods.

Both blood and breast milk can be used for monitoring contaminant concentrations. The preference for blood monitoring in the Arctic is based on a need for information on both males and females, multiple age groups (children, adolescents, adults, senior citizens) and both POPs and metals. Several studies and data provided in previous AMAP assessments indicate that contaminant concentrations in blood and breast milk are well correlated and inter-comparable.

The results presented in this chapter illustrate the need for continued monitoring of organochlorines and metal concentrations in human populations in the Arctic, especially for mothers or women of reproductive age and children. These data are important to allow a more complete assessment of trends in contaminant concentrations in a broader range of Arctic populations. The issue of decreasing contaminant exposure and decreasing traditional food consumption is very important in a number of circumpolar countries and is specifically addressed in Chapter 9.

5.2. Emerging contaminants of concern for humans in Arctic regions

In addition to the legacy POPs discussed in section 5.1, a growing number of compounds are being detected in humans from the Arctic regions of the world. Some of these are fairly 'new' compounds whereas others have been around for decades but have only recently been detected due to advances in analytical techniques. The main compounds addressed in this section are the brominated flame retardants and the perfluorinated compounds, in particular the polybrominated diphenylethers (PBDEs), perflourooctane sulfonate (PFOS), and perflourooctanoic acid (PFOA). Until recently, there were few data available on human concentrations of these compounds.

Concentrations of PBDEs in the Arctic are low in general, with the exception of Alaska where concentrations are much higher. Reported concentrations in Alaska are comparable to, or even higher than, those that have been reported in the U.S. general population. Concentrations in the Canadian Arctic were considerably lower than in Alaska, but higher than in the European Arctic. BDE_{47} was the predominant PBDE congener. Other brominated flame retardants investigated were tetrabromobisphenol A (TBBPA) and hexabromocyclodecane (HBCD), which showed low exposures based on limited data. Concentrations of PFOS were generally high throughout the Arctic, and comparable to concentrations reported in several other heavily populated areas. There were minor inter-country differences, but comparisons were limited by small sample sizes. Concentrations of PFOA were much lower than concentrations of PFOS but were elevated compared to the legacy POPs, and were clearly distributed throughout the Arctic. Limited data from Nunavik (Canada) showed an increase in ΣPBDE concentrations and a decrease in PFOS concentrations. There is, however, a clear need for ongoing monitoring of these compounds. Several other compounds of concern, such as short-chain chlorinated paraffins (SCCPs), parabenes and siloxanes plus metabolites of PCBs, should also be screened at regular intervals.

5.2.1. **Brominated flame retardants**

PBDEs, polybrominated biphenyls (PBBs), TBBPA and HBCD are some of the predominant brominated flame retardants. The PBBs are no longer in production due to a voluntary phase-out by producers. It is well known that the physical properties of PBDEs encourage long-range transport and accumulation, and this is supported by measured concentrations of PBDEs in air and biological samples from remote areas of the Arctic. This is the first AMAP assessment presenting human plasma data on PBDEs.

The PBDEs consist of three technical mixtures: the penta-, octa-, and decaBDEs, each varying in degree of bromination and application. Of these technical mixtures, the penta and octa formulations were banned in 2004 by the European Union and are soon to be banned by the United States and Canada (Vonderheide et al., 2008). Great Lakes Chemicals ceased production of the penta and octa mixtures in North America at the end of 2004 (de Wit et al., 2006). Therefore, decabrominated diphenylether (decaBDE) accounts for most of the PBDE produced, with an annual production of 56 000 tonnes (www.bsef.com). TBBPA is dominating the global production of brominated flame retardants together with decaBDE and HBCD (Law et al., 2006). Some applications of TBBPA as a flame retardant are bound in the product, and the environmental release is thus expected to be considerably less than for the PBDEs which are simply mixed in the final product.

In humans, the predominant brominated flame retardants are the PBDEs. The highest human concentrations are reported in North America, particularly in the United States, where concentrations are up to one order of magnitude higher than in other parts of the world (Sjodin et al., 2008). In the United States, concentrations of PBDEs still seem to be increasing, whereas human concentrations have been reported to be leveling off or declining since 1998/99 in Norway and Sweden (Meironytè-Guvenius, 2002; Lind et al., 2003; Schecter et al., 2005; Thomsen et al., 2007).

In environmental biological samples, including humans, the lower brominated congeners (BDE47 and/or BDE99) predominate, although BDE209 is also observed and seems to be of increasing importance. BDE153 has a longer half life and with the phase-out of the penta and octa mix, a shift towards BDE153 dominating human samples is expected. With a longer half life, BDE153 is also expected to persist for longer in the environment and might be expected to be related more to the food chain than the other PBDEs (Thomsen et al., 2002; Thuresson et al., 2006b; Sandanger et al., 2007). BDE153 is also present in both the penta and octa mix, as opposed to BDE47 which is primarily in the penta mix.

PBDEs are being found in concentrations approximately one order of magnitude lower than for PCBs. Exceptions are observed in North America, where concentrations of PBDEs are reported to be comparable to those for PCBs (Sandanger et al., 2007). In general, potential exposure routes for PBDEs and other brominated flame retardants are more complex than exposures routes to legacy POPs for which food is the main contributor. In industrialized or westernized countries, there are indications that food and indoor dust/air are the predominant pathways; however, conclusive data are lacking. In remote communities with fewer consumer products, exposure through the food chain is more likely to be the main route of exposure. In relation to the different exposure scenarios, differences in the congener pattern are expected due to differences in half lives and bioaccumulation factors.

For other brominated flame retardants such as TBBPA and HBCD, there are few biomonitoring data. There are many analytical challenges related to these compounds, and there is therefore a lack of data. However, the few data that do exist indicate that concentrations of these compounds are also increasing in the Arctic. Considering the large quantities of the compounds that are produced globally, this is of great concern. Production has increased with the phasing-out of the penta- and octaBDEs, and there are currently no limitations on their production or use. In southern Norwegian archived samples, no time trend was observed for TBBPA, and it was concluded that the short half life of this compound could explain the lack of accumulation with time (Thomsen et al., 2007).

5.2.2. **Perfluorinated compounds**

The chemical properties of the perfluorinated compounds, and their production and use were described in previous AMAP assessments (AMAP, 2003, 2004); however, due to analytical challenges, the perfluorinated compounds have received less attention than deserved (Hekster et al. 2003). The analytical methodology has, however, improved considerably over the last few years, and so the amount of data on human concentrations has increased considerably, with a focus on PFOS and PFOA.

PFOS and PFOA seem to be retained in the human body and to resist metabolic breakdown. Half lives for PFOS and PFOA are reported to be in the range of four to eight years, with PFOS having the longer half life (Olsen et al., 2005, 2007a). Due to their widespread use and bioaccumulative properties (Martin et al., 2003; Powley et al., 2008), PFOS and PFOA are detected in blood/serum/plasma samples of the general population worldwide, as well as in umbilical cord blood (Inoue et al., 2004; Karrman et al., 2006a,b; Calafat et al., 2007). A short review of the possible toxic effects of perfluorinated compounds is presented in Chapter 8, section 8.3.2.1.2.

POPs bioaccumulate and increase with age, but PFOS and PFOA are present at similar concentrations in all age groups (Olsen et al., 2003, 2004; Calafat et al., 2007), although some very recent data indicate an increase with age in women (Rylander, C., pers. comm., 2008). Significantly lower concentrations have been reported for women compared to men (Harada et al., 2004; Calafat et al., 2007; Fromme et al., 2007b). PFOS and PFOA concentrations have been reported to have increased from 1974 to 1989 and from 1977 to 2003 in southern

industrial countries (Harada et al., 2004; Olsen et al., 2005). However, more recent data from the United States provide strong evidence of concentrations having started to decline since the phase-out in 2000. A study on blood from American Red Cross donors showed that PFOS and PFOA concentrations were significantly lower (60% and 25%, respectively) in 2006 compared to 2000/2001 (Olsen et al., 2008). Calafat et al. (2007) also reported a significant decline when comparing 1999/2000 samples with 2003/2004 samples from the U.S. population (Calafat et al., 2007).

Both food and indoor dust seem to be important sources of potential human exposure, even though it was recently concluded that the main exposure route was through the diet (Fromme et al., 2008).

Long-range transport to the Arctic and the potential precursors is a complex process and not discussed here.

Wet weight concentrations of perfluorinated compounds in human plasma are high compared to those of legacy POPs; however, in contrast to POPs, perfluorinated compounds are not associated with lipids and so are not stored in body fat. Concentrations of perfluorinated compounds are therefore only reported on a wet weight basis.

5.2.3. Halogenated phenolic compounds

5.2.3.1. Pentachlorophenol

Pentachlorophenol (PCP) has been known as an environmental contaminant for many years, with its chemical properties and use described in a previous AMAP assessment (AMAP, 2003). Despite PCP being recognized as a globally distributed contaminant, there have been few human studies on this compound. However, in the few studies that have been undertaken, PCP is one of the major halogenated phenolic compounds in human plasma (Sandau et al., 2002; Guvenius et al., 2003). PCP is an important environmental chemical due to its toxicity, contamination by dioxins, and ubiquitous distribution in the environment (Schulz and Butte, 2007).

5.2.3.2. Hydroxylated PCBs

PCBs are biotransformed by the cytochrome P-450 monooxygenases, and in most of the known metabolic pathways the formation of the hydroxylated PCBs (OH-PCBs) is the initial step. The OH-PCBs can also be formed by direct hydroxylation of the parent PCBs, and have been found to be the main metabolites excreted in feces and/or urine (Letcher et al., 1999; Guvenius et al., 2002).

A number of OH-PCBs have been identified in human plasma, and as many as 38 different OH-PCB congeners were reported in a study by Hovander et al. (2002). Concentrations of OH-PCBs are generally one order of magnitude lower than for the parent PCBs (Bergman et al., 1994; Sandau et al., 2000, 2002), even though concentrations comparable to the PCBs have been reported (Klasson-Wehler et al., 1997).

5.2.4. Short-chain chlorinated paraffins

The properties, production, and use of SCCPs have been described in previous reports. There are still few data on these compounds, primarily due to analytical difficulties. In contrast to most other xenobiotic compounds, the high number of SCCP congeners poses a substantial analytical challenge. No congener-specific analysis exists because the individual components are not resolved, resulting in major difficulties in the quantification of SCCPs. A high degree of variability has also been reported in the quantification, depending on the analytical technique used.

SCCPs appear to illicit fewer acute and chronic toxic effects than PCBs, but knowledge is very limited.

Owing to concerns about their possible environmental impact, use of SCCPs has been declining, although a proper screening of human samples from the Arctic is still needed to assess the current status of contamination.

5.2.5. Pharmaceutical and personal care products

5.2.5.1. Cyclic siloxanes

Cyclic siloxanes have widespread use in a variety of applications including fermentation processes, instant coffee production, paper coatings and sizing, diet soft drinks, waste yeast tanks, food washing solutions, adhesives, textiles, deasphalting, boiler treatments, detergents, cleaning solutions, surfactants, cosmetic products, and polishes. Examples of such compounds are hexamethylcyclotrisiloxane, octamethylcyclotetrasiloxane, decamethylcyclopentasiloxane, and dodecamethylcyclohexasiloxane. In personal care products, the siloxane/cyclosiloxane content can be as high as 40% to 60% by weight (Luu and Hutter, 2001).

Octamethylcyclotetrasiloxane has a partitioning coefficient between octanol and water (K_{OW}) of 5.10 and is thus expected to adsorb onto suspended solids and sediment. Furthermore, a bioconcentration factor of 12400 indicates a very high potential for bioconcentration in aquatic organisms. Dimethyl siloxanes in general are highly resistant to biodegradation (NIH, 2007) and siloxanes are on the list of potential new contaminants in the Arctic (Muir and Howard, 2006).

Human data are limited, particularly for the Arctic where, to our knowledge, there are currently no data available. Analysis of the siloxanes is challenging because these compounds are present at high concentrations in many aspects of the environment, including vacutainers used to sample blood. Therefore, considerable care is needed when these substances are to be analyzed.

5.2.5.2. Parabenes

Parabenes are used as preservatives in topical antibiotic or corticosteroid preparations and in food and cosmetics.

Methylparabene, butylparabene, ethylparabene, and propylparabene have been detected in sewage treatment plant influent and effluent water, and sludge (Remberger et al., 2006). Also, an estimated bioconcentration factor of 110 and a log K_{OW} of 3.57 suggests that the potential for bioconcentration in aquatic organisms is high. Parabenes are not expected to undergo hydrolysis in the environment. Biodegradation of methylparabene, which fully degraded after six days in sludge with an acclimation period of two days using a Zahn-Wellens test, suggests that biodegradation may be an important environmental fate process in water. Butylparabene was estrogenic at 10 mg/kg body weight (NIH, 2007).

Parabenes have been determined in different human matrices including breast tissue, human serum, and urine, where methylparabene has been the predominant compound (Darbre et al., 2004; Darbre and Harvey, 2008).

5.2.6. **National results**

5.2.6.1. **Alaska, United States**

The PBDE and perfluorinated compound data from Alaska shown in Table 5.30 comprise data from two different communities. The concentrations of PBDEs determined in the Yupik peoples from the Yukon Kuskokwim River Delta are the highest reported in this assessment and are thus the highest known human PBDE concentrations in the Arctic. These concentrations are similar to those seen in national surveys in the southern United States. BDE47 is clearly the predominant congener. The PFOS data were measured in a different community to the PBDEs and the concentrations appear to fall within the lower range of the data presented in this assessment.

5.2.6.2. **Canada**

Data for Canada are available from three regions: Nunavik data are presented in Table 5.31 and data from the Inuvik and Baffin regions are presented in Table 5.32.

In all three communities, the predominant PBDE was BDE47, but for men from Nunavik, BDE153 concentrations were only slightly lower than for BDE47. Concentrations of BDE47 seemed comparable for all three regions (the mean for all communities was about 6 μg/kg lipids) with the exception of the non-indigenous community from Inuvik for which concentrations were slightly higher (mean about 11 μg/kg lipids); however, only six samples were analyzed from this population so firm conclusions were not possible.

In Nunavik, a wider range of brominated compounds were measured, including BDEs 47, 99, 100 and 153, but only BDEs 47 and 153 were detected in more than 50% of samples with concentrations ranging from less than the detection limit to 343.5 μg/kg lipids and 134.6 μg/kg lipids, respectively. PBB153, pentabromophenol (PBP), TBBPA as well as two tetrabromophenols were measured, but only 2,3,4,6-TBP was detected in more

Table 5.30. Concentrations of emerging contaminants (μg/kg lipids) in Yupik maternal serum from the Yukon-Kuskokwim River Delta, Alaska. Data are geometric means (min – max) for 2004 – 2006. Source: Berner, J. pers. comm. (2008).

	Yukon-Kuskokwim River Delta (Yupik) 2004 – 2006 26 [a] n = 180 – 202 [b]
BDE47	26 (1.2 – 455)
BDE99	6.3 (0.15 – 1359)
BDE100	5.3 (0.1 – 87)
BDE153	8.0 (0.3 – 76)
BDE209	1.9 (1.2 – 15)
PFOS	7.4 (< 0.2 – 28) [c, d]
PFOA	1.0 (< 0.1 – 4.3) [c, d]

n: Range of number of individuals sampled.
[a] Arithmetic mean age of group sampled for PFOS and PFOA, age of group sampled for PBDEs not available; [b] range of number of individuals sampled; [c] concentrations for PFOS and PFOA expressed in μg/L plasma, all other data are expressed in μg/kg lipids; [d] PFOS and PFOA were measured in a different community to the PBDEs.

Table 5.31. Concentrations of emerging contaminants (μg/kg lipids) in plasma for men, women and women of childbearing age among Inuit from Nunavik, Canada. Data are geometric means (min – max) for 2004. Source: Ayotte, P., pers. comm. (2008).

	Men 2004 37 (18 – 74) [a] n = 344 – 412 [b]	Women 2004 37 (18 – 74) [a] n = 431 – 501 [b]	Women of childbearing age 2004 28 (18 – 39) [a] n = 264 – 301 [b]
BDE47	6.0 (< LOD – 101)	6.0 (< LOD – 344)	6.7 (< LOD – 344)
BDE99	< LOD (< LOD – 97)	< LOD (< LOD – 82)	< LOD (< LOD – 82)
BDE100	< LOD (< LOD – 78)	< LOD (< LOD – 83)	< LOD (< LOD – 83)
BDE153	4.0 (< LOD – 135)	2.1 (< LOD – 58)	4.0 (< LOD – 58)
TBBPA	< LOD (< LOD – 0.5)	< LOD (< LOD – 0.3)	< LOD (< LOD – 0.3)
PCP	1.0 (0.2 – 10)	0.7 (0.1 – 18)	0.7 (0.2 – 9.3)
PFOS	21 (2.8 – 470) [c]	16 (0.5 – 200) [c]	13 (2.3 – 97) [c]
4-HO-CB107	0.2 (< LOD – 2.9)	0.2 (< LOD – 3.2)	0.1 (< LOD – 1.0)
4-HO-CB146	0.1 (< LOD – 4.9)	0.1 (< LOD – 3.3)	0.07 (< LOD – 0.6)
4-HO-CB187	0.2 (0.007 – 4.3)	0.1 (< LOD – 4.2)	0.07 (< LOD – 0.8)

LOD: Limit of detection.
[a] Arithmetic mean age and range of group sampled; [b] range of number of individuals sampled; [c] concentrations for PFOS expressed in μg/L plasma, all other data are expressed in μg/kg lipids.

Table 5-32. Concentrations of PBDEs (µg/kg lipids) in Dene-Métis, Inuit and non-Aboriginal mothers in the Inuvik and Baffin regions of Canada. Data are geometric means (min – max) for specified sampling period. Source: Van Oostdam, J. pers. comm. (2008).

	Non-Aboriginal	Dene-Métis	Inuit	
	Inuvik 2005 – 2006 32 (23 – 40) [a] n = 6 [b]	Inuvik 2005 – 2006 25 (16 – 36) [a] n = 17 [b]	Inuvik 2005 – 2006 26 (17 – 38) [a] n = 52 [b]	Baffin 2007 24 (15 – 39) [a] n = 99 [b]
BDE47	11 (3.6 – 102)	6.9 (1.8 – 30)	6.7 (1.8 – 468)	6.3 (1.1 – 174)
BDE99	2.2 (1.2 – 14)	1.6 (1.2 – 6.8)	2.2 (1.2 – 152)	1.9 (0.7 – 145)
BDE100	2.1 (1.2 – 12)	1.4 (1.2 – 4.2)	1.9 (1.2 – 90)	1.7 (0.7 – 30)
BDE153	1.3 (0.6 – 5.3)	1.8 (0.6 – 4.3)	2.5 (0.6 – 68)	2.1 (0.5 – 22)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

than 50% of samples with concentrations ranging from 1 ng/L to 1395 ng/L. PFOS, a perfluorinated compound, was measured and detected in the blood of all participants. Mean concentrations were 21 µg/L plasma, 16 µg/L plasma and 13 µg/L plasma in men, women, and women of childbearing age, respectively.

Seventeen hydroxylated metabolites of PCBs, PBDEs, and heptachlorostyrene were measured; all except 2-OH-BDE68, 2-OH-BDE75 and 4-OH-CB193 were detected in more than 50% of samples. The most abundant metabolites were 4-OH-CB107, 4-OH-CB146 and 4-OH-CB187.

Blood concentrations of PCP, BDE153 and PFOS were significantly higher in men than women ($p < 0.001$), whereas BDE47 concentrations were similar in both genders ($p = 0.284$). There was a significant increase in concentrations of PCP ($p = 0.004$) and PFOS ($p < 0.001$) in relation to age group, with the highest mean concentration found in people aged 45 – 74 years. BDE47 did not show an age-related change in concentration ($p = 0.081$), whereas BDE153 showed a non-significant increase with age ($p = 0.061$). Slightly higher concentrations of BDE47 were found in women aged 18 – 39 years, but this difference relative to other age groups was not statistically significant.

In Nunavik and southern Quebec, breast milk samples collected in 1990 were archived and newer samples collected in 2002 (Pereg et al., 2003). All samples were analyzed at the same laboratory in 2003 and in the same laboratory that conducted the other PBDE analyses reported in this assessment. BDE47 was the predominant congener in the breast milk samples. The sum of PBDE congeners in breast milk for these two populations increased between these two dates but to a much greater extent in the southern Quebec population (Figure 5.15). This increase is similar to the increasing concentrations seen in many other southern populations in North America over the 1990s, but the difference in concentration between Nunavik and southern Quebec mothers should not be over-interpreted as there were only ten mothers from Nunavik in each sampling period (1990 and 2002). Also, the report by Pereg et al. (2003) only supplied limited information on these groups.

Data have recently become available for PFOS in the blood of women of child-bearing age from Nunavik which indicate a marked decline in concentration since 1992. In 1992, 2004, and 2007, mean concentrations of PFOS dropped from 21 (8 – 130) µg/L plasma, to 11 (3 – 20) µg/L plasma, to 5.9 (1.5 – 15) µg/L plasma (Pereg, 2008), respectively. The study reported a significant annual decline over this period on both an adjusted (age and region) and unadjusted basis although the comparability of all the age groups to the 1992 baseline survey was not fully outlined in the 2008 report. This decline in PFOS concentrations is similar to declines seen in other southern populations following the 2000/02 phase-out of perfluorooctanesulfonyl-fluoride-based materials by the primary global manufacturer, 3M Company (Olsen et al., 2007b).

Potential associations between PCP, BDE47, BDE153, and PFOS concentrations with traditional food consumption were also investigated in the Nunavik study. Consumers of marine mammal fat have significantly higher concentrations of PFOS ($p = 0.0001$) and slightly higher concentrations of PCP ($p = 0.05$) than non-consumers. However, consumption of marine mammal fat was not positively associated with plasma concentrations of BDE153 and BDE47. Consumers of marine mammal fat have significantly lower BDE47 blood concentrations ($p = 0.03$) than non-consumers. Blood concentrations of PCP, BDE47 and BDE153 were not associated with consumption of country fish expressed in quartiles, whereas PFOS concentrations increased with quartile of fish consumption ($p < 0.0001$). However, there is no difference in PFOS mean concentrations between the third and fourth quartile of fish consumption.

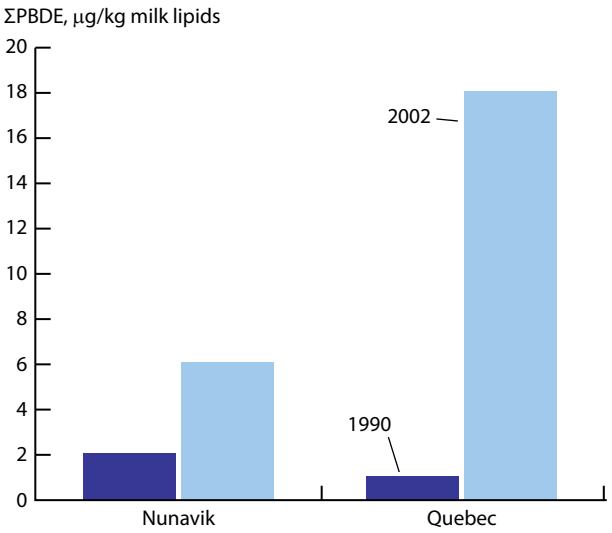


Figure 5-15. Comparison of concentrations of sum of PBDEs in two Quebec populations (Pereg et al., 2003).

5.2.6.3. **Greenland**

There are no data on emerging contaminants for Greenland.

5.2.6.4. **Faroe Islands**

No new data are presented in this assessment for the Faroe Islands; however, a recent paper published is cited in the discussion (Weihe et al., 2008).

5.2.6.5. **Norway**

Maternal data from Bodø are presented in Table 5.33. Maternal plasma samples were collected and analyzed for PBDEs in 2004 and 2006. The 2006 study was initiated in order to sample larger volumes of plasma so as to enable a proper determination of the nona and deca brominated congeners. In 2004, the predominant PBDE congener was BDE47 together with BDE153 (with no data for BDE209). In 2006, the predominant congener was BDE209 together with BDE207. It should be emphasized that the uncertainty for the higher brominated PBDEs is greater than for the lower brominated PBDEs (as mentioned, BDE209 is very susceptible to contamination issues). Nevertheless, concentrations were well above blank values and thus indicate their presence in the Norwegian human samples. Besides the nona and deca congeners, the predominant congeners were BDE47 and BDE153, which had comparable concentrations (mean about 1 μg/kg lipids). TBBPA concentrations were extremely low and detected in only 30% of samples, with no values above the limit of detection.

The predominant perfluorinated compound was PFOS (mean 16 μg/L plasma, and with a narrow range of 9.0 to 29 μg/L plasma). This was followed by PFOA which was present at much lower concentrations (mean 2.3 μg/L plasma, range 1.7 to 7.0 μg/L plasma). PCP was detected in all samples but at very low concentrations (mean 1.2 μg/L plasma).

5.2.6.6. **Sweden**

The Swedish data for PBDEs and perfluorinated compounds in 25 maternal plasma samples are presented in Table 5.34. The women had lived for more than 20 years in the Kiruna area and for all women this was their first delivery. PBDE concentrations were all low with most congeners below the detection limit for the majority of samples. The predominant congener was BDE47 (mean < 1.6 μg/kg lipids). The maximum value for BDE153 was slightly lower than the maximum for BDE47. BDE209 was not determined. PFOS was detected in all samples (mean 8.1 μg/L plasma). PFOA concentrations were considerably lower (mean 1.6 μg/L plasma).

5.2.6.7. **Finland**

The only data available on emerging contaminants in Finland were for PBDEs in breast milk. Considering the good comparability of lipid-adjusted data in different matrices, the data are included in Table 5.35. The data are

Table 5·33. Concentrations of emerging contaminants (μg/kg lipids) in maternal plasma, Bodø, Norway. Data are geometric means (min – max) for specified sampling period. Source: SPFO (2006, 2007).

	2004 39 (29 – 48) [a] n = 12 [b]	2006 28 (19 – 36) [a] n = 29 [b]
BDE47	1.3 (0.6 – 2.8)	0.9 (0.1 – 4.6)
BDE99	0.5 (0.3 – 0.9)	na
BDE100	< 0.4 (< 0.2 – 1.0)	na
BDE153	1.2 (0.8 – 2.3)	0.8 (0.4 – 1.7)
BDE183	< 0.3 (0.1 – 1.5)	< 0.1 (< 0.04 – < 0.3)
BDE209	na	1.6 (< 0.5 – 19)
TBBPA	< 0.001 (< 0.001 – 0.009)	na
PCP	1.1 (0.7 – 3.2)	na
PFOS	16 (9.0 – 29) [c]	na
PFOA	2.3 (1.7 – 7.0) [c]	na

na: Not available.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] concentrations for PFOS and PFOA expressed in μg/L plasma, all other data are expressed in μg/kg lipids.

Table 5·34. Concentrations of emerging contaminants (μg/kg lipids) in maternal plasma, Kiruna, Sweden. Data are geometric means (min – max) for 2006. Source: Messner, T. pers. comm. (2008).

	2006 27 (22 – 33) [a] n = 25 [b]
BDE47	< 1.6 (< 1.155)
BDE99	< 0.3 (< 0.2 – 15)
BDE100	< 0.3 (< 0.2 – 17)
BDE153	< 0.3 (< 0.2 – 33)
BDE183	< 0.3 (< 0.2 – 2.1)
PFOS	8.1 (1.2 – 22) [c]
PFOA	1.6 (< LOD – 3.6) [c]

LOD: Limit of detection.

[a] arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] concentrations for PFOS and PFOA expressed in μg/L plasma, all other data are expressed in μg/kg lipids.

Table 5·35. Concentrations of PBDEs (μg/kg lipids) in pooled breast milk from primipara mothers in southern (non-Arctic), central (non-Arctic), and northern (Arctic) Finland in 2005. Source: Kiviranta, H. pers. comm. (2007).

	Southern Finland 2005 29 (20 – 39) [a] n = 35 [b]	Central Finland 2005 27 (19 – 40) [a] n = 31 [b]	Northern Finland 2005 26 (21 – 41) [a] n = 11 [b]
BDE47	2.3	1.8	2.1
BDE99	0.6	0.4	0.6
BDE100	0.5	0.4	0.4
BDE153	0.7	0.8	1.6
BDE183	0.04	0.02	0.02

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

from pooled samples, and so there are no indications of ranges in concentration for the different congeners. Pooled samples from northern, central, and southern Finland were analyzed separately. Concentrations were low with BDE47 the predominant congener (mean about 2 μg/kg lipids). There seemed to be no differences between the three regions in terms of concentration, except for BDE153 which seemed higher in the sample from northern Finland, where it was only a little lower than for BDE47.

HBCD was also measured in the samples from northern and central Finland and all concentrations below the detection limit (< 0.4 μg/kg lipids).

5.2.6.8. **Russia**

Human data presented in this assessment are from maternal samples from Taymir and Naryan Mar (Pechora River basin) (see section 5.1; Tables 5.21 and 5.22).

Samples collected in 2002 from Naryan Mar and Taymir were analyzed together with the samples from Bodø (Norway) in 2004/05 as part of a pilot study on emerging contaminants. The results are presented in Table 5.36. The PBDE concentrations were all low with the majority of congeners below the detection limit in most samples; this was especially the case in Naryan Mar where even the mean concentration for BDE47 was < 0.6 μg/kg lipids. BDE209 was not measured in these samples due to limited sample volumes. The predominant congener in the samples from Taymir was BDE47 (mean 1.0 μg/kg lipids). TBBPA was below the detection limit in all samples from both communities. Concentrations of PFOS were higher in Naryan Mar (mean 16 μg/L plasma, range 5.0 to 49 μg/L plasma) compared than in Taymir (mean 9.3 μg/L plasma, range 5.1 to 14 μg/L plasma). PFOA concentrations were lower and comparable in the two communities.

Table 5.36. Concentrations of emerging contaminants (μg/kg lipids) in maternal plasma, Naryan Mar and Taymir, Russia. Data are geometric means (min – max) for 2002. Source: SPFO (2006).

	Taimyr 2002 26 (20 – 35) [a] n = 12 [b]	Naryan Mar 2002 30 (22 – 35) [a] n = 12 [b]
BDE47	1.0 (0.4 – 1.7)	< 0.6 (< 0.5 – 0.8)
BDE99	0.6 (< 0.3 – 1.0)	< 0.4 (< 0.3 – < 0.6)
BDE100	< 0.2 (< 0.1 – 0.4)	< 0.1 (< 0.1 – < 0.2)
BDE153	0.6 (< 0.3 – 0.9)	< 0.5 (< 0.2 – 2.3)
BDE183	< 0.2 (< 0.1 – 0.4)	< 0.2 (< 0.1 – 0.6)
TBBPA	< 0.001	< 0.001
PCP	1.6 (0.8 – 12)	1.7 (1.0 – 3.4)
PFOS	9.3 (5.1 – 14) [c]	16 (5.0 – 49) [c]
PFOA	2.2 (1.2 – 5.7) [c]	1.7 (0.8 – 5.2) [c]

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] concentrations for PFOS and PFOA expressed in μg/L plasma, all other data are expressed in μg/kg lipids.

5.2.7. **Discussion**

5.2.7.1. **Polybrominated diphenylethers**

Elevated human concentrations of PBDEs are now reported in the Arctic, but these findings seem to be limited to Alaska (U.S. Arctic). Levels in mothers for all other countries reporting PBDE concentrations in this assessment are considerably lower with concentrations from the European Arctic being the lowest (Figure 5.16). The concentrations reported from Alaska are comparable to, or even somewhat higher than, those recently reported for the general U.S. population (Sjodin et al., 2008).

The mean BDE47 concentration in Alaska (Yupiks) was reported to be 26 μg/kg lipids, which is considerably higher than that reported for the Canadian communities, with mean concentrations of 6 to 11 μg/kg lipids. Concentrations in the European Arctic are considerably lower, with mean concentrations for BDE47 in the range < 0.6 to 2.2 μg/kg lipids. Within Canada, concentrations seem slightly higher in the non-indigenous population from Inuvik compared to Dene-Métis and Inuit from the Inuvik, Baffin, and Nunavik regions, although the sample size among non-indigenous northern Canadians is quite small. Concentrations in Norway, Russia, and Finland are comparable, even though the Naryan Mar data seem slightly lower than for the other populations. Again, these concentrations are all low and close to detection limits, and are thus associated with greater uncertainty. The predominant PBDE is still BDE47, but data from Norway indicate that BDE209 is found in comparable concentrations to BDE47. The finding of elevated concentrations of BDE209 together with BDE207 is supported by a Swedish study where high concentrations of BDE207, together with BDE209 and BDE47, were observed (Karlsson et al., 2007). Despite the higher uncertainty associated with BDE207 and BDE209, this clearly indicates the need to determine this compound in future assessments.

The ratio of BDE153 to BDE47 is highly variable between the countries, with BDE153 concentrations constituting only 25% of BDE47 concentrations in the Alaskan data. In other countries like Norway and Canada, concentrations are comparable. The reason for this could be that the diet constitutes a larger proportion of the exposure for people that are exposed to lower concentrations. As indicated by Sandanger et al. (2007), the proportion of BDE153 in these individuals is higher than in the more exposed individuals. One reason for this is possibly the difference in half lives (6.5 years for BDE153 compared to 1.8 years for BDE47; Geyer et al., 2004), resulting in a slower decrease in BDE153 concentrations after the phase-out of the penta and octa mixtures. This is supported by the findings in Nunavik where the men had significantly higher BDE153 concentrations than the women. The men also consumed more traditional food and thus a larger proportion of BDE153. The differences in exposure to

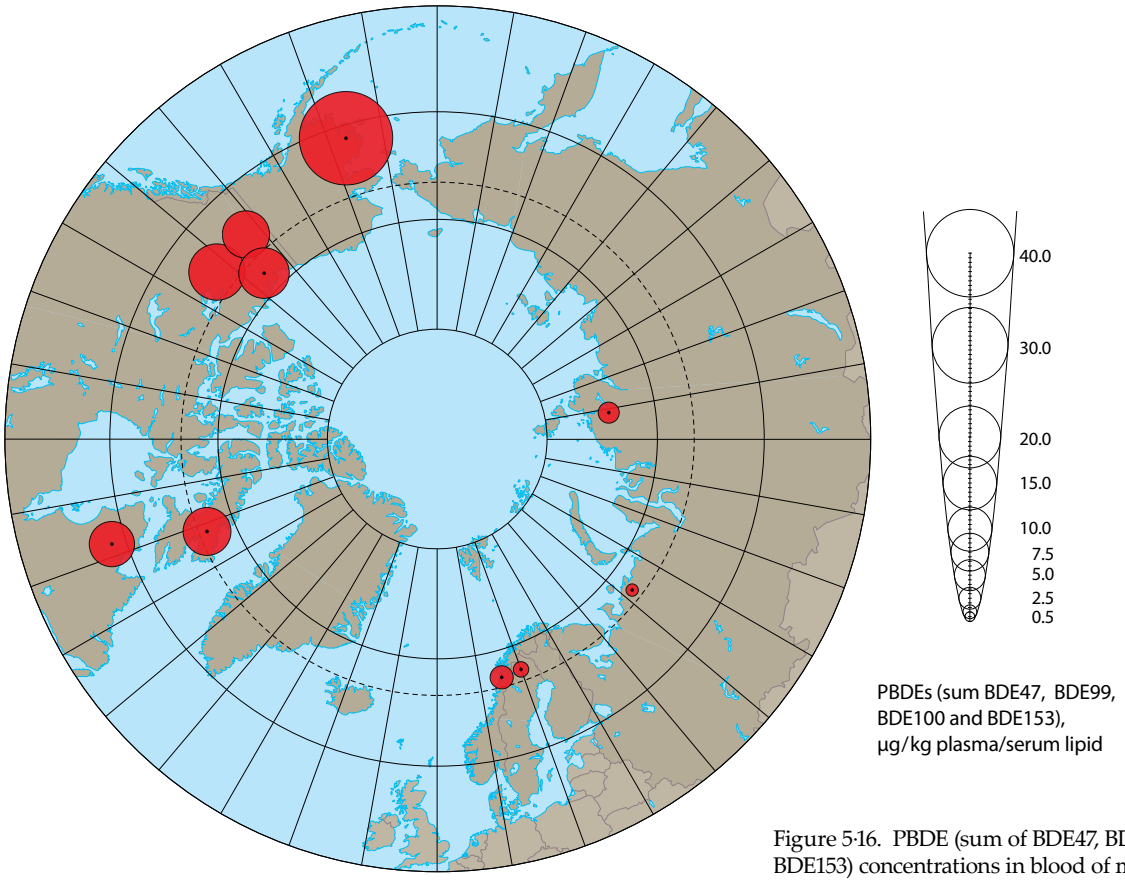


Figure 5-16. PBDE (sum of BDE47, BDE99, BDE100 and BDE153) concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

the different mixtures in different countries may also contribute to higher concentrations of BDE47 relative to BDE153. Therefore, a shift towards BDE153 and a decrease in BDE47 is expected in the most remote Arctic communities where exposures are more related to the food chain. Others have also reported that there seems to be a general trend with increasing proportions of BDE153 in populations with non-occupational exposure (Thuresson et al., 2006a).

There are few available data on trends in these compounds in humans from the Arctic. An increasing trend in PBDE concentrations has recently been demonstrated in Nunavik (Canada). In contrast, concentrations are reported to be leveling off or decreasing in the southern parts of Sweden and Norway. For the more persistent congeners like BDE153 it might take longer before a similar decline occurs because this will dominate in the marine food chain.

The limited human data on TBBPA and HBCD show that concentrations are still low and mostly undetected (Knutsen et al., 2008; Thomsen et al., 2008).

5.2.7.2. **Perfluorinated compounds**

The main perfluorinated compound reported here is PFOS with only limited data on PFOA. Discussions are therefore focused on PFOS. It should be noted that this is a compound with greater analytical uncertainty than the legacy POPs. There is reason to believe that the estimated concentrations are associated with an uncertainty of 10% to 40% depending on the laboratory. PFOS and PFOA were only recently introduced in the AMAP ringtest (see Chapter 4). In addition, PFOS is not associated with lipids and thus only wet weight concentrations of this compound are considered here.

Of all the contaminants reported in this assessment, PFOS is currently the predominant compound in human plasma. The maximum concentration reported in this assessment is 470 µg/L plasma (mean 20.6 µg/L plasma), found in an Inuit male from Nunavik.

Even though it is by far the predominant compound in plasma, the fact that PFOS is not associated with lipids implies that the total burden of PFOS might not be higher than the more lipid-soluble compounds (legacy POPs). However, this has not been completely evaluated and PFOS is also associated with organs such as the liver in addition to plasma.

The geographical distribution of human PFOS exposure across the Arctic provides no clear spatial distribution or distinct differences between countries (Figure 5.17). In addition, sample size for most countries is limited, reducing the availability of firm conclusions. However, concentrations reported from Sweden, Alaska, and Naryan Mar (Russia) (mean concentrations 8.1 µg/L plasma, 7.4 µg/L plasma, and

9.3 µg/L plasma, respectively) seem slightly lower than the majority of the other concentrations. The highest mean concentration (20.6 µg/L plasma) was reported among men from Nunavik. It should be noted that in Nunavik, a larger number of individuals was assessed than in any of the other communities and countries. All mean concentrations (women) for PFOS reported here were lower than the mean concentration of 18.4 µg/L plasma reported for U.S. women above the age of 12 (Calafat et al., 2007). In comparison, the median value reported for 12 Faroese women was 23.7 µg/L plasma (Weihe et al., 2008). This indicates that human plasma concentrations in the Faroe Islands are higher than any of the other means reported here. Initial time trend data for women of child-bearing age in Nunavik suggest PFOS concentrations are decreasing; however, trend data are not available from other Arctic regions for comparison.

For Nunavik, gender-specific data indicated that men had significantly higher concentrations of PFOS than women from the same communities. Significantly higher concentrations among men are in accord with the findings by Calafat et al. (2007).

The range of PFOS exposure in the different populations is narrow compared to other contaminants, with considerable uncertainty linked to the possible routes of exposure. Dietary data were only available from Nunavik, where increasing concentrations of PFOS were associated with the consumption of fish and marine mammal meat. Marine mammal meat was also identified as a source of PFOS exposure in a recent study on the Faroe Islands (Weihe et al., 2008). Fromme et al. (2007a) summarized the overall exposure assessment for adults, and concluded that dietary exposure is the dominant intake pathway for both PFOS and PFOA for the western European population.

Another issue regarding PFOS in humans is the reported differences in isomer patterns in different populations (Karrman et al., 2007b). This difference was also apparent when comparing isomers in samples from Taymir and Naryan Mar (Russia) and Bodø (Norway). In the samples from Naryan Mar, the branched isomers had comparable intensity to the linear isomer. The women from Naryan Mar were also more exposed than the women from Taymir; women from Naryan Mar do have a higher intake of fish but there are few data on this and a small sample size.

The isomeric patterns still require investigation and future data should be isomer specific, if possible. It is unclear if people are reporting PFOS concentrations as a sum of the isomers, or only the linear isomer that dominates the standard and technical mixtures.

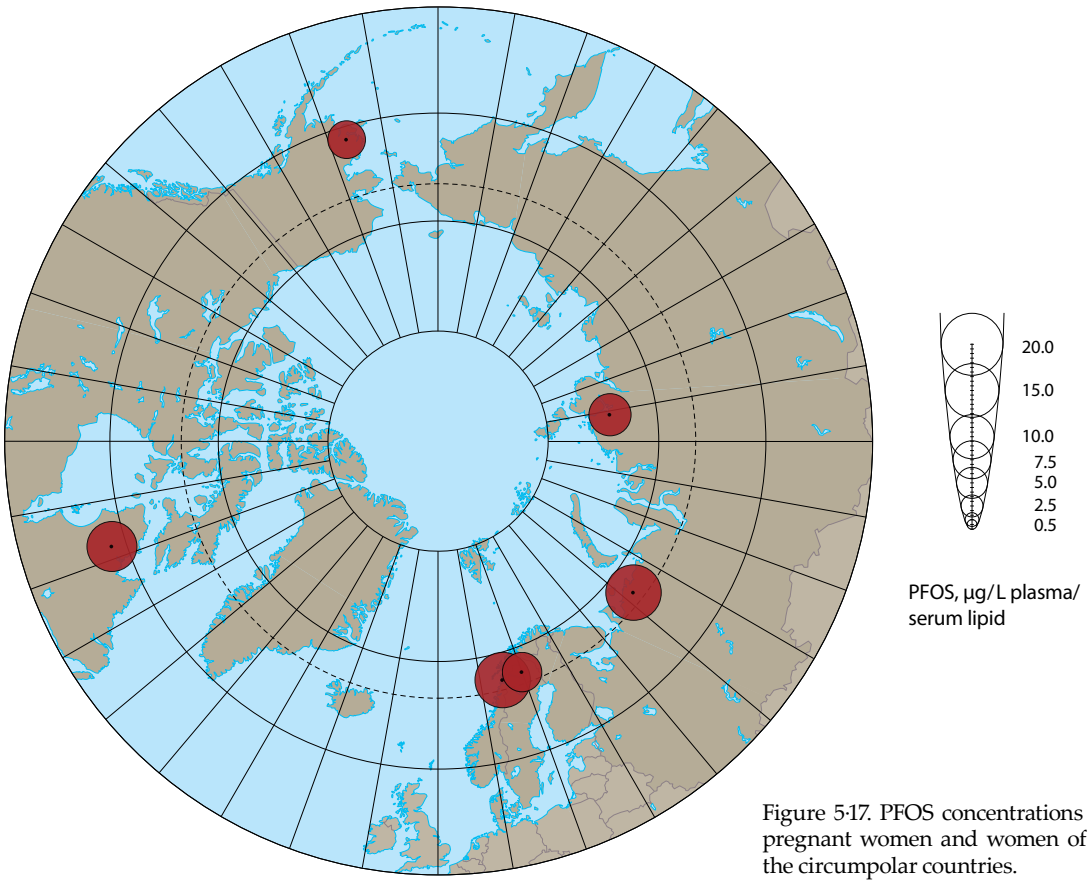


Figure 5-17. PFOS concentrations in blood of mothers, pregnant women and women of child-bearing age in the circumpolar countries.

Powley et al. (2008) found branched/linear distributions of PFOS in fish and seals in the western Canadian Arctic that were markedly different from each other and from the expected isomer distribution found in technical grade PFOS. It was suggested that branched PFOS was eliminated significantly faster in seals than linear PFOS if their diet consisted primarily of Arctic cod (*Boreogadus saida*), because the branched isomer content of PFOS in Arctic cod was approximately 50% (relative peak areas), but only 4% in seal matrices. Powley et al. (2008) concluded that biological monitoring does not reflect the exposure concentration isomer ratios, and that differential pharmacokinetic behavior plays an important role in the observed patterns in biological samples.

PFOA data are only available from Norway, Russia, and Alaska. The data from these countries are comparable and the concentrations are considerably lower than for PFOS. Nevertheless, compared to legacy POPs, concentrations are high, which is of concern considering that higher concentrations of this compound are reported in cord plasma than maternal plasma. More data on PFOA are required to understand both trends and spatial distribution.

5.2.7.3. **Pentachlorophenol and hydroxylated PCBs**

There are no international intercomparisons or certified reference materials available for the determination of PCP and OH-PCBs in human plasma, increasing the uncertainty of the data. This should be considered when comparisons are made. There are also limited data available.

PCP data are only available from Canada, Norway, and Russia where PCP is detected in all samples. PCP concentrations in Nunavik (Canada), Bodø (Norway), and Taymir and Naryan Mar (Russia) seem comparable, with a slightly higher mean concentration among the Russian data. There is also a broad range of values in some of the communities, indicating large differences in exposure. Elevated concentrations of PCP are detected in humans throughout the Arctic, but data are still limited geographically and exposure routes and time trends are not elucidated.

Data on the OH-PCBs are only available from Canada where the concentrations are considerably lower than for PCP. The only Arctic comparison is the data from Uelen (Russia) presented by Sandanger et al. (2004), where the concentrations were considerably higher.

Of the hydroxylated compounds determined, PCP predominated in all populations except among the Chukchi from Uelen, where concentrations of some of the OH-PCBs were found to be higher. The samples were from both men and women and the median concentration of the predominant OH-PCB, 4-OH-PCB107, was reported to be 1.67 μg/L plasma. This is considerably higher than reported among the Inuit (Nunavik) in this assessment, where the mean concentration was 0.16 μg/L plasma for this congener. The maximum concentration reported among the Inuit for this congener was 3.2 μg/L plasma, and comparable to the maximum concentration among the Chukchi from Uelen (3.95 μg/L plasma), indicating a broad exposure range. The ratio of OH-PCBs to PCB has in the majority of studies been reported to be approximately 0.1 to 0.2 or even less. In Uelen (Russia), the median ratio was, however, as high as 0.4 and several unknown OH-PCBs were detected (Sandanger et al., 2004). This indicates that there is still limited knowledge of these metabolites in the Arctic and that there also seem to be large differences between populations within the Arctic. Further assessments are needed in relation to health studies, although a full monitoring program is not required.

5.2.8. **Conclusions and recommendations**

5.2.8.1. **Polybrominated diphenylethers and other brominated flame retardants**

Concentrations of PBDEs in the Canadian Arctic are higher than those in the European Arctic, with concentrations in Alaska (U.S. Arctic) being the highest of the circumpolar countries. Of the PBDEs studied, BDE47 had the highest plasma concentrations in the samples; however, there are studies showing that BDE153, which has a longer half life, will become more highly concentrated than BDE47 in the future. PBDEs should be routinely monitored in humans from the Arctic, because there is currently a lack of data from some regions. There is also an urgent need for more data to enable evaluations of time trends in future assessments.

Even though the limited data for TBBPA and HBCD indicate that concentrations are still low, the large production volumes indicate a need for further data and screening. Considering the large amounts of brominated flame retardants produced worldwide and that these production volumes will remain high, it is essential to assess all new compounds of importance and initiate early screenings in order to detect potential contaminants of concern. More data are needed on the higher brominated congeners including the deca and nona BDEs.

5.2.8.2. **Perfluorinated compounds**

PFOS is currently the predominant perfluorinated compound in human plasma in Arctic regions worldwide. The mean maternal plasma concentrations of PFOS in the different Arctic countries seem comparable. The only available dietary data from Nunavik indicate that consumers of fish and marine mammal meat have significantly higher concentrations of PFOS; however, these data are limited. Further studies are needed to understand spatial distribution, sources of exposure and time trends. Isomeric distributions for PFOS and higher fluorinated sulfonates need to be included as part of this work. Currently, PFOS and PFOA are monitored in some regions and need to be included in all regions.

5.2.8.3. **Pharmaceutical and personal care products**

Siloxanes and parabenes are potential new contaminants in the Arctic, although there are currently no known human data available in the circumpolar region. However, siloxanes have been detected in biota in the Arctic and both compound groups are produced in large quantities worldwide. There are strong indications that these groups of compounds should be screened in future assessments for some compounds due to high potential for bioaccumulation in aquatic organisms, and high resistance to biodegradation.

5.2.8.4. **Short-chain chlorinated paraffins**

Knowledge of SCCPs is limited, although due to the concerns about potential impacts on the environment, use of SCCPs has been declining. There are currently no SCCP human health data available for this assessment due to analytical difficulties. To assess the effects of SCCPs on human health in the Arctic, analytical protocols need to be developed to allow human screening.

5.2.8.5. **Hydroxylated PCBs and pentachlorophenols**

There are variable differences in exposure to OH-PCBs and PCPs among Arctic communities, although concentrations are fairly consistent across countries with available data (Canada, Russia, as well as Norway for PCPs). The majority of OH-PCB concentrations are considerably lower than for the PCBs. In Uelen, Russia, concentrations were however comparable, indicating some large regional differences. PCP is often the hydroxylated compound found at the highest concentrations in human tissue. However, comparisons of PCP concentrations to those of OH-PCBs show inconsistent results, with PCPs higher than OH-PCBs in Nunavik (Canada) and lower in Uelen (Russia). Further research should attempt to clarify spatial differences in these compounds, exposure routes and trends over time.

In general, the timeframe of contaminant production, transport to the Arctic, and first detection in humans remains too long, causing a lag in the time taken to enable bans and reduce their production. To decrease this period, more resources are needed for exploratory analysis for early detection of unknown compounds. Non-target screening is encouraged to detect unknown contaminants. Enhanced communication between researchers and industry is also required to assess and respond efficiently to contaminants of potential concern to human health.

Appendix 5·1: Wet Weight Data Tables.

To facilitate comparisons, the tables in this Appendix have been numbered to correspond to the equivalent (lipid weight data tables) tables in Chapter 5.

Table A 5·3. Contaminant concentrations (µg/L plasma) in Dene-Métis, Inuit and Caucasian mothers from the Inuvik region, NWT, Canada. Data show geometric mean (and range) for specified period of sampling. Source: baseline study (Tofflemire, 2000), follow-up study (Armstrong et al., 2007).

	Dene- Métis			Inuit			Caucasian		
	Baseline study 1998 – 1999	Follow-up study 2005 – 2006	Significant difference, $p < 0.05$	Baseline study 1998 – 1999	Follow-up study 2005 – 2006	Significant difference, $p < 0.05$	Baseline study 1998 – 1999	Follow-up study 2005 – 2006	Significant difference, $p < 0.05$
	24 (18 – 35) [a] n = 42 [b]	24 (16 – 36) [a] n = 17 [b]		23 (15 – 37) [a] n = 31 [b]	26 (17 – 38) [a] n = 52 [b]		31 (19 – 45) [a] n = 21 [b]	32 (23 – 40) [a] n = 6 [b]	
Oxychlordane	0.03 (0.01 – 0.22)	0.01 (0.00 – 0.04)	SD [e]	0.15 (0.03 – 1.06)	0.07 (0.00 – 1.00)	SD [d]	0.04 (0.02 – 0.07)	0.01 (0.01 – 0.03)	SD [d]
p,p'-DDE	0.51 (0.17 – 1.80)	0.30 (0.11 – 1.20)	SD [c]	1.08 (0.40 – 3.79)	0.65 (0.05 – 7.40)	SD [d]	0.57 (0.22 – 2.07)	0.33 (0.15 – 0.95)	ns [f]
Toxaphene, parlar 50	na	na	na	na	na	na	na	na	na
CB153	0.12 (0.02 – 1.05)	0.30 (0.11 – 1.20)	SD [d]	0.26 (0.06 – 0.88)	0.14 (0.00 – 1.30)	SD [d]	0.11 (0.03 – 0.27)	0.04 (0.02 – 0.08)	SD [d]

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.; [c] SD (p = < 0.05 – 0.01); [d] SD (p = 0.01 – 0.001); [e] SD (p = 0.001 – <0.0001); [f] not significant (p > 0.05).

Table A 5·5. Trends in contaminant concentrations (µg/L plasma) in pregnant Inuit women from Nunavik, Québec, Canada. Data show geometric mean (and range) for specified period of sampling. Source: 1992 (Santé Québec, 1994), 1996 – 2001 (Dallaire et al., 2003), 2004 (Dewailly et al., 2007a,b), 2007 (Pereg et al., 2008).

	1992 24 [a] (18 – 35) [a] n = 11 [b]	1996 24 [a] (17 – 34) [a] n = 25 [b]	1997 25 [a] (15 – 41) [a] n = 53 [b]	1998 25 [a] (15 – 37) [a] n = 46 [b]	1999 26 [a] (17 – 36) [a] n = 26 [b]	2000 26 [a] (17 – 39) [a] n = 36 [b]	2001 27 [a] (17 – 39) [a] n =20 [b]	2004 27 [a] (18 – 42) [a] n = 29 [b]	2007 24 [a] (18 – 37) [a] n = na	Significant difference, $p < 0.05$ [c, d]
Oxychlordane	0.57 (0.21 – 2.8)	0.34 (0.05 – 1.7)	0.36 (0.08 – 3.9)	0.26 (0.05 – 2.7)	0.32 (0.07 – 1.5)	0.27 (0.04 – 2.3)	0.24 (0.04 – 1.2)	0.27 (0.06 – 1.9)	na	0.0006
p,p'-DDE	4.70 (1.9 – 18)	2.38 (0.54 – 9.7)	2.79 (0.54 – 14.4)	2.01 (0.34 – 17.9)	1.98 (0.63 – 9.9)	1.85 (0.37 – 15.0)	1.55 (0.38 – 12.8)	1.78 (0.43 – 7.7)	na	< 0.0001
CB153	1.27 (0.46 – 3.3)	0.87 (0.15 – 3.9)	0.95 (0.21 – 6.1)	0.63 (0.14 – 5.6)	0.79 (0.15 – 3.0)	0.65 (0.08 – 5.2)	0.56 (0.08 – 3.8)	0.55 (0.12 – 2.0)	na	< 0.0001

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] special analysis, Pereg, D. pers. comm. (2007); [d] using anova adjusted for age and region (Hudson or Ungava), regression adjusted for age and region (Hudson or Ungava) and smoking status (smoker, ex-smoker, non-smoker).

Table A 5·6. Contaminant concentrations (µg/L plasma) in Inuit women and men from Nunavik, Quebec, Canada. Data show geometric mean (and range) for specified period of sampling. Source: 1992 (Santé Québec, 1994), 1994 (Dewailly et al., 2007a,b).

	Inuit women 1992 35 (18 – 73) [a] n = 282 [b]	Inuit women 2004 37 (18 – 74) [a] n = 498 [b]	Significant difference, $p <$ 0.05 [c]	Inuit men 1992 36 (18 – 74) [a] n = 210 [b]	Inuit men 2004 37 (18 – 74) [a] n = 408 [b]	Significant difference, $p <$ 0.05 [c]
Oxychlordane	0.72 (0.02 – 11)	0.41 (0.01 – 16)	$p < 0.0001$	0.87 (0.01 – 21.0)	0.40 (0.005 – 9.3)	$p < 0.0001$
p,p'-DDE	6.2 (0.42 – 74)	2.9 (0.19 – 54)	$p < 0.0001$	7.51 (0.76 – 96.0)	2.81 (0.076 – 49.0)	$p < 0.0001$
CB153	1.6 (0.11 – 16.0)	0.98 (0.04 – 41)	$p < 0.0001$	2.14 (0.07 – 19.0)	1.15 (0.051 – 20.0)	$p < 0.0001$

na: Not available.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·7. Contaminant concentrations (μg/L plasma) in Inuit mothers from the Baffin Region, Nunavut Territory, Canada. Data show geometric mean (and range) for specified period of sampling. Source: baseline study (Butler-Walker et al., 2003, 2006), follow-up study (Potyrala, M., unpubl., 2008).

	Baseline study 1997 24 (15 – 39) [a] n = 30 [b]	Follow-up study 2005 – 2007 24 (15 – 39) [a] n = 99 [b]	Significant difference, $p < 0.05$
Oxychlordane	0.58 (0.093 – 2.4)	0.23 (0.04 – 1.9)	< 0.0001
p,p'-DDE	2.1 (0.55 – 6.0)	1.1 (0.13 – 5.9)	< 0.0001
Toxaphene, parlar 50	0.13 (0.03 – 0.66)	0.076 (0.007 – 1.0)	0.0008
CB153	1.0 (0.25 – 3.9)	0.37 (0.077 – 2.2)	< 0.0001

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·8. Trends in contaminant concentrations (μg/L plasma) in pregnant Inuit women from Disko Bay, Greenland. Data show geometric mean (and range) for specified period of sampling. The statistical analysis was a linear regression using log variables adjusted for age. Source: Deutch and Hansen (2000), Deutch et al. (2007), Deutch unpubl. data.

	1994 25 (20 – 35) [a] n = 10 [b]	1995 27 (20 – 35) [a] n = 94 [b]	1996 27 (20 – 35) [a] n = 63 [b]	1997 25 (20 – 35) [a] n = 12 [b]	1999 26 (22 – 34) [a] n = 21 [b]	2006 27 (20 – 35) [a] n = 20 [b]	Significant difference, $p < 0.05$
Oxychlordane	0.56 (0.1 – 4.0)	0.63 (0.02 – 4.7)	0.48 (0.02 – 2.0)	0.52 (0.04 – 1.9)	0.22 (0.01 – 0.8)	0.11 (0.02 – 0.5)	$p < 0.0001$
p,p'-DDE	4.4 (2 – 8)	3.0 (0.5 – 21)	3.1 (0.6 – 10)	4.1 (1.1 – 17)	1.5 (0.4 – 4.3)	1.03 (0.2 – 3.5)	$p < 0.0001$
CB153	1.3 (0.5 – 6)	1.9 (0.3 – 10)	1.5 (0.4 – 5)	1.9 (0.6 – 6)	0.67 (0.2 – 2.0)	0.40 (0.02 – 1.2)	$p < 0.0001$

na: Not available, ns: not significant.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·10. Trends in contaminant concentrations (μg/L plasma) in Inuit men from Nuuk, Greenland. Data show geometric mean (and range) for specified period of sampling. Trend analysis based on linear regression analysis with adjustment for age. Trends and statistics calculated from log transformed concentrations. Source: Deutch et al. (2004, 2007), Deutch, B., pers. comm. (2007).

	Sisimiut 2002 – 2003 31 (20 – 50) [b] n = 51 [c]	Qaanaaq 2003 34 (20 – 50) [b] n = 41 [c]	Nuuk 2005 44 (30 – 50) [b] n = 19 [c]	Quegertarsuaq 2006 35 (20 – 50) [b] n = 35 [c]	Narsaq 2006 39 (20 – 50) [b] n = 28 [c]	All Greenland [a] 1999 – 2006 35 (19 – 50) [b] n = 314 [c]
Oxychlordane	0.39 (0.03 – 3.0)	2.64 (0.5 – 24)	1.23 (0.2 – 4.1)	0.7 (0.07 – 3.1)	0.6 (0.06 – 2.9)	1.33 (0.03 – 24)
Trans-nonachlor	0.87 (0.05 – 8.8)	4.1 (0.8 – 35)	2.8 (0.5 – 8.5)	1.6 (0.16 – 6.7)	1.3 (0.15 – 5.2)	2.24 (0.05 – 35)
p,p'-DDT	0.04 (0.01 – 0.7)	0.23 (0.01 – 2.8)	0.12 (0.01 – 0.52)	0.08 (0.02 – 0.5)	0.07 (0.02 – 0.24)	0.15 (0 – 2.75)
p,p'-DDE	2.8 (0.5 – 24)	6.45 (1.8 – 55)	6.2 (1.7 – 16)	4.8 (0.78 – 16)	4.9 (0.5 – 18)	6.1 (0.46 – 55)
DDE:DDT	78 (16 – 360)	28 (6.2 – 277)	51 (19 – 170)	60 (23 – 260)	71 (26 – 375)	43 (6.2 – 3.75)
HCB	0.55 (0.12 – 3.5)	1.56 (0.33 – 104)	1.4 (0.3 – 4.4)	1.1 (0.14 – 4.2)	0.71 (0.12 – 27)	1.13 (0.12 – 10.5)
β-HCH	0.07 (0.01 – 0.64)	0.34 (0.08 – 2.1)	0.16 (0.01 – 0.44)	0.09 (0.01 – 0.37)	0.08 (0.02 – 0.26)	0.19 (0.01 – 2.6)
Mirex	0.07 (0.01 – 0.39)	0.25 (0.06 – 1.7)	0.21 (0.05 – 0.82)	0.09 (0.02 – 0.4)	0.12 (0.01 – 0.5)	0.2 (0.01 – 2.2)
Total Toxaphene	0.30 (0.02 – 4.5)	1.33 (0.13 – 13)	0.84 (0.14 – 2.5)	0.72 (0.05 – 3.2)	0.56 (0.06 – 2.4)	0.89 (0 – 13)
parlar 26	0.11 (0.01 – 1.9)	0.52 (0.04 – 5.7)	0.29 (0.05 – 0.90)	0.27 (0.02 – 1.2)	0.21 (0.02 – 1.0)	0.35 (0 – 5.7)
parlar 50	0.18 (0.01 – 2.6)	0.8 (0.09 – 7.5)	0.55 (0.1 – 1.60)	0.45 (0.03 – 2.0)	0.34 (0.04 – 1.4)	0.55 (0 – 7.5)
PCBs						
Aroclor 1260	11.2 (1.8 – 85)	39 (13 – 151)	28 (9.3 – 87)	15 (2.8 – 58)	19 (3.4 – 62)	29.4 (1.8 – 40)
CB118	0.16 (0.01 – 2.4)	0.59 (0.08 – 4.1)	0.51 (0.1 – 1.5)	0.31 (0.04 – 1.2)	0.22 (0.2 – 0.8)	0.43 (0.01 – 4.1)
CB138	0.61 (0.1 – 4.5)	1.95 (0.7 – 6.6)	1.6 (0.4 – 4.9)	0.84 (0.06 – 3.7)	1.17 (0.2 – 3.5)	1.74 (0.06 – 17.9)
CB153	1.5 (0.2 – 12)	5.5 (1.7 – 22)	3.9 (1.3 – 12)	2.0 (0.35 – 7.4)	2.4 (0.4 – 8.3)	3.86 (0.24 – 60)
CB180	0.7 (0.14 – 4.6)	2.6 (0.7 – 9.6)	2.1 (0.8 – 6.3)	1.1 (0.17 – 3.9)	1.24 (0.2 – 4.6)	2.06 (0.14 – 5.6)
Σ14 PCBs	3.67 (0.02 – 32)	14.3 (4.4 – 56)	10.6 (3.6 – 31)	5.8 (1.0 – 22)	6.7 (1.1 – 22)	10.7 (0.02 – 180)

ns: Not significant.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·11. Concentrations of POPs (μg/L plasma) in Inuit women of reproductive age from Greenland. Data show geometric mean (and range) for specified period of sampling. Source: Deutch et al. (2004, 2007), Deutch, B., pers. comm. (2007).

	Sisimiut 2002 – 2003 33 (20 – 50) [b] n = 42 [c]	Qaanaaq 2003 33 (20 – 50) [b] n = 34 [c]	Nuuk 2005 36 (30 – 50) [b] n = 45 [c]	Quegertarsuaq 2006 34 (20 – 50) [b] n = 44 [c]	Narsaq 2006 35 (20 – 50) [b] n = 42 [c]	All Greenland [a] 1999 – 2006 33 (18 – 50) [b] n = 299 [c]
Oxychlordane	0.22 (0.01 – 1.7)	1.06 (0.03 – 9.0)	0.16 (0.02 – 1.7)	0.28 (0.02 – 2.7)	0.43 (0.05 – 5.5)	0.53 (0.01 – 14.8)
Trans-nonachlor	0.48 (0.05 – 3.3)	1.8 (0.1 – 12)	0.39 (0.05 – 32)	0.62 (0.07 – 4.6)	0.89 (0.11 – 9.5)	0.97 (0.05 – 11.7)
p,p′-DDT	0.02 (0.01 – 0.53)	0.13 (0.01 – 1)	0.02 (0.01 – 0.16)	0.04 (0.02 – 0.32)	0.07 (0.02 – 1.0)	0.08 (0.01 – 2.8)
p,p′-DDE	1.55 (0.22 – 8.5)	3.7 (0.15 – 25)	1.8 (0.28 – 11)	2.3 (0.2 – 16)	3.7 (0.26 – 20)	3.59 (0.15 – 43)
DDE:DDT	65 (13 – 270)	28 (8.5 – 120)	66 (9.5 – 280)	51 (10 – 270)	50 (5.2 – 410)	42.2 (5.2 – 410)
HCB	0.42 (0.07 – 1.9)	0.98 (0.07 – 4.9)	0.33 (0.12 – 1.8)	0.61 (0.07 – 6.1)	0.59 (0.11 – 2.5)	0.66 (0.07 – 6.1)
β-HCH	0.04 (0.01 – 0.2)	0.19 (0.01 – 1.0)	0.02 (0.01 – 0.26)	0.04 (0.01 – 0.41)	0.06 (0.01 – 0.31)	0.09 (0.01 – 2.0)
Mirex	0.05 (0.01 – 0.22)	0.11 (0.01 – 0.7)	0.03 (0.01 – 0.33)	0.04 (0.01 – 0.38)	0.07 (0.01 – 0.6)	0.08 (0.01 – 1.3)
Total Toxaphene	0.19 (0.02 – 1.3)	0.65 (0.02 – 4.7)	0.16 (0.02 – 0.9)	0.34 (0.03 – 2.6)	0.43 (0.03 – 5.8)	0.43 (0.02 – 7.0)
parlar 26	0.08 (0.01 – 0.55)	0.26 (0.01 – 1.9)	0.06 (0.01 – 0.3)	0.13 (0.01 – 0.92)	0.17 (0.01 – 2.3)	0.17 (0.01 – 2.9)
parlar 50	0.11 (0.01 – 0.8)	0.39 (0.01 – 2.8)	0.1 (0.01 – 0.6)	0.22 (0.02 – 1.7)	0.27 (0.02 – 3.5)	0.26 (0.01 – 4.1)
PCBs						
Aroclor 1260	5.9 (1.0 – 27)	18.2 (1.2 – 114)	6.2 (1.5 – 46)	6.9 (0.9 – 4.3)	13.9 (1.7 – 87)	14.3 (0.9 – 263)
CB118	0.13 (0.02 – 0.72)	0.37 (0.02 – 2.1)	0.12 (0.01 – 0.8)	0.18 (0.02 – 1.6)	0.22 (0.03 – 1.2)	0.28 (0.01 – 4.5)
CB138	0.34 (0.06 – 1.6)	1.0 (0.01 – 5.0)	0.37 (0.11 – 2.4)	0.43 (0.06 – 2.7)	0.90 (0.12 – 5.0)	0.90 (0.06 – 15)
CB153	0.79 (0.12 – 3.7)	2.49 (0.16 – 17)	0.8 (0.18 – 6.3)	0.89 (0.11 – 6.0)	1.77 (0.2 – 12)	1.84 (0.11 – 38)
CB180	0.34 (0.05 – 1.5)	1.1 (0.11 – 9.0)	0.40 (0.07 – 3.4)	0.45 (0.04 – 3.5)	0.82 (0.1 – 4.9)	0.91 (0.04 – 29)
Σ14 PCBs	2.18 (0.4 – 9.8)	6.73 (0.5 – 43)	2.27 (0.54 – 16)	2.67 (0.3 – 16.5)	4.97 (0.62 – 29)	5.35 (0.3 – 106)

[a] The eight regions in Greenland were Ittoqqortoormiit 1999, Uummannaq 1999, Tassiilaq 2000, Sisimiut 2002 – 2003, Qaannaq 2003, Nuuk 2005, Quegertarsuaq 2006 and Narsaq 2006; [b] arithmetic mean age and range of group sampled; [c] number of individuals sampled.

Table A 5·12. Concentrations of POPs (μg/L plasma) in Inuit men from Nuuk, Greenland by age class. Data show geometric range mean (and range) for 2005. Source: Deutch et al. (2007), Deutch, B., pers. comm. (2007).

	36 (35 – 38) [a] n = 3 [b]	46 (42 – 50) [a] n = 16 [b]	61 (51 – 77) [a] n = 31 [b]	All ages 55 (35 – 77) [a] n = 50 [b]
Oxychlordane	0.68 (0.6 – 0.8)	1.27 (0.2 – 0.4)	2.88 (0.7 – 15)	2.02 (0.2 – 15)
Trans-nonachlor	1.39 (1.2 – 1.6)	2.97 (0.5 – 8.5)	6.04 (2.0 – 3.3)	4.38 (0.5 – 33)
p,p'-DDT	0.1 (0.09 – 0.11)	0.12 (0.01 – 0.52)	0.20 (0.06 – 0.93)	0.16 (0.01 – 0.93)
p,p'-DDE	5.28 (3.1 – 9.0)	5.94 (1.7 – 16)	11.93 (2.8 – 9.0)	9.01 (1.7 – 90)
DDE:DDT	54.6 (28 – 104)	51.1 (19.3 – 170)	57.9 (28 – 101)	55.1 (19.3 – 170)
HCB	0.79 (0.6 – 1.1)	1.47 (0.3 – 4.4)	2.6 (0.9 – 10)	2.1 (0.3 – 10)
β-HCH	0.09 (0.07 – 0.11)	0.17 (0.01 – 0.44)	0.32 (0.14 – 1.3)	0.24 (0.01 – 1.3)
Mirex	0.14 (0.09 – 0.21)	0.21 (0.05 – 4.1)	0.56 (0.13 – 2.8)	0.37 (0.05 – 2.8)
Total Toxaphene	0.71 (0.7 – 0.73)	1.48 (0.23 – 4.1)	2.24 (0.67 – 12.3)	1.83 (0.23 – 12.3)
parlar 26	0.145 (0.14 – 0.15)	0.31 (0.05 – 0.9)	0.49 (0.17 – 2.7)	0.39 (0.05 – 2.7)
parlar 50	0.29 (0.28 – 0.30)	0.59 (0.09 – 1.6)	0.87 (0.25 – 4.8)	0.72 (0.09 – 4.8)
PCBs				
Aroclor 1260	21.4 (17 – 27)	28.3 (9 – 87)	59.1 (22 – 240)	43.5 (9 – 240)
CB118	0.40 (0.2 – 0.7)	0.50 (0.09 – 1.5)	1.1 (0.4 – 4.7)	0.80 (0.09 – 4.7)
CB138	1.23 (1.0 – 1.6)	1.56 (0.45 – 4.9)	3.0 (1.3 – 11)	2.28 (0.5 – 11)
CB153	2.93 (2.4 – 3.6)	3.88 (1.3 – 12)	8.31 (2.9 – 35)	6.06 (1.3 – 35)
CB180	1.45 (1.1 – 1.9)	2.14 (0.8 – 6.3)	5.27 (1.8 – 23)	3.61 (0.8 – 23)
Σ14 PCBs	7.81 (6.1 – 10)	10.62 (3.6 – 31)	23.1 (8.4 – 97)	16.7 (3.6 – 97)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·15. Concentrations of POPs (μg/L plasma) in Icelandic mothers. Data show geometric mean (and range) for specified period of sampling. Lipid normalization of data based on average lipid concentrations from 1995. Source: Olafsdottir, K., pers. comm. (2007).

	Reykjavik 1995 30 (18 – 41) [a] n = 40 [b], p = 1.9 [c]	All Iceland 1999 28.7 (20 – 42) [a] n = 39 [b], p = 1.9 [c]	All Iceland 2004 30.3 (20 – 40) [a] n = 40 [b], p = 1.8 [c]	SD [d]
Oxychlordane	0.05 (0.02 – 0.16)	0.03 (0.01 – 0.17)	0.05 (0.01 – 0.17)	ns
p,p'-DDE	0.87 (0.33 – 4.3)	0.78 (0.26 – 2.41)	0.42 (0.15 – 1.78)	$p < 0.0001$
CB153	0.52 (0.20 – 1.2)	0.48 (0.19 – 1.65)	0.32 (0.15 – 0.77)	$p < 0.0001$

ns: Not significant.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] parity; [d] significant differences using Kruskal-Wallis Test (Nonparametric ANOVA) between 1995 and 2004.

Table A 5·16. Concentrations of POPs (µg/L plasma) in maternal blood from Icelandic mothers, by region. Lipid normalization of data based on average lipid concentrations from 1995. Data show geometric mean (and range) for 2004. Source: Olafsdottir, K., pers. comm. (2007).

	Reykjavik 2004 31 (20 – 40) [a] n = 20 [b], p = 1.5 [c]	Akureyri 2004 31 (22 – 39) [a] n = 10 [b], p = 2.4 [c]	Vestmannaeyjar 2004 29 (22 – 39) [a] n = 10 [b], p = 1.8 [c]	All regions 2004 30 (20 – 40) [a] n = 40 [b], p = 1.8 [c]
Oxychlordane	0.05	0.05	0.08	0.04
Trans-nonachlor	0.06	0.05	0.06	0.05
p,p'-DDT	0.02	0.02	0.03	0.02
p,p'-DDE	0.42	0.46	0.38	0.40
DDE:DDT	19.2	24.4	14.1	20.3
HCB	0.22	0.22	0.20	0.23
β-HCH	0.07	0.08	0.10	0.04
Toxaphene				
parlar 26	0.01	0.01	0.01	0.01
parlar 50	0.03	0.03	0.03	0.03
PCBs				
Aroclor 1260	2.63	2.56	2.49	2.76
CB118	0.08	0.08	0.09	0.08
CB138	0.18	0.18	0.18	0.19
CB153	0.32	0.32	0.30	0.34
CB180	0.18	0.17	0.18	0.19
Σ14 PCBs	1.03	0.98	1.01	1.05

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] parity.

Table A 5·17. Concentrations of POPs (µg/L plasma) in maternal plasma from northern Norway. Data show geometric mean (and range) for specified period of sampling. Source: Kirkenes (AMAP, 1998), Bodø (SPFO, 2005).

	Kirkenes 1996 29 (19 – 44) [a] n = 66 [b]	Bodø 2004 30 (20 – 35) [a] n = 10 [b]
Oxychlordane	0.03	0.02
p,p'-DDE	0.61	0.40
CB153	0.41	0.14

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·18. Contaminant concentrations (µg/L plasma) in pregnant women from the Kiruna region in northern Sweden. Data show geometric mean (and range) for specified period of sampling. Source: 1996 (Van Oostdam et al., 2004), 2007 (Messner, T., pers. comm., 2008).

	Northern Sweden 1996 29 (22 – 33) [a] n = 40	Northern Sweden 2007 27 (22 – 33) [a] n = 25	Significant difference, $p < 0.05$
Oxychlordane	0.02 (0.01 – 0.05)	nd	
p,p'-DDE	0.84 (0.33 – 5.5)	0.27 (0.06 – 0.96)	$p < 0.001$
CB153	0.70 (0.31 – 2.0)	0.21 (0.07 – 0.46)	$p < 0.001$

nd: Not detected.

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5-21 Concentrations of POPs (μg/L plasma) in pregnant women by area and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007), Anda, E., pers. comm. (2008), Sandanger et al. (2003), Dudarev et al. (2003), Konoplev et al. (2005, 2006), Dudarev and Chashchin (2006).

	Chukotka Peninsula		Kola Peninsula[2]	Pechora River Basin	Taymir Peninsula	Norilsk	Kamchatka
	Coastal	Inland					
	Chukchi & Inuit	Chukchi	Saami, Nenets & Komi	Nenets	Dolgan	Ethnic Russian	Koryak & Even
	26 (15 – 41) [a] n = 68 [b]	25 (18 – 40) [a] n = 58 [b]	22 (18 – 32) [a] n = 16 [b]	23 (16 – 38) [a] n = 38 [b]	27 (16 – 42) [a] n = 69 [b]	27 (16 – 37) [a] n = 59 [b]	21 (15 – 39) [a] n = 8 [b]
Oxychlordane	0.59 (0.01 – 7.9)	0.03 (0.01 – 0.35)	0.02 (0.01 – 0.07)	0.02 (0.01 – 0.12)	0.03 (0.02 – 0.44)	0.02 (0.01 – 0.10)	0.05 (0.01 – 0.15)
Trans-non-achlor	0.44 (0.05 – 3.7)	0.05 (0.02 – 0.26)	0.03 (0.02 – 0.13)	0.03 (0.02 – 0.31)	0.08 (0.02 – 0.44)	0.02 (0.02 – 0.11)	0.11 (0.03 – 0.53)
p,p'-DDT	0.22 (0.06 – 1.2)	0.21 (0.06 – 1.0)	0.25 (0.06 – 0.80)	0.26 (0.06 – 1.9)	0.21 (0.06 – 0.85)	0.33 (0.09 – 6.3)	0.11 (0.06 – 0.34)
p,p'-DDE	2.3 (0.74 – 7.0)	1.42 (0.07 – 6.4)	2.06 (0.77 – 6.6)	1.6 (0.06 – 5.4)	1.5 (0.21 – 7.7)	3.2 (0.79 – 20)	1.7 (1.0 – 2.5)
HCB	1.3 (0.33 – 6.0)	0.52 (0.14 – 2.7)	0.34 (0.15 – 1.6)	0.56 (0.15 – 2.1)	0.57 (0.07 – 2.1)	0.26 (0.08 – 1.2)	0.29 (0.19 – 0.55)
β-HCH	1.7 (0.33 – 7.6)	0.67 (0.09 – 2.5)	0.16 (0.02 – 1.7)	0.33 (0.02 – 1.1)	0.65 (0.02 – 3.0)	1.0 (0.02 – 5.7)	0.48 (0.30 – 1.1)
PCBs							
Aroclor 1260	7.6 (1.5 – 30)	1.67 (0.44 – 8.47)	2.49 (0.44 – 5.4)	3.21 (0.44 – 15)	3.2 (0.78 – 12)	2.3 (0.44 – 10)	2.1 (0.87 – 3.2)
CB99	0.28 (0.06 – 0.88)	0.07 (0.03 – 0.73)	0.09 (0.03 – 0.20)	0.07 (0.03 – 0.23)	0.13 (0.03 – 0.36)	0.14 (0.03 – 0.49)	0.08 (0.03 – 0.19)
CB118	0.35 (0.07 – 1.5)	0.17 (0.03 – 1.4)	0.17 (0.03 – 0.60)	0.12 (0.03 – 0.30)	0.22 (0.03 – 0.86)	0.21 (0.06 – 1.4)	0.16 (0.06 – 0.26)
CB138	0.34 (0.09 – 1.2)	0.12 (0.05 – 0.72)	0.22 (0.05 – 0.57)	0.15 (0.05 – 0.56)	0.21 (0.05 – 0.74)	0.16 (0.05 – 0.58)	0.10 (0.05 – 0.19)
CB153	1.1 (0.19 – 4.8)	0.20 (0.04 – 0.98)	0.26 (0.04 – 0.50)	0.45 (0.04 – 2.4)	0.40 (0.10 – 1.6)	0.28 (0.04 – 1.4)	0.29 (0.12 – 0.52)
CB180	0.23 (0.06 – 1.0)	0.06 (0.02 – 0.29)	0.09 (0.02 – 0.28)	0.18 (0.02 – 1.30)	0.14 (0.02 – 0.56)	0.08 (0.02 – 0.36)	0.09 (0.05 – 0.12)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Table A 5·22. Concentrations of POPs (μg/L plasma) in women (general population) by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007), Anda, E., pers. comm. (2008), Sandanger et al. (2003), Dudarev et al. (2003), Konoplev et al., 2005, 2006), Dudarev and Chashchin (2006).

	Chukotka Peninsula		Kola Peninsula		Pechora River Basin	Taymir Peninsula	Commander Islands
	Coastal	Inland	Lovosero	Krasnoschelye			
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Saami, Nenets and Komi	Nenets	Dolgan	Aleuts
	38 (21 – 69) [a] n = 26 [b]	37 (19 – 81) [a] n = 28 [b]	47 (26 – 76) [a] n = 17 [b]	44 (18 – 78) [a] n = 47 [b]	37 (18 – 65) [a] n = 31 [b]	44 (20 – 72) [a] n = 40 [b]	34 (18 – 46) [a] n = 49 [b]
Oxychlordane	0.58 (0.05 – 5.1)	0.07 (0.01 – 1.2)	0.03 (0.01 – 0.13)	NA[6]	0.03 (0.01 – 0.17)	0.08 (0.01 – 0.54)	0.04 (0.01 – 0.46)
Trans-non-achlor	0.87 (0.11 – 5.8)	0.11 (0.02 – 1.5)	0.09 (0.04 – 0.26)	0.04 (0.02 – 0.62)	0.04 (0.02 – 0.28)	0.09 (0.02 – 0.83)	0.16 (0.03 – 1.4)
p,p′-DDT	0.17 (0.06 – 0.70)	0.11 (0.06 – 0.48)	0.36 (0.15 – 1.0)	0.43 (0.12 – 4.1)	0.40 (0.06 – 3.2)	0.21 (0.06 – 1.2)	0.20 (0.06 – 1.3)
p,p′-DDE	2.1 (0.46 – 6.8)	1.1 (0.30 – 2.5)	2.91 (0.37 – 9.1)	2.47 (0.08 – 45)	2.1 (0.23 – 12)	1.2 (0.06 – 4.6)	2.3 (0.05 – 29)
HCB	0.69 (0.08 – 3.4)	0.75 (0.25 – 2.6)	0.75 (0.39 – 1.2)	0.57 (0.05 – 1.7)	0.80 (0.26 – 2.3)	1.3 (0.05 – 3.6)	0.62 (0.17 – 2.7)
β-HCH [d]	1.71 (0.22 – 8.2	0.18 (0.02 – 1.6)	0.98 (0.09 – 4.2)	0.75 (0.02 – 3.8)	0.58 (0.15 – 3.7)	1.1 (0.13 – 3.9)	0.62 (0.17 – 2.7)
PCBs							
Aroclor 1260	13.17 (2.4 – 78)	1.8 (0.67 – 8.3)	3.83 (1.8 – 10)	4.00 (0.53 – 13)	3.3 (0.44 – 29)	2.94 (0.60 – 9.3)	4.2 (1.4 – 27)
CB99	0.32 (0.05 – 1.2)	0.07 (0.03 – 0.28)	0.10 (0.03 – 0.19)	0.26 (0.03 – 4.0)	0.13 (0.03 – 8.8)	0.08 (0.03 – 0.51)	0.15 (0.03 – 1.2)
CB118	0.44 (0.07 – 1.8)	0.15 (0.03 – 0.56)	0.26 (0.11 – 0.71)	0.29 (0.03 – 1.3)	0.19 (0.03 – 5.6)	0.17 (0.03 – 0.83)	0.22 (0.03 – 1.8)
CB138	0.73 (0.14 – 4.2)	0.11 (0.05 – 0.39)	0.25 (0.10 – 0.82)	0.31 (0.05 – 1.0)	0.22 (0.05 – 2.8)	0.20 (0.05 – 0.73)	0.29 (0.08 – 1.8)
CB153	11 (0.309 – 10.913)	0.23 (0.08 – 1.2)	0.48 (0.19 – 1.2)	0.44 (0.05 – 1.7)	0.40 (0.04 – 2.8)	0.35 (0.07 – 1.3)	0.51 (0.16 – 3.3)
CB180	0.46 (0.07 – 3.7)	0.07 (0.02 – 0.34)	0.23 (0.12 – 0.64)	0.14 (0.02 – 0.70)	0.11 (0.02 – 1.1)	0.10 (0.02 – 0.49)	0.17 (0.02 – 1.1)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled; [c] thirty samples were missing from Krasnoschelye; [d] ten samples for β-HCH were missing from one lab, all in the same area (Kanchalan), thus will give an artificially low estimate.

Table A 5-23. Concentrations of POPs (μg/L plasma) in men (general population), by region and ethnicity in Russia. Data show geometric mean (and range) for 2001 – 2003. Source: Dudarev, A., pers. comm. (2007), Anda, E., pers. comm. (2008), Sandanger et al. (2003), Dudarev et al. (2003), Konoplev et al. (2005, 2006), Dudarev and Chashchin (2006).

	Chukotka Peninsula		Kola Peninsula		Pechora River Basin	Taymir Peninsula	Commander Islands
	Coastal	Inland	Lovosero	Krasnoschelye			
	Chukchi & Inuit	Chukchi	Saami, Nenets and Komi	Saami, Nenets and Komi	Nenets	Dolgan	Aleuts
	35 (19 – 68) [a] n = 24 [b]	32 (19 – 54) [a] n = 14 [b]	44 (18 – 77) [a] n = 4 [b]	44 (18 – 77) [a] n = 15 [b]	25 (18 – 62) [a] n = 13 [b]	39 (18 – 69) [a] n = 12 [b]	39 (18 – 58) [a] n = 40 [b]
Oxychlordane	1.7 (0.01 – 9.7)	0.07 (0.01 – 0.41)	0.03 (0.01 – 0.14)	0.03 (0.01 – 0.12)	0.04 (0.01 – 0.44)	0.06 (0.01 – 1.2)	0.01
Trans- non-achlor	1.8 (0.02 – 7.0)	0.13 (0.04 – 0.56)	0.16 (0.08 – 0.26)	0.08 (0.02 – 0.28)	0.08 (0.02 – 0.34)	0.14 (0.02 – 0.36)	0.20 (0.02 – 1.3)
p,p'-DDT	0.20 (0.06 – 0.73)	0.14 (0.06 – 0.24)	0.58 (0.27 – 1.9)	0.26 (0.14 – 0.58)	0.29 (0.06 – 0.63)	0.17 (0.06 – 0.51)	0.20 (0.06 – 7.0)
p,p'-DDE	3.5 (1.3 – 8.3)	1.7 (1.1 – 3.2)	4.8 (1.9 – 17)	2.1 (0.43 – 7.0)	1.7 (0.11 – 10)	1.8 (0.91 – 4.2)	2.9 (0.67 – 9.9)
HCB	0.93 (0.02 – 3.4)	0.62 (0.35 – 1.4)	0.97 (0.62 – 1.3)	0.67 (0.20 – 2.0)	0.83 (0.33 – 2.3)	1.4 (0.57 – 6.0)	0.24 (0.02 – 0.73)
β-HCH	2.2 (0.02 – 6.4)	0.45 (0.02 – 4.8)	0.90 (0.41 – 1.6)	0.67 (0.27 – 1.6)	0.49 (0.26 – 1.2)	1.0 (0.47 – 1.9)	0.14 (0.02 – 2.0)
PCBs							
Aroclor 1260	32 (6.1 – 109)	2.7 (1.8 – 4.2)	10 (8.6 – 13)	5.5 (1.9 – 14)	4.0 (1.1 – 16)	4.8 (2.5 – 11)	3.2 (0.44 – 17)
CB99	0.62 (0.16 – 1.4)	0.12 (0.07 – 0.19)	0.18 (0.13 – 0.20)	0.10 (0.03 – 0.30)	0.12 (0.03 – 1.3)	0.10 (0.03 – 0.24)	0.03 (0.03 – 0.50)
CB118	0.75 (0.14 – 1.6)	0.24 (0.09 – 0.45)	0.43 (0.17 – 0.74)	0.20 (0.07 – 0.44)	0.13 (0.06 – 0.33)	0.19 (0.06 – 0.62)	0.04 (0.03 – 0.40)
CB138	1.7 (0.36 – 5.3)	0.18 (0.13 – 0.27)	0.59 (0.45 – 0.85)	0.34 (0.13 – 1.2)	0.25 (0.05 – 1.0)	0.31 (0.18 – 0.66)	0.26 (0.05 – 1.4)
CB153	4.4 (0.82 – 16)	0.33 (0.20 – 0.59)	1.4 (1.2 – 2.0)	0.70 (0.21 – 1.7)	0.51 (0.15 – 2.0)	0.61 (0.30 – 1.5)	0.30 (0.04 – 2.2)
CB180	1.3 (0.26 – 5.1)	0.11 (0.05 – 0.26)	0.64 (0.47 – 1.1)	0.38 (0.08 – 1.0)	0.22 (0.05 – 1.5)	0.23 (0.07 – 0.67)	0.15 (0.02 – 2.1)

[a] Arithmetic mean age and range of group sampled; [b] number of individuals sampled.

Chapter 6

Genetics and Contaminants

Eva Cecilie Bonefeld-Jørgensen

Summary

This chapter describes the concepts of natural and selected gene diversity in relation to different populations, with emphasis on the Inuit and the possible link with and consequences of chemical exposures. Maternal inheritance of mitochondrial DNA (mtDNA) has been used to elucidate the ancestry of the Inuit and has demonstrated a close similarity in the circumpolar region with the hypothesis that the genetic impact of Neo-Inuit (Thule groups) interbred with existing Dorset populations in Canada and Greenland.

Differences in the occurrence of diseases between Inuit and Caucasian populations have been reported and the possible relation to gene polymorphism is speculated but needs further study. Serum lipids and apolipoproteins are risk factors for atherogenesis. Apolipoprotein E (APOE) differs between populations and APOE polymorphisms were found to be associated with atherosclerosis in U.S. white and black people that seems independent of serum lipids. However, the risk of coronary heart disease in Canadian Inuit was lower despite a higher incidence of disease-related *APOE* alleles. Nor was any association found between *APOE* genotypes and atherosclerotic lesions in Greenlandic Inuit. Studies have supported the hypothesis that the risk of coronary heart disease in Inuit is influenced by inherited genes as well as by diet and lifestyle.

In contrast to their Asian ancestors, the Inuit do not seem to be genetically protected against alcoholism. Co-exposure to alcohol and environmental chemicals might influence metabolism because some of the genes involved in metabolism of both types of exposure are identical. Ethnic differences in lactose tolerance are well known and a low range of lactose tolerance is found in Inuit. Future studies might elucidate whether changes in diet and lactose tolerance have any impact on health risk.

The balance between xenobiotic absorption and elimination rates in metabolism are important factors in detoxification and prevention of chemical carcinogenesis. Approximately 80% of all cancers have been estimated from epidemiological studies to be related to environmental factors, and cancer susceptibility can result from differences in genetic background for metabolism, DNA repair, and altered gene expressions of tumor-related genes. Thus gene polymorphism in metabolizing enzymes, for example cytochrome P450, is suspected to influence susceptibility to environmental carcinogens. Studies have suggested a link between gene polymorphism in metabolizing genes, levels of persistent organic pollutants (POPs) and the risk of, for example, breast cancer in Caucasians. The incidence of breast cancer in Inuit is low and the very few studies on polymorphism in metabolizing genes in Inuit awaits further studies with respect to the risk of breast cancer.

Epigenetics is a new paradigm in toxicology and teratology, a phenomenon that can be hereditary without any change in primary DNA sequence but which reflects a change in control of gene activity that arises from the interplay of DNA methylation, histone modification, and RNA-mediated pathways. Epigenetic regulation is a part of normal development and differentiation; however, by misdirection it can cause diseases including cancer. Environmental exposure to polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs), which are effective promoters in two-step-cancer models, implies the involvement of epigenetic mechanisms, and epigenetic hypermethylation of the tumor suppressor Breast Cancer *BRAC1* gene has been related to breast and ovarian tumors. *In vitro* studies showed that non-coplanar PCBs can decrease the *BRACA1* expression implying epigenetic mechanisms. A link between epigenetic mechanisms, exposure to γ-hexachlorocyclohexane (HCH) and risk for breast and prostate cancer has also been suggested. Recent data for Greenlandic Inuit showed a link between the levels of serum POPs and the level of 'global' DNA methylation, and further studies are needed to elucidate these cellular and biological epigenetic responses in relation to health.

POPs are well known for their potential to suppress the immune system. Lower incidence of asthma is observed in Inuit and studies have suggested that genotype differences might be involved in the lower incidence compared to Caucasians. However, the exact mechanisms are not yet known.

The ethnic differences in apolipoprotein gene polymorphisms related to fatty acid metabolism are described in this chapter, and a slightly higher frequency of the *APOE*4* allele in Inuit compared to other populations was reported. However, no associations between *APOE* genotypes and atherosclerotic lesions, serum lipids, glucohemoglobin levels or adiposity were found. The paraoxonase gene family (*PON1*, *PON2*, *PON3*) expresses serum paraoxonase that are associated with high-density lipoprotein (HDL) particles. The common genetic *PON1 M55* variant, associated with atherosclerosis and lipoprotein metabolism and higher plasma triglycerides, was found to be related to traits in plasma lipoprotein metabolism in indigenous Canadians.

Studies have reported that the genetic background and risk factors for cardiovascular diseases differs between Inuit and Caucasians (Danes) with a lower risk for Inuit from a genetic point of view. The risk allelels include apolipoproteins, fibrinogen, factor V, glycoproteins, plasmonogen activator and inhibitor, angiotensin-converting enzyme and angiotensin.

Extensive research for the underlying genetic factors of diabetes type II has not succeeded and very little is reported for Arctic populations. Variations in the vitamin D receptor genotype were reported to influence bone turnover. A genetic adaption to dietary constraint was suggested. However, whether the reported associations between POPs exposure and osteoporosis in Greenlandic women are genetically linked awaits further studies.

Finally, the chapter describes ethnic gene polymorphism for the aryl hydrocarbon receptor (*AHR*), the androgen receptor (*AR*), and the estrogen receptor (*ER*). For the *AHR* gene similar polymorphism was found for Caucasians and Inuit and was different to that for Japanese and African populations. Ethnic differences in the *ERα* gene have been reported and related to PCB exposure and breast cancer. However, no report on *ER* polymorphisms was found for Arctic Inuit people. *In vitro* studies have shown complex patterns of responses following exposure to natural as well as to synthetic estrogens (e.g., hydroxyl-PCBs) dependent on the cell context and ER form that must encourage researchers to elucidate the possible interaction between POPs exposure, *ER* polymorphism, and health.

In summary, genetic background affects the impact and susceptibility to contaminant exposure and thus health risk. To date, little research on genetic polymorphism especially in relation to diseases has been undertaken on Arctic populations. Future studies should include genetics in parallel with lifestyle and contaminant exposure in order to provide a better insight into individual and population vulnerability to contaminants.

6.1. Introduction

This chapter provides an introduction to the ancestry of the Inuit in order to understand their genetic background as a result of population movements and adaptation to the environment. The polymorphism of genes used as biomarkers of effect by environmental chemicals is described in terms of a comparison between Inuit and Caucasians. To date, relatively little is known about the specific genetic polymorphism of Inuit in relation to contaminants. The known genetic polymorphism in other populations, for example Caucasians, is given as a guide to future research into which genes should be investigated in order to understand the possible strengths and weaknesses of Inuit to combat the high level of contaminants in their environment. Cross references are made where necessary to other chapters of this assessment.

6.2. Genetic diversity

Most genetic diversity in humans is thought to be neutral, that is, not affected by natural selection. 'Neutral diversity' can be used to record the history of humans. The global neutral diversity is known due to the DNA typing and DNA sequencing technologies that have been applied to samples from many human populations.

Selected diversity, diversity that is not neutral, can also be of interest to history, but of more importance is whether 'selected diversity' is a consequence of random mutation and natural selection, and how it might affect human health and well-being. Many rare genetic disorders belonging to this category that have health consequences are leftovers – adaptations to past environments – for example lactose intolerance, hemochromatosis and sickle cell heterozygotes, with the latter giving some protection against malaria (Harpending and Cochran, 2006).

Diversity within the 'older' population of sub-Saharan Africa is greatest within Africa and declines away from Africa into the New World; declining 15% to 20% from Africa to northeast Asia and 30% into the New World. The movement out of Africa was suggested to involve small movements and adaptive natural selection favoring the modern genotype (Eller, 1999; Eswaran, 2002).

Chemical contamination can cause population reduction via heritable genetic somatic and germ-line mutations initiating a cascade of responses on health, such as on reproduction and population genetics. Mutagenic and non-mutagenic (e.g., endocrine disrupting) chemicals can affect the reproductive success of a population and ultimately lead to decreased genetic diversity, extirpation and/or adaptation to a contaminated environment (Bickham et al., 2000). The loss of genetic variability may become permanent once variability is lost and the population cannot recover to what it was prior to the environmental impact (assuming the absence of gene flow from other populations) – unless the population survives for a very long time (Figure 6.1).

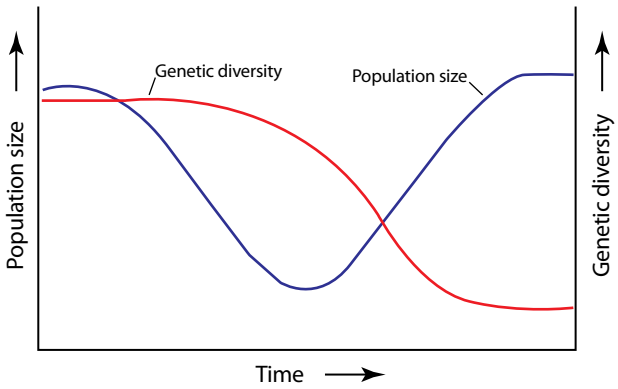


Figure 6.1. Relationship between genetic diversity and population numbers. Source: adapted from Bickham et al. (2000).

6.2.1. Mitochondrial DNA as a tool to determine the ancestry of Inuit

The unique genetic properties of mtDNA, including its maternal inheritance, its complete mapping, and its high mutation rate have been used to determine the ancestry of populations (Thrasher, 2000). Previous studies of mtDNA variation in the circumpolar region have demonstrated a close similarity between the mtDNA pools of Siberian, Chukchi, and Greenlandic Inuit (Saillard et al., 2000). This was interpreted as a recent population expansion in the area and a signal of the genetic impact of Thule groups (Neo-

Box 6·1. Genes, alleles, genetic polymorphy, haplotypes, and haplogroups

Genetic diversity can be explained by the following concept: genes exist in more than one form (*allele*), and no one (except one-egged twins) carries the same forms (*alleles*) of genes and are so everyone is a genetic polymorph. An allele can be dominant or recessive meaning that the dominant allele can alone dominate over the recessive allele, whereas the recessive allele can only express its phenotype when together with the same allele form. *Haplotypes* are a group of close-set genetic polymorphisms on the same chromosome that are inherited as a bloc. Because many different haplotypes exist they are grouped into superior *haplogroups*. With respect to mtDNA, the Inuit carry only haplotype cluster A2 and D3 out of the four primary mtDNA A–D haplotype groups.

Inuit) expanding eastward from Alaska within the last 1000 years and replacing any existing groups (Saillard et al., 2000). However, knowing that Inuit carry considerable differences in the frequencies of genetic mtDNA haplotypes (Box 6.1) has cast doubt on the hypothesis that contemporary Inuit have all their ancestry to the so-called Thule groups expanding from Alaska. Discrepancies in mutational divergence and their putative source of mtDNA pool from Siberia/Alaska seems more consistent with the possibility that expanding Thule groups interbred with existing Dorset populations in Canada and Greenland (Helgason et al., 2006) (Figure 6.2).

Mutations in germ cells and mtDNA can be passed to offspring and these heritable mutations can lower the reproductive output of an affected population because of lower viability and fertility. Mutations with severe effects might be only the tip of the iceberg, and because most mutations are only slightly deleterious they are difficult to detect over short time periods and with low numbers of samples (Bickham et al., 2000). Thus population-genetic effects of environmental contaminants should be a focus of evolutionary toxicology.

6.3. Diseases and genetics in Inuit

The Inuit gene pool is in many respects similar to that of East Asian populations. In the circumpolar regions Inuit have been living in almost genetic isolation for more than 5000 years. During this period the Inuit have been subject to a harsh selective pressure concerning climate and diet, resulting in distinct ethnic features that might explain the differences between Inuit and Western pathology. In Greenland, Danish–Norwegian colonization during the 18th century started a genetic admixture that increased after the Second World War in most Arctic populations. Exploitation of Arctic resources and military involvement led to a further Westernization and genetic admixture (Harvald, 1989).

Table 6.1 lists some polymorphisms with clinical implications; ecogenetic effects under certain environmental conditions for Greenlandic Inuit.

Differences in the occurrence of diseases between Inuit and Caucasians, possibly related to gene polymorphism between the two ethnic populations, were reported for Upernavik in Greenland (Harvald, 1989). Table 6.2 compares the observed incidences of various diseases in Inuit from Upernavik against the expected incidences of these diseases based on Caucasians (Danes). Of eleven examples, only apoplexy and epilepsy (grand mal only) occurred more frequently in the Inuit than expected, while the incidences of peptic ulcer, acute myocardial infarction, psoriasis, bronchial asthma, diabetes mellitus, thyrotoxicosis and multiple sclerosis diseases were lower than expected.

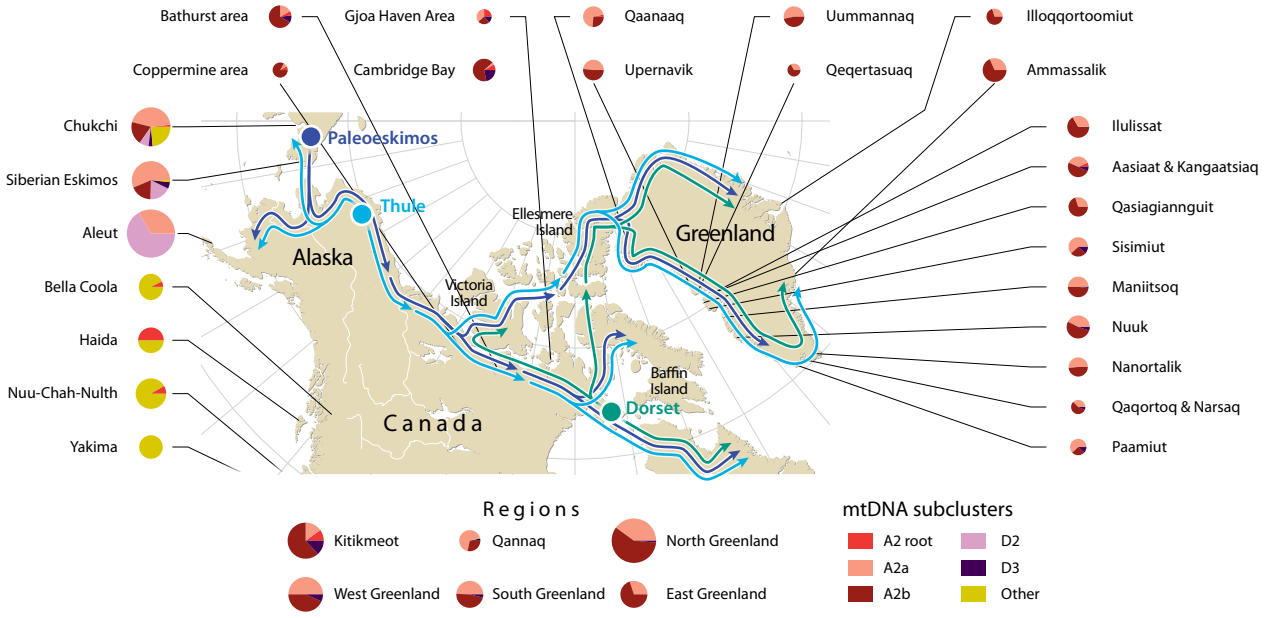


Figure 6·2. North American circumpolar region showing schematically possible source and migration routes of three Arctic cultures and frequency of mtDNA subcluster in Arctic and North American populations. Source: adapted from Helgason et al. (2006).

Table 6·1. Polymorphism with clinical implications; ecogenetic effects under certain environmental conditions for Greenlandic Inuit.

Clinical effect	Consequences
Lactase deficiency	Malabsorption
Sucrose deficiency	Malabsorption
Rare occurrence of Spartein / desbrisoquine (poor metabolizers) Isoniazide slow activators	Fast elimination of certain drugs
C3F-allele rare	Coronary protection
d-allele (rhesus) rare	No rhesus immunization
HLA-B27 frequent	Reactive arthritis frequent
HLA-B8 rare	No insulin-dependent diabetes mellitus
Low number of HLA-alleles	High risk of trophoblastic neoplasma

Table 6·2. Observed incidence of various disease compared to the expected incidence of these disease for Danes over the period 1950 to 1974 in Upernavik. Source: Harvald (1989).

Disease	Observed incidence	Expected incidence
Cancer (all forms)	46	53
Apoplexi	25	15
Epilepsy (grand mal only)	16	8
Peptic ulcer	19	29
Rheumatic fever	11	na
Rheumatoid arthritis	9	na
Psychosis	10	8
Chronic glomerulonephritis	4	na
Chronic pyelonephritis	2	na
Acute myocardial infarction	3	40
Psoriasis	3	40
Bronchial asthma	1	25
Diabetes mellitus	1	9
Thyrotoxicosis	0	7
Multiple sclerosis	0	2

na: not available.

6.4. Serum lipids of Greenlandic Inuit in relation to genetic heritage

It has been suggested that Inuit have a lower incidence of coronary artery disease than Caucasians, despite their higher fat intake (reviewed by Kutryk and Ramjiawan, 2003). Serum levels of total cholesterol, oxidized cholesterol, triglycerides, and apolipoproteins (apo) are risk factors for atherogenesis. Studies have given some insight into the relative contributions of genetic and environmental factors in the development of ischemic heart disease.

Inuit on the east coast of Greenland had little contact with Caucasians in the past and so were expected to have a gene pool similar to that of the original Inuit. Consequently, the level of lipoprotein(a) (Lp(a)) was found to be significantly higher for east coast Inuit than for Inuit from the west coast of Greenland and Danes (Caucasians). Inuit from the east coast of Greenland also differed from the west coast Inuit and/or Danes with respect to small apo(a) molecules (S1, S2, B, F), which were absent from the east coast Inuit but present in west coast Inuit and /or Danes. In contrast, the large apo(a) variant (VS4) was found in Inuit (west and east Inuit) but was very rare in Danes. Common to all three study regions was an inverse relationship between Lp(a) and apo(a) size (Klausen et al., 1995). Apolipoprotein E (APOE) also differs in different human populations and APOE polymorphisms were reported to have a direct association with the extent of atherosclerosis in U.S. blacks and U.S. whites that might be independent of serum lipid, whereas genetic risk for coronary heart disease in northwest Canadian Inuit was lower than in the rest of Canada despite a higher incidence of four disease-related alleles, including *APOE E4* (Hegele et al., 1997). A significant association between *APOE* genotypes and the extent of atherosclerotic lesions was not found for Greenlandic Inuit (Boudreau et al., 1999). Kamboh et al. (1989) found a monomorphic apolipoprotein D (*APO D*) locus in Aleuts of the Pribilof Island, Inuit from Kodiak Island and St. Lawrence Island, U.S. whites and Amerindian populations from Mexico and Canada, but did not find this to be the case for U.S. blacks and Nigerian blacks. Support for the hypothesis that risk of coronary heart disease in Inuit is influenced by inherited genes as well as by diet and lifestyle changes was provided by a study of Greenlandic Inuit living in Greenland or Denmark, which showed that risk factors such as cholesterol and triglyceride differed between genetically-pure and genetically-mixed Inuit depending on the degree of Western lifestyle (Bjerregaard et al., 2004a).

6.5. Gene polymorphism and ethanol metabolism in various ethnic groups

Genetic differences among individuals and their capacity to metabolize alcohol play a role in the large inter-individual variations in alcohol use. Twin, family and adoption studies have shown that vulnerability to alcoholism is determined by genetic factors and influenced by the environment. Alcohol use in Inuit has been high and because alcohol metabolism needs genes (enzymes) (P4502E1, Table 6.3) that are also involved in metabolism and cellular protection against environmental chemicals, epidemiological data obtained from studies on the impact of environmental chemicals on human health must corrected for alcohol intake.

Heavy drinking and alcoholism among North American Indians and Inuit is both a public health and social economic problem and there have been considerations as to whether this is a cultural or genetic

problem. Of several candidate genes for alcoholism, the alcohol-metabolizing enzymes alcohol dehydrogenase (ADH, that oxidizes ethanol to acetaldehyde) and aldehyde dehydrogenase (ALDH, that oxidizes acetaldehyde to acetate), were shown to be involved in the risk of alcoholism. The ADH and ALDH polymorphism among Alaska Natives under treatment for alcoholism showed that Alaska Natives are not protected against

Table 6·3. Relative importance of polymorphism of humans P450. Source: adapted from Ingelman-Sundberg (2005).

Enzyme	Fraction, %	Substrates	Major allelic variants	Clinical effects of the polymorphism	Significance, polymorphism
CYP1A1	5	Carcinogens	None	None	-
CYP1A2	2	Drugs/carcinogens	*CYP1A2*1k*	Less expression/inducibility	+
CYP1B1	-	Carcinogens	Rare defect alleles	None	-
CYP2A6	2	Nicotine, drugs, carcinogens	*CYP2A6*4* *CYP2A6*9*	Altered nicotine metabolism	+
CYP2B6	2 – 4	Drugs	-	Relatively high	+
CYP2C8	1	Drugs	*CYP2C8*3*	Taxol metabolism	+
CYP2C9	10	Drugs	*CYP2C9*2* *CYP2C9*3*	Side effects Drug dosage	++ +++
CYP2C19	5	Drugs	*CYP2C19*2* *CYP2C19*3*	Drug dosage Drug efficiency	+++ +++
CYP2D6	25 – 30	Drugs	*CYP2D6*2nx* *CYP2D6*4* *CYP2D6*10* *CYP2D6*17* *CYP2D6*41*	Non response Side effects Drug dosage Drug dosage Drug dosage	+++ +++ ++ + ++
CYP2E1	2 – 4	Carcinogens, solvents,drugs	-	Not shown	-
CYP3A4	45 – 50	Drugs/carcinogens	Rare	Not shown	-
CYP3A5	< 1	Drugs	*CYP3a5*3*	Not shown	-

An updated version of the polymorphisms in human P450 genes encoding enzymes active in biotransformation of xenobiotic compounds can be found at http://www.imm.ki.se/cypalleles.

Box 6·2. Gene polymorphism and ethanol metabolism

Of several candidate genes for alcoholism the alcohol-metabolizing enzymes alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), that oxidize ethanol to acetaldehyde and acetaldehyde to acetate, respectively, were shown to be involved in the risk of alcoholism. About 10% of ethanol is metabolized by P4502E1 depending on the saturation of ADH. During metabolism reactive oxygen species and radicals causing oxidative stress can cause ethanol-induced liver damage. For detoxification of radicals glutathione S-transferase plays a role. All these enzymes are polymorphic giving rise to altered phenotypes (Gemma et al., 2006). A variant of ADH (ADH2) and ALDH (ALDH2) is found more frequently among Chinese, Japanese and other Mongoloid populations than among Caucasian and black populations (Agarwal and Goedde, 1992). The polymorphic *ADH* and *ALDH* encode different subunits of the enzymes that differ in the rate of alcohol metabolism. The ALDH2 isozyme is inactive and reported to be found in up to about half of Japanese and Chinese livers, whereas this abnormality was not found in Caucasians and black people (Agarwal and Goedde, 1992). Asians that possess the atypical ALDH2 are more sensitive to acute responses to alcohol and it tends to counteract intake of alcohol and consequently alcohol-related disorders. Studies have determined further polymorphism in gene loci influencing alcoholism, *ADH2*, *ADH3* and *ALDH2*, among ethnic groups in China (Han, Mongolian, Korean, and Elunchun) (Shen et al., 1997). Within each population one or more of the three loci protected against alcoholism. The *ADH2*2* alleles were found at much lower frequency in Elunchun's, and low frequency of the *ALDH2*2* alleles occurred in both Elunchun and Mongolian groups. The protective alleles, *ALDH2*2*, *ADH2*2* and *ADH3*1*, encode enzymes that either rapidly metabolize ethanol to acetaldehyde or slow the conversion of acetaldehyde to acetate causing flushing and other unpleasant symptoms. Similarly, in a study of alcoholic and non-alcoholic Japanese individuals, differences were found in the *ADH2*, *ADH3* and *ALDH2* loci (Nakamura et al., 1996), where both homozygous *ALDH2*1/1* and heterozygous *ALDH2*1/2* genotypes, and for the latter in combination with *ADH2*1*, were suggested to increase the development of alcoholism. Interestingly, nearly all Caucasians tested were homozygous for the *ALDH2*1/1* genotype suggesting a possible sensitivity to the development of alcoholism (Goedde et al., 1992).

Alaska Natives were homozygous for *ADH1*1*, *ADH2*1* and *ALDH2*1* alleles with variation in the *ADH3* genotype, and no differences in these genes were found compared to the general population but differences were found when compared with four Asian groups. In conclusion, Alaska Natives are not protected against alcoholism via the *ALDH2*2* genotype, in contrast to Asians that are (Segal, 1999).

alcoholism via the protective *ALDH2*2* genotype, in contrast to Asians that are (Segal, 1999) (Box 6.2).

High alcohol intake is also a social problem for Greenlandic Inuit. A comparison of Inuit living in Greenland and Denmark showed that the latter had the higher alcohol intake and that this depended on the length of stay in Denmark. In contrast, a higher proportion of individuals with episodes of heavy drinking and alcohol dependence were seen in large communities in Greenland (Madsen et al., 2005). A small study of the polymorphism of genes suggested to be involved in alcoholism that compared Greenlandic Inuit and Danes showed no significant differences between the two populations (Autrup, H., pers. comm., 2008), and based on the previously described studies of Asian, Caucasian and Alaska Natives it might be suggested that Greenlandic Inuit are not protected against alcoholism. If so, the speculation is then whether this difference relative to their Asian ancestors is a 'selected diversity' resulting from mutation and/or natural selection or is a leftover from health consequences.

6.6. Genetic interpretation of ethnic differences in lactose tolerance and intolerance

The lactose molecule, the carbohydrate found in milk, can only be absorbed when the molecule is converted into glucose and galactose. Ethnic lactose tolerance/intolerance has been related to genetic differences across adult groups. The symptoms of lactose intolerance are bloating, cramps and diarrhea. The tolerance range from 90% in subjects of European ancestry to fewer than 10% for most Africans, Orientals, Indians and Inuit indicates that most humans are intolerant (Johnson et al., 1981). Experts of genetics, anthropology, nutrition and gastroenterology agree that the ability to digest lactose once infancy has passed is dependent on having a single autosomal dominant allele (Box 6.1 and Box 6.3), and that the dominant allele is a mutant, whereas the wild-type allele leads to cessation of lactase production after infancy. The presence of the dominant allele follows populations having a long tradition (~ 6000 to 9000 years ago) of cattle herding and use of raw milk, and includes northern Europeans and certain African and Arabian nomadic tribes. This contrasts with populations showing lactose intolerance, for example, non-herding, non-milk using groups such as Inuit, Australian Aborigines, Kung Bushmen and American Indians. Orientals and Asians, in general, show about 90% lactose intolerance (reviewed by Johnson et al., 1981).

Whether lactose intolerance and the impact of environmental chemicals affect the health risk of Arctic populations awaits future research. In a recent study (Long et al., 2007a) the TCDD toxic equivalence of serum dioxin-like activity (AHR-TEQ) (see Chapter 8, Box 8.3) of the combined data of Nuuk, Sisimiut and Qaanaaq showed a statistically significant positive correlation with the consumption of dairy food, suggesting that dairy products may be one source of dioxin-like and/or AhR-activating compounds for Inuit living in West Greenland.

Box 6.3. Ethnic differences in lactose tolerance and intolerance

Hollox et al. (2001) have shown that the element responsible for lactase persistence/non-persistence polymorphism in humans is *cis*-acting to the lactase gene (*LCT*) and that a 70-kb lactase haplotype (*LCT*P*) is associated with lactase persistence in Europeans. Moreover, they showed that difference in lactase persistence frequency is generated by point mutations and recombinations giving rise to the four globally common haplotypes A, B, C, and U. These are not closely related and have different distributions and frequencies; the frequency of A is high in northern Europeans only; U is virtually absent from Indo-Europeans* and is found at reasonable frequencies in other populations, being highest in Siberian, Chinese, Japanese and San from northwest Namibia.

Gene selection and drift were suggested to be important in the generation of the lactase haplotype diversity, which is higher in 'Old World' sub-Saharan Africans than in non-Africans.

* The Indo-European languages being a proxy for the spread of haplotypes comprise a family of several hundred related languages and dialects, including most of the major languages of Europe, the Iranian plateau (Southwest Asia), much of Central Asia and the Indian subcontinent (South Asia). The Indo-European (Indo refers to the Indian subcontinent, because geographically the language group spreads from Europe in the west to India in the east) group has the largest numbers of speakers of the recognized families of languages in the world today, with its languages spoken by approximately three billion native speakers.

6.7. Differences in gene polymorphism between Caucasian and Asian populations; focusing on genes involved in metabolism and/or as mediators of health effects of POPs

Researchers in evolutionary biology, population management and conservative biology routinely investigate genetic variability but few have addressed the effects of chemical contamination on genetic diversity. Induced mutations can be passed to the offspring (see section 6.2.1), lowering the fitness of the population, a process known as 'mutational load'. Acute exposure such as following an oil spill is not expected to seriously affect population genetics because the more deleterious the mutations the more quickly selection excises them (Bickham et al., 2000). However, chronic exposure to chemical contamination may be only slightly deleterious and new mutations can be hard to detect in small populations over a short period of time (Mukai, 1964; Crow, 1997).

As hypothesized by Bickham et al. (2000), population genetic responses to chemical exposures might cause increased genetic variation (resulting from new induced mutations) or decreased genetic variation (through selection that also affects allele frequencies)

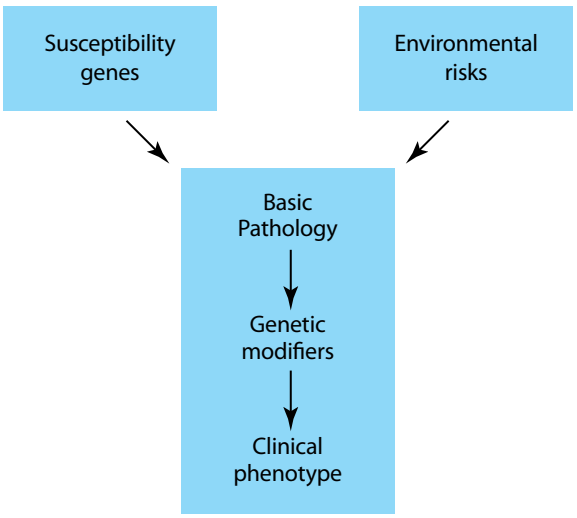


Figure 6·3. The paradigm of interactions between genes and environment and development of a clinical phenotype.

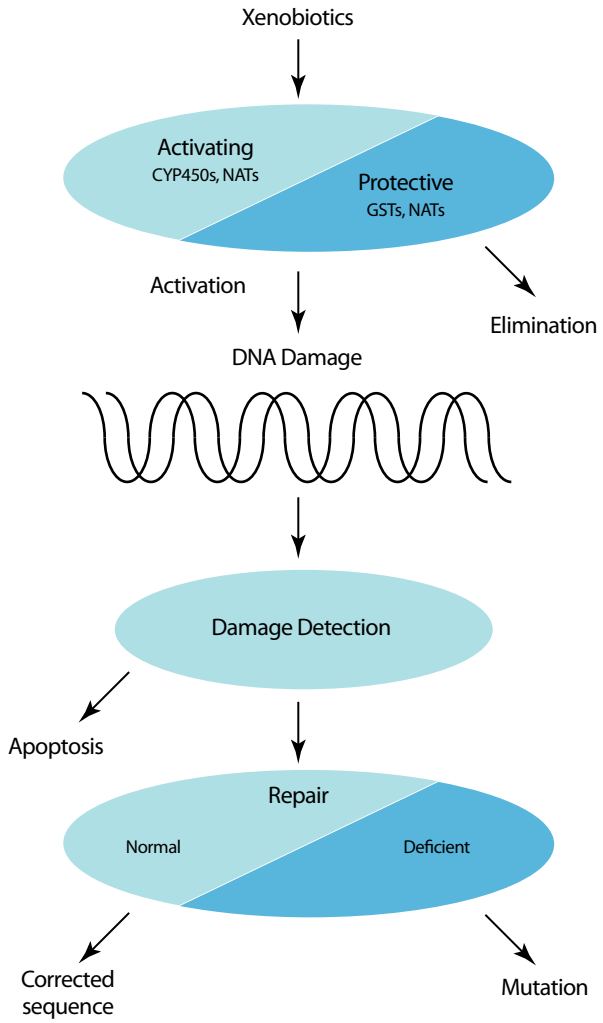


Figure 6·4. Genetic variability in susceptibility to toxicants. Source: adapted from Miller et al. (2001).

(Box 6.1), and both can be a consequence of adaptation to a contaminated environment. The paradigm of interactions between genes and the environment and the development of a clinical phenotype is shown schematically in Figure 6.3.

Epidemiological studies indicate that about 80% of all cancers are related to environmental factors, and that cancer susceptibility can result from differences in genetic background for metabolism, DNA repair, altered expression of proto-oncogenes and tumor suppressor genes in association with nutritional status (Figure 6.4). The balance between xenobiotic absorption and elimination rates in metabolism are important factors in detoxification and prevention of chemical carcinogenesis. Individual differences in the capability to detoxificate and/or activate xenobiotics have been related to gene polymorphisms in genes of detoxification enzymes and thus differences in chemical susceptibility (Hatagima, 2002).

6.7.1. Gene polymorphism differences in cytochrome P450 phase I and phase II genes

The cytochrome P450 superfamily comprises at least ten known and characterized families and many subfamilies, including enzymes involved in the biotransformation of xenobiotics and the biosynthesis of steroid hormones, biliary acids, fat-soluble vitamins, and fatty acids. Most carcinogenic chemicals are not toxic in themselves but are metabolically activated. Biotransformation involves two phases: phase I which mainly involves the P450 (CYP) family and phase II which is catalyzed by conjugation enzymes such as glutathione S-transferase (GST), UDP-glucuronosyltransferase, and N-acetyltransferase (NAT). Phase I enzymes promote the activation of drugs and pro-carcinogens to reactive compounds, while phase II enzymes generally inactivate the Phase-I induced reactive compounds by conjugation to cofactors transforming them into highly water-soluble and easily secreted compounds in urine or bile.

The balance between expression of phase I and phase II enzymes can be critical for susceptibility to cancer following exposure to carcinogens (Hatagima, 2002; Lampe, 2007). Several polymorphic detoxification enzymes are implicated in cancer risk: CYPs (e.g., CYP1A1, CYP1A2, CYP2A6, CYP2E1); N-acetyltransferases (e.g., NST1, NAT2); microsomal epoxide hydroxylase; catechol *O*-methyltransferase; GSTs (e.g., GSTA1, GSTM1, GSTT1, GSTP1); UDP-glucuronosyltransferases (UGTs, e.g.,UGT1A1, UGT1A6, UGT2B7, UGT2B15), and sulfotransferases (SULT, e.g., SULT1A2) (Lampe, 2007). Based on the occurrence of mutations in P450 genes, and gene deletions and duplications, the human population has been divided into poor (PM), intermediate (IM), efficient (EM), or ultra rapid (UM) drug metabolizers. The PM group lacks the enzyme in question, IM individuals are often heterozygous for a gene defect, EM individuals are homozygous for a non-defect gene with effective enzyme activity and UM individuals have either a genotype with high efficient enzyme

Table 6·4. Major polymorphic variants of cytochrome P450 and their allele frequencies (adapted from Ingelman-Sundberg, 2005).

Enzyme	Number of functional variants [a]	Major variant	Mutation	Consequence	Allele frequency [b]	
					Caucasians	Orientals
CYP2A6	16	*CYP2A6*2*	L160H	Inactive enzyme	1 – 3	0
		*CYP2A6*4*	Gene deletion	No enzyme	1	15
CYP2C9	12	*CYP2C9*2*	R144C	Reduced affinity for P450 reductase	8 – 13	0
		*CYP2C9*3*	I1359L	Altered substrate specificity	7 – 9	2 – 3
CYP2C19	16	*CYP2C19'2*	*Aber. splice* site	Inactive enzyme	13	23 – 32
		CYP2C19'3	Stop codon	Inactive enzyme	0	6 – 10
CYP2D6	46	*CYP2D6*2xn*	Gene duplication	Increased activity	1 – 5	0 – 2
		*CYP2D6*4*	Defect splicing	Inactive enzyme	12 – 21	1
		*CYP2D6*5*	Gene deletion	No enzyme	4 – 6	6
		*CYP2D6*10*	P36S, S486T	Unstable enzyme	1 – 2	50
		*CYP2D6*17*	T107I, R296C, S486T	Reduced affinity for substrates	0	In blacks
CYP2E1	2	*CYP2E1*2*	R76H	Less enzyme expressed	0	1
		*CYP2E1*3*	V389I	No effects	< 1	0
		*CYP2E1*4*	V179I	No effects	< 1	nd
CYP3A4	19	Only very rare variants with no major functional effects				

nd: not determined

[a] The number of variant alleles is as shown at the Human CYP allele Nomenclature Web site (http://www.imm.ki.se/cypalleles) and includes only those with separate allelic numbers; [b] the allele frequencies are from many different studies provided, partly summarized by Ingelman-Sundberg et al. (1999).

Table 6·5. Classic studies of ethnic differences in the frequency of deletions of GSTT1. Source: adapted from Bolt and Their (2006).

Country / region	GSTT1 carriers (*GSTT1*1*), %	GSTT1 non-carriers (*GSTT1*0*), %
East Asia (Korea, China)	38	62
China (Shanghai)	51	49
USA (whites)	80	20
USA (African American)	78	22
USA (Mexican American)	90	10
Germany	75	25
Turkey	80	20
Scandinavia	85	15

activity and/or multiple gene copies of a single allele (Ingelman-Sundberg, 2004, 2005).

Inter-ethnic differences are a genetic drift that can be caused by migration of populations with a specific genotype and might also involve genetic selection. Some major inter-ethnic polymorphic variants of P450 enzymes and *GST* alleles are shown in Tables 6.3 and 6.4, and inter-ethnic differences in Tables 6.5 and 6.6, respectively. In particular, *GST1-1* is relevant for deactivation of carcinogenic intermediates of polycyclic hydrocarbons. Evidence suggests that *GST1-1* and/or *GSTM1-1* play a role in the deactivation of reactive oxygen species involved in cellular processes of inflammation, ageing and degenerative diseases. *GSTM-1* and *GSTT1-1* are genetically deleted (non-functional alleles *GSTM1*0* and *GSTT1*0*) in a high percentage of the human population, with major ethnic differences (Table 6.6). The combination of *GSTM1*0* with genetic traits of *CYP1A1* and *GSTP1* may predispose the respiratory and digestive tracts (and the lungs especially in smokers)

Table 6·6. Allele frequencies of *GSTT1*0* and *GSTM1*0* in different ethnic groups. Source: adapted from Bolt and Their (2006).

Allele	Ethnicity	Frequency	Homozygous (mean and range)
*GSTM1*0*	Caucasians	10514	0.531 (0.42 – 0.60)
	Asians	1511	0.529 (0.42 – 0.54)
	Africans	479	0.267 (0.16 – 0.36)
*GSTT1*0*	Caucasians	5577	0.197 (0.13 – 0.26)
	Asians	555	0.470 (0.35 – 0.52)
*GSTM1*0* plus *GSTT1*0*	Caucasians	5537	0.104
	Asians	407	0.246

Table 6-7. Ethnic variations in *CYP3A* allele frequencies.

Allele	Chinese, Japanese, %	African-American, %	Caucasian, %
*CYP3A4*1B*	0	35 – 67	2 – 10
*CYP3A5*3*	65 – 85	27 – 50	70 – 90
*CYP3A7*1C*	-	6	3

to a higher risk of cancer, *GSTM1*0* also appears to be associated with bladder cancer, consistent with a *GSTM1* interaction with carcinogenic tobacco smoke constituents (Bolt and Thier, 2006). Extensive reviews have been published on gene polymorphism in ethnic groups for enzymes involved in xenobiotic metabolism including in selected cancer sites, and for some genes this differs between Asians and Inuit, and Caucasians (Hatagima, 2002; Dorne, 2004; Gresner et al., 2007). This is the case for *CYP2E1* and *CYP2C9* (Table 6.3) where the Inuit genotype for the latter indicates no or few poor metabolizers among the population (Gaedigk, 2000; Gaedigk et al., 2001).

The human CYP3A subfamily plays a more dominant role in the metabolic elimination of drugs and carcinogens than for any other biotransformation enzyme localized in the liver and small intestine. Inter-individual differences in enzyme expression may be due to several factors, including variable control mechanisms, disease state, up- and down-regulation by environmental stimuli (smoking, drug intake, diet), and genetic mutations. Unlike other P450 enzymes such as CYP2D6 and CYP2C19 there is no evidence of a null allele for *CYP3A4*, but more than 30 single nucleotide polymorphisms have been identified in the gene (reviewed by Lamba et al., 2002). In the coding region less than 5% of the allele frequencies are found and they are not likely to contribute to the differences in clearance by the CYP3A4 inter-individually. Most variants are found in the gene regulating 5′-flanking region, an A-392-G transition with ethnic allele differences (Table 6.7). This allele has been linked to various diseases, such as prostate cancer, leukemia, and early puberty. CYP3A5, an extrahepatic CYP3A isoform is suggested to be implicated in disease risk, the metabolism of endogenous steroids or xenobiotics, and is polymorphic with ethnic variations in allele frequencies (Table 6.7) where the *CYP3A5*3* allele confers low protein expression and catalytic activity. An allele of the major fetal liver CYP3A enzyme *CYP3A7*1C* showed increased gene transcription (Lamba et al., 2002).

In summary, gene polymorphism in metabolizing enzymes may influence susceptibility to environmental carcinogens, thus affecting the risk of cancer (Hatagima, 2002; Lampe, 2007).

6.7.2. POPs, gene polymorphism, hormone metabolism, and health risks

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 among 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

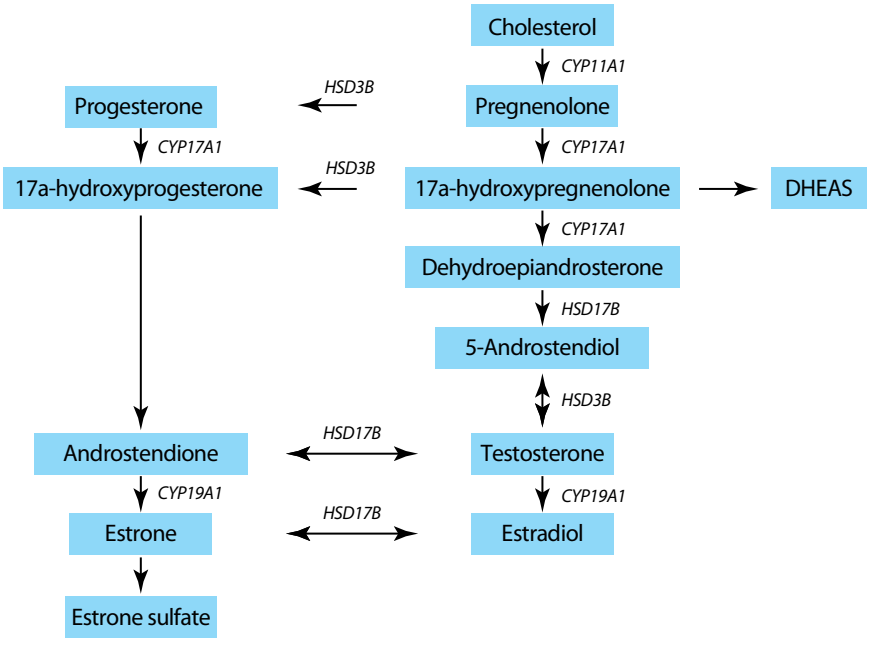


Figure 6-5. Schematic illustration of the pathways of steroid hormone biosynthesis. Source: adapted from Olson et al. (2007).

may result in genetic dysfunction. Mutations in genes inherited or induced by environmental factors, may thus result in reproductive effects, birth defects, and cancer (Nei and Saitou, 1986).

Polymorphism in the genes involved in the maintenance of the endogenous hormonal balance, such as estrogen biosynthesis (e.g., *CYP17* and *CYP19*) (Figure 6.5) and estrogen metabolism (e.g., *CYP1A1*, *CYP1A2*, *CYP1B1* (Table 6.3), and catechol-*O*-methyltransferase (COMT)) may affect the synthesis and degradation of estrogens and so may possibly result in adverse health effects. Elucidating whether genotype influences steroid hormone state can aid the understanding of hormonally-mediated conditions.

Examples of interactions between exposure to environmental contaminants and gene polymorphism and increasing susceptibility to adverse health are described for *CYP1A1*, *CYP1A2* and *CYP1B1*, *COMT*, *CYP17*, and *CYP19*.

CYP1A1 encodes aryl hydrocarbon hydrolase (AHH), an enzyme involved in the production of reactive epoxide intermediates from polycyclic aromatic hydrocarbons (PAHs), steroid hormones, and other aromatic compounds (Crofts et al., 1994). On the basis of this model, individuals with higher *CYP1A1* activity would be at increased risk of breast cancer when exposed to high levels of PCBs. Exposure to PCB and the risk of breast cancer were reported to be linked to the M2 and M3 polymorphism of the *CYP1A1* gene (Box 6.4) (Li et al., 2005a). The *M3* polymorphic *CYP1A1* gene combined with high PCB levels was found to result in a three-fold risk of postmenopausal breast cancer, compared to women with two wild-type alleles and low levels of PCB (Negri et al., 2003). For the *M2 CYP1A1* gene polymorphism Ile/Ile vs. Val/Ile (heterogeneous), Val/Val (mut), the latter two are known to be associated with breast cancer risk in Caucasians with high PCB body burdens (adjusted Odds Ratio 2.9) (Moysich et al., 1999).

A recent study showed that 80% of 65 Greenlandic Inuit tested had the *Val/Ile* or *Val/Val* genotype in contrast to Europeans tested in parallel where only 17% had the *Val/Val* or *Val/Ile* genotype (Bonefeld-Jorgensen, E.C., Centre of Arctic Environmental Medicine, University of Aarhus, unpubl., 2008). The incidence of breast cancer in Greenlandic women is much lower than in Danish women. However, the frequency of diagnosed breast cancers in Greenland has been increasing since the mid-1980s. Whether this is due to better screening and diagnostic capabilities and/or to the predominant *CYP1A1* 'mutant/heterogeneous' gene polymorphism found in Inuit awaits the outcome of further studies.

CYP1A2 and CYP1B1 enzymes are involved in the metabolic activation of several carcinogens, including aromatic and heterocyclic amines, nitroaromatic compounds, mycotoxins and estrogens, and individual differences in CYP1A2 and CYP1B1 activity may influence individual susceptibility to cancer. As a generalization, slow and intermediate CYP1A2 metabolizers represent about 50% of Caucasians, while their frequency in Japanese subjects seems to be much lower. Increased risk of colon cancer and bladder cancer in subjects with the rapid 2 activity was suggested, and a higher level of 4-aminobiphenyl-hemoglobin adducts was found in moderate smokers with the rapid CYP1A2 phenotype than in subjects with slow activity (Landi et al., 1999). Moreover, *CYP1A1* and *CYP1B1* gene polymorphisms may modify the relation between environmental exposure to POPs and advanced endometriosis risk (Tsuchiya et al., 2007). In addition, for the dioxin-exposed Seveso subjects the *CYP1B1*3* variant was linked to an increase in eczema and urticaria 20 years after the exposure (Landi et al., 2005). Studies have suggested a possible interaction between environmental exposure (e.g., waste incinerators, agriculture products for farming) and a *CYP1B1* polymorphism (valine to leucine, codon 432) with change in catalytic activity increasing breast cancer risk (Saintot et al., 2004) and meta analyses suggested an increased breast cancer risk for Caucasian but not Asian women (Paracchini et al., 2007).

Sixty-five Greenlandic Inuit were genotyped for this *CYP1B1* polymorphism and results showed that 75% had the variant leucine polymorphism compared to 22% to 34% for the Europeans tested (Eva C. Bonefeld-Jørgensen, Centre of Arctic Environmental Medicine, Aarhus University, unpubl., 2008). Future studies might elucidate whether this *CYP1B1* polymorphism also affects the risk of breast cancer in Inuit.

The *COMT* gene is involved in Phase II metabolic inactivation for catechol estrogens, and polymorphism in the *COMT* gene, which codes for a low activity variant of the COMT enzyme, is associated with increased risk of developing breast cancer. For the COMT polymorphism, the *COMT-L* allele is associated with increased breast cancer risk in premenopausal women, but decreased

Box 6·4. *CYP1A1* polymorphism

CYP1A1 encodes aryl hydrocarbon hydrolase (AHH), an enzyme involved in the production of reactive epoxide intermediates that can increase the risk of oxidative stress and cancer. Several polymorphisms have been identified in CYP1A1, some of which lead to more highly inducible AHH activity (Crofts et al., 1994). *CYP1A1* polymorphisms include *M1* (T→C substitution at nucleotide 3801 in the 3'-noncoding region), *M2* (A→G substitution at nucleotide 2455 leading to an amino acid change of isoleucine to valine at codon 462), *M3* (T→C substitution at nucleotide 3205 in the 3'-noncoding region), and *M4* (C→A substitution at nucleotide 2453 leading to an amino acid change of threonine to asparagine at codon 461). Studies of CYP1A1 in cultured human lymphocytes showed significantly elevated levels of inducible enzyme activity among individuals with *M2* genotypes. Crofts et al. (1994) reported that *M2* alleles were associated with increased *CYP1A1* inducibility at the mRNA level, and a three-fold elevation in AHH enzyme activity. The *M1* allele also encodes an inducible form of *CYP1A1* (reviewed by Li et al., 2005a).

risk in postmenopausal women (Miyoshi and Noguchi, 2003). *In vitro* data have shown that COMT activity is protective against oxidative DNA damage. Dioxin-induced E2 metabolism and oxidative DNA damage is inhibited by COMT but not when the COMT was inhibited, suggesting that the low activity variant of COMT can increase the risk of oxidative DNA damage. The data also suggest that in breast tissue of women with low COMT activity, an increase in oxidative DNA damage mediated through the estrogen catechols may be a contributory factor in the development of breast cancer (Lavigne et al., 2001).

Many chemicals of environmental relevance (e.g., atrazine, roundup, 4-octylphenol, diethylstilbestrol) are shown, *in vivo* in aquatic species and *in vitro* in human cell lines, to affect adrenocortical function involving enzymes in the steroidogenic pathway, such as CYP17 and CYP19 (Figure 6.5) (Majdic et al., 1996; Harvey and Everett., 2003). TCDD affects normal Sertoli cell function (Lai et al., 2005). Using various human cell lines and rats, TCDD, dioxin-like (e.g., CB126) and non-dioxin-like PCBs (such as CB28 and CB105), PCB mixtures, pesticides (e.g., toxaphenes) and PCB metabolites have been shown to affect testicular androgenesis in rats (Andric et al., 2000, 2003), to act as CYP19/aromatase inhibitors (Drenth et al., 1998; Woodhouse and Cooke, 2004; Heneweer et al., 2005), and a TCDD-induced inhibition of CYP17 causing a decrease in estradiol production in human luteinized granulosa cells (Moran et al., 2003).

Box 6·5. *CYP17* polymorphism

A single T to C base substitution at position 1931 creates an additional Sp-1-type (CCACC box) promoter motif 34 bp upstream from the site of initiation of translation in the variant allele *A2*.

Studies indicate that this polymorphism increases enzyme activity resulting in increased serum estrogen and progesterone levels in pre-menopausal women and oestrone and dehydroepiandrosterone in postmenopausal women. The urine ratio of 2-OHE:16αOHE was lowest in women with the *CYP17A2/A2* genotype. Although based on controversial data, the *CYP17A2/A2* genotype has been reported to be associated with breast cancer in women and men.

In men, the promoter variant *CYP17* is associated with testosterone levels 20% or higher in men with the C/C compared with the T/T genotype, whereas heterozygous men had intermediate hormone levels (p = 0.019). Men with the C/C genotype were also nearly 3 cm taller (Zmuda et al., 2001).

The *CYP17*A2* allele has also been linked with prostate hyperplasia (Azzouzi et al., 2002), a recent meta-analysis suggested that the *CYP17* polymorphism is unlikely to increase the risk of sporadic prostate cancer (Ntais et al., 2003). The *CYP17*A2* allele has also been linked with osteoporosis in postmenopausal women (Somner et al., 2004). No data were found concerning *CYP17* polymorphism and testis development and/or sperm quality/fertility.

Box 6·6. *CYP19* polymorphism

In *CYP19*, a tetranucleotide (TTTA) simple tandem repeat polymorphism, which varies from 7 to 13 repeats in intron 4, and additional 3bp deletion in the 7-repeats allele, were investigated and found to be associated with breast cancer and prostate cancer (Miyoshi and Noguchi, 2003; Ntais et al., 2003). Moreover, a polymorphism at codon 264 (Arg to Cys; a C to T substitution in exon 7) was also reported to be associated with breast cancer and prostate cancer. The TTTA polymorphism at lower numbers (< 9 repeats) has also been reported to be associated with lower estradiol levels and lower bone mass density and increased risk of osteoporosis in women and men (Gennari et al., 2004).

The CYP17 gene encodes the P450c 17α enzyme primarily expressed in ovary of women and the adrenal cortex. The enzyme is involved in the biosynthesis of androgens/estrogen from cholesterol (Figure 6.5). The *CYP17* gene product is involved in steroidogenesis in mammal fetal testis and its enzyme activity is down-regulated by endocrine disrupters (e.g., phthalates) resulting in reduced production of testosterone (Lehmann et al., 2004). Gene polymorphism causing increased enzyme activity (Box 6.5) has been linked to breast cancer (Setiawan et al., 2007), prostate hyperplasia (Azzouzi et al., 2002), and osteoporosis in postmenopausal women (Somner et al., 2004).

The CYP19 gene encodes the aromatase enzyme (Figure 6.5) converting C-19 androgens to estrogens. Aromatase is present in ovary, testis, prostate, placenta, brain, and peripheral adipose tissues (the main source of estrogens in postmenopausal women) (Miyoshi et al., 2003; Ntais et al., 2003). In breast cancer patients aromatase plays an important role in intra-tumoral biosynthesis of estrogens.

Inactivating mutation of the aromatase gene was reported to elicit increased luteinizing hormone, follicle-stimulating hormone and testosterone levels and to elicit undetectable estradiol levels, and decreased sperm count and viability (Rochira et al., 2001). Two different polymorphisms were found to be associated with breast cancer and prostate cancer (Box 6.6).

There are several reports on the effect of endocrine disrupters on *CYP19* gene expression and/or aromatase activity (Cheshenko et al., 2008), such as for bisphenol-A and nonylphenols (Bonefeld-Jorgensen et al., 2007), PCBs (Hany et al., 1999; Woodhouse and Cooke, 2004; Wojtowicz et al., 2005; Xu et al., 2006; Li, 2007), methyl sulfonyl PCB metabolites (Heneweer et al., 2005), TCDD and CB126 (Drenth et al., 1998), and brominated flame retardants and brominated dioxins (Ding et al., 2007).

Thus, environmental contaminants have the potential to alter the gene and gene activities playing a role in sex hormone processes, and polymorphisms in the genes involved modulate the activity of the related enzymes in the steroid hormone biosynthesis. Future studies are needed to explore whether gene-environmental contaminant interaction plays a role in sex hormone processes in the Arctic populations including Inuit.

Box 6·7. Epigenetics

A noteworthy example regarding epigenetic roles in fetal development includes the intake of folic acid during pregnancy. Folic acid prevents neural-tube defects by enhancing the transfer of methyl groups to DNA methyl transferases responsible for methylation of CpG motifs, and also prevents the risk of a reduced pool of progenitor cells in the fetal forebrain (Hilakivi-Clarke and de Assis, 2006). Furthermore, in mice: (1) coat color association with metabolic defects (obesity, hyperinsulinemia, and shorter life span) could be reversed by maternal intake of a methyl-supplemented diet resulting in increased methylation of CpG motifs in a retrotransposon, and (2) epigenetic mechanisms were involved in the increased risk of prostate carcinogenesis upon exposure to endocrine disrupters (bisphenol A and estradiol). Maternal exposure to the synthetic estrogen di-ethyl-distilbestrol, another endocrine disrupter, was related in both animals and humans to increased uterine, breast and multi-generational cancer; hypomethylation of CpG causing persistent expression in uterine genes (*c-fos, lactoferrin*) and histone modification of the permanent *Hoxa-11* gene expression was suggested to play an important role in epigenetic mechanisms (Hilakivi-Clarke and de Assis, 2006).

6.8. Epigenetics: a new paradigm in toxicology and teratology

Aberrant fetal and child development and the risk of cancer may result from inherited mutations in the germ line, from changes in DNA sequences arising in somatic tissues during life, and from aberrations of genomic DNA methylation including hyper- and hypomethylation of genes (e.g., increased or inhibited transfer of methyl groups via methyltransferases to CpG motifs) (Box 6.7).

Epigenetics is a phenomenon that can be hereditary without any change in the primary DNA sequence, but is due to changing controls of gene activities. Such controls arise from the interplay of DNA methylation, histone modifications, and RNA-mediated pathways. Epigenetic regulation is a part of normal development and differentiation; however, this can be misdirected causing a number of diseases including cancer and metabolic disorder (Table 6.8) (see also Chapter 7 and 8).

Table 6·8. Epigenetic modifications in the genome during fetal development. Source: adapted from Hilakivi-Clarke and de Assis (2006).

Modification	Consequences
Hypermethylation of CpG sites	Loss of gene expression
Hypomethylation of genomic DNA	Gene over-expression
Modifications of histones	Activation and inactivation of chromatin
Imprinting	Mono-allelic expression of genes
Loss of imprinting	Bi-allelic expression of genes
RNA interference	Inactivation of chromatin

Exposure *in utero* or early in life to dietary and environmental factors can have a profound effect on the epigenetic code, the epigenome, resulting in birth defects and diseases later in life (Reamon-Buettner and Borlak, 2007).

There are increasing examples of effects from environmental exposures that can be attributed to epigenetic causes and the research challenge is to evaluate and understand the contribution of epigenetic influences of environmental exposures. PCBs and PBBs are effective promoters in two-stage cancer models, which implies that epigenetic mechanisms are involved (Jensen et al., 1982; Safe, 1989; Silberhorn et al., 1990; van der Plas et al., 2000). There are several indications that both coplanar as well as non-coplanar PCBs are involved in epigenetic mechanisms and can act as tumor promoters. The coplanar PCBs mediate their toxicity via the AHR, resulting in adverse effects such as liver damage, thymus atrophy, skin lesions, a wasting syndrome, and tumor promotion (Van den Berg et al., 1998). In contrast, the non-coplanar PCBs do not significantly activate the AHR and exhibit a different spectrum of toxic actions such as modulation of steroid hormones and intracellular Ca^{2+} signaling, being linked to oxidative stress, metabolic disorder (see Chapter 7 and 8), neurotoxicity, immunotoxicity, endocrine disruption and tumor promotion (Hansen, 1998; Brouwer et al., 1999; Bonefeld-Jorgensen et al., 2001; Robertson and Hansen, 2001; Dean et al., 2002). Thus the data imply that nongenotoxic but epigenetic mechanisms are involved in their carcinogenic potential. The exact modes of action of non-coplanar PCBs are still unclear. However, the accepted toxic equivalency factors approach (see Chapter 8, Box 8.3) is based exclusively on AHR-mediated toxicity data, whereas in this system the more prevalent non-coplanar PCBs have zero toxic potency (Van den Berg et al., 1998), despite their known toxicity (also Chapter 7, section 7.3.1.1).

Mutation in the *BRCA1* gene is responsible for ovarian cancer and for about 50% of familial breast cancer, but mutation cannot explain the incidence of sporadic breast cancers. However, several studies have reported that *BRACA1* was epigenetically silenced by hypermethylation in breast and ovarian primary tumors and cell lines (Jacinto and Esteller, 2007). The potential of non-coplanar PCBs (CBs 138, 180, 153) to interfere with expression of the tumor suppressor gene *BRCA1* (that pays an important role in cell-cycle control, DNA repair and genomic stability) without any sign of cell toxicity suggests that epigenetic mechanisms might be involved (Rattenborg et al., 2002). Machala et al. (2003) reported that non-coplanar PCBs, but not coplanar PCBs, were potent inhibitors of gap junctional intracellular communication, which belong to a critical epigenetic event in tumor promotion.

Also, non-cytotoxic/genotoxic but epigenetic mechanisms were suggested for the potential of the environmental contaminant γ-HCH (lindane) to

induce increases in micronuclei and factors critical for cell survival (Bcl-2, Bax, $P21^{waf1/Cip1}$) in breast and prostate cells at low doses (Kalantzi et al., 2004).

Many regulatory regions (promoters) of genes encoding proteins that are involved in critical cellular processes and/or have tumor suppressor functions have been identified to be hypermethylated in prostate tumors, resulting in inactivation and gene silencing (Li et al., 2004). Epigenetic mechanisms were found to affect the expression of two members of the dioxin-AHR inducible cytochrome *P*450 *CYP* supergene family, *CYP1A1* and *CYP1B1* (Table 6.3) in human prostate cancer: inactivation by hypermethylation was demonstrated for the *CYP1A1* gene (Okino et al., 2006), whereas the *CYP1B1* gene was reported to be hypomethylated and over-expressed (Tokizane et al., 2005). Both genes encode an enzyme that metabolizes PAHs and contributes to both their detoxification and, paradoxically, their bioactivation into toxic and mutagenic intermediates, and aberrant expression of the genes may play an important role in prostate cancer. Although the mechanisms controlling the tissue-specific and cancer-specific expression of *CYP1B1* are not known it is found over-expressed in a variety of human tumor cells such as in lung, breast, liver, gastrointestinal tract, and ovarian cancer and seems to have a potentially crucial role in tumor development and progression. Moreover, the AHR, having relevant functions in cell proliferation, is silenced by gene-promoter epigenetic hypermethylation in human lymphoblastic leukemia (Mulero-Navarro et al., 2006) and rat hepatoma cells (Gudas and Hankinson, 1987).

A recent study of the relationship between plasma POPs concentrations and global DNA methylation in DNA of 70 Greenlandic Inuit has shown that global hypomethylation increased with increasing blood plasma levels of many of the POPs investigated (Rusiecki et al., 2008). Global hypomethyltion due to impaired DNA-methyltransferase activity has been related to multiple malignancies in mice (Gaudet et al., 2003). Moreover, reduced levels of CpG sequence methylation globally have been found in many cancer cells and pre-malignant adenomas (Feinberg and Tycko, 2004). Studies of larger populations are needed for further evaluation of the relationship between POPs exposure and epigenetic effects on gene expressions and human health risks.

Although there has been considerable progress in the definition of critical windows for programming cardiovascular and metabolic outcomes in the rat, there is still a lack of detailed information on such critical windows for programming in humans. Perturbations of the intrauterine environment have major effects. The nature of the epigenetic, structural, and functional adaptive responses which result in a permanent programming of cardiovascular and metabolic function, and the role of the interaction between the pre- and postnatal environment in determining final health outcomes, has been reviewed extensively by McMillen and Robinson (2005).

6.9. The immune system and POPs

Environmental contaminants can induce immune dysfunctions (Silkworth and Loose, 1981). Dioxins, dioxin-like PCBs and PAHs suppress the immune system and children exposed to synthetic estrogens *in utero* show altered immune function (Carpenter et al., 1998), and both synthetic and natural estrogens suppress the immune system (Kendall et al., 1992). The AHR is a key mediator of toxic effects induced by a number of organic pollutants. AHR ligands such as dioxins and dioxin-like PCBs can activate inflammatory reactions by multiple mechanisms, for example, by activation of the nuclear factor κB (NF-κB) and proinflammatory cytokines that in turn (e.g., tumor necrosis factor, TNF-α) suppress the expression of *CYP1A1*, probably due to a mutual inhibitory interaction between the signal pathway of AHR and NF-κB (reviewed by Umannova et al., 2007). TNF and interleukine (cytokine) IL-1β are important mediators of dioxin toxicity in rodents (Taylor et al., 1992; Fan et al., 1997) and maturation of the immune system is especially vulnerable to POPs during pre-and/or postnatal life (Bonefeld-Jorgensen and Ayotte, 2003).

6.9.1. Gene frequencies and immunoglobulins in Inuit

Inuit wandered and settled along the north coast of America arriving in Greenland approximately 2000 BC (Figure 6.2). Different cultures succeeded each other. The Inugsuk culture was the origin of the present Greenlandic population. Today 27% of the West Greenland gene pool is estimated to be of European origin (Lamm et al., 1992), whereas East Greenland was first visited by Europeans in 1884 and stayed isolated until after the Second World War. The East Greenland gene pool is thus considered closest to that of the original Inugsuk Inuit.

The discovery by Hirsfeld and Hirsfeld (1919; cited by Allan, 1963) that the ABO blood group allele frequencies vary among different populations opened the door to potential genetic analyses. Moreover, the human leukocyte antigen system (HLA) and the antibody gammaglobulin (GM) were concluded to be useful systems for characterizing populations based on the number of haplotypes specific to populations (Callegari-Jacques et al., 1993). Studies of the ABO blood group system, the HLA and Gm allotypes supported the hypotheses of Asian ancestry for the Arctic Inuit populations, the historical isolation of East Greenland, and gene drifting (Box 6.8).

6.9.2. Genotype-phenotypes related to the cytokine system (atopy and allergy)

The frequency of bronchial asthma was found to be much lower for Greenlandic Inuit than Danes (Table 6.2). Studies in Alaska also indicate a lower asthma risk for rural Natives than urban residents (Gessner, 2003; Gessner and Neeno, 2005; Martinez and Weiss, 2006).

Box 6·8. The ABO blood group system and the human leukocyte antigen system in Inuit

The ABO blood group system

The antigens of A, B, and H of the *ABO* blood group system are found as alcohol-soluble substances on the red blood cell membrane and are also secreted by mucous glands in water-soluble glycoprotein in various body fluids, including saliva. The non-secretors status of the ABH blood group substances is associated with pathological conditions of mucous membranes, particularly with duodenal ulcer and gastric (pre)malignancies and probably also with pulmonary dysfunction. A high frequency of non-secretors is found among Icelanders. Like many other Arctic populations of the Mongolian race the Greenlandic Inuit also have a low frequency of non-secretors (Eriksson et al., 1986).

The human leukocyte antigen system

Serological human leukocyte antigen (HLA) tissue typing and gene frequencies were determined in Tasiilaq (Ammassalik, East Greenland) and compared to other populations by Welinder et al. (2000). The genomic data confirmed the serological estimates. In contrast to other Greenlandic populations the Tasiilaq Inuit are genetically homogenous with little ad-mixture with Europeans. Moreover, their pattern of alleles indicates close genetic relationships with other Inuit. Similar frequencies of serological data were obtained with high frequencies of HLA-A24, B40 (B61), Cw3, DR4 and DQ3 (DQ7) with the exception of B27 which is rare in East Greenland Inuit. The frequencies for B62 (B15) and B48 are unusual for Native Americans and are not an admixture with Scandinavians having low frequencies of the two antigens. The data confirm the historical isolation of East Greenland, and genetic drift has been suggested as a plausible explanation (Welinder et al., 2000).

Gamma globulin allotypes

Populations and family studies of gamma globulin (*Gm*) allotypes have demonstrated a large amount of intra-and inter-population polymorphism as well as 'en bloc' transmission of specific allotypic combinations (haplotypes). Moreover, genes linked to the Gm system may influence immune responsiveness and disease susceptibility. The *Gm* (and *IgA*) alleles among Caucasians, black peoples and Asians have been reported to differ (Vyas and Fudenberg, 1969). Callegari-Jacques et al. (1993) reported the Gm haplotype distribution in 60 groups including Inuit, North, Central and South American Indians (22 808 individuals in total), and provided detailed insight into the observed differences. The *Gm* allotypes of humans are inherited differences located on the heavy chains of immunoglobulin G (IgG). The *Gm* results revealed clear differences among North, Central and South American Indian populations. The two haplotypes mainly responsible for these differences are *GM*axg* and *Gm*abOst*. Comparison of the Gm haplotypes for Amerindians and Inuit, showed that Inuit differed distinctly from the other groups. Because the Gm system is involved in immune responses, the variability observed may be related to unknown selective pressures and might also cause differences between the groups with respect to immune responses.

Whether these differences are due to genetics or lifestyle differences awaits further research based on the current knowledge of atopy and allergy.

Most 'single-gene' diseases following the Mendelian pattern of inheritance (e.g., cystic fibrosis and sickle cell disease) are rare and first signs are evident in childhood. In common multifactoral diseases, what is inherited is a higher risk of developing the disease through a complex interaction between susceptible genes and environmental risk factors making the event more or less likely (Figure 6.3). The pathologic event is influenced by genetic modifiers such as cytokines.

Cytokines are intracellular signal molecules that coordinate inflammatory responses to injury including interleukins, tumor necrosis factors, interferons and hematopoietic growth factors (Duff, 2006). Inflammatory responses are involved in attack on pathogens and repairing injured tissues but inflammation also plays an important role in many chronic diseases, such as rheumatoid arthritis, asthma, psoriasis, ulcerative colitis, postmenopausal osteoporosis, hypertension, obesity and Alzheimer disease (reviewed by Duff, 2006).

At least ten members of the IL-1 cytokine family are known to be involved in acute inflammatory and autoimmune responses. Three pro-inflammatory genes have been well characterized, *IL-1α* and *IL-1β* and the anti-inflammatory IL1 receptor antagonist (*IL-1Ra*). There is some evidence that *IL-1* polymorphism affects gene expression and that this might influence chronic diseases.

Rheumatoid arthritis is a multifactorial inflammatory disease with some familiar clustering linked to the histocompatibility complex HLA-DRB1 and there is evidence for linkage of several markers in the *IL-1* gene cluster in a subset of rheumatoid arthritis patients heterozygous for HLA-DRB1. Polymorphisms of the *IL-1* gene cluster have also been linked with cholesterol levels and increased risk of coronary disease (Box 6.9).

Box 6·9. The *IL-1* gene cluster and risk of coronary diseases

Odds ratios (OR) in patients for risk of coronary occlusion associated with cholesterol (1.74), lipoprotein(a) (2.55), smoking (3.92), and *IL-1B* allele homozygous for a common *IL-1* gene polymorphism (*IL-1B(-511)*) allele 2, had an OR of 3.88 being almost as high as for smoking (reviewed by Duff, 2006). Stratifying patients according to total cholesterol the *IL-1* genotype had no effect on the OR at concentrations < 200 mg/dL, whereas for patients with concentrations > 239 mg/dL the OR increased from 2.7 to 5.9 for patients homozygous for *IL-1B(-511)* allele 1 and *ILB-1B(-511)* allele 2, respectively. A similar pattern was observed for LDL cholesterol.

An intermediate frequency of *IL-1β(-511)* for Chinese (50%) compared to Caucasian (35%) and African (69%) populations was reported by Jin et al. (2003). Rheumatoid arthritis is relatively rare in Inuit, whether this is related to genetics or nutrients (e.g., n-3 fatty acids) awaits further studies because no reports on *IL-1β* genotypes for Inuit were found in the literature.

The *IL-4RA* polymorphism has been identified in Greenlandic Inuit (Khoo et al., 2006). Atopy is characterized by increased IgE production in response to common allergens and is strongly associated with asthma and rhinitis. The *IL-R* receptor α gene is a candidate gene that might be involved in the pathogenesis of atopy. Khoo et al. (2006) evaluated whether *IL-4RA* polymorphisms (Ala57Thr and Ile50val) were associated with atopy in 1295 Inuit (living in Denmark or Greenland) in parallel with 1329 individuals from seven populations with different global locations. The novel *IL4RA Ala57Thr* (Thr57) polymorphism was common (33%) in the Inuit but rare (< 0.6%) in all other populations. In Inuit living in Denmark, the *Thr57* allele and the Ile50/Thr57 haplotype were associated with a lower risk of atopy, with similar trends observed for atopic rhinitis and atopic asthma. In Inuit living in Greenland, the *Thr57* allele was not associated with atopy or atopic diseases, but Ile50 was weakly associated with a lower risk of atopy. Thus, a full investigation of genotype-phenotype relationships in a given population can only be achieved if each gene is screened for novel polymorphisms in that population.

The pro-inflammatory interleukine-6 (*IL-6*) gene is another gene which differs among ethnic groups. A polymorphism (G/C) within the regulatory promoter region (-174) of the gene alters the expression of this cytokine. The fraction of individuals having the GG genotype is generally 80% to 100% in non-Caucasian populations and 30% to 45% in Caucasian populations. The *-174G* genotype has been set in relation to colorectal and breast cancer and an increased incidence of type II diabetes mellitus in Native Americans. However, the exact mechanisms are still unknown (Berger, 2004).

6.10. Gene polymorphism related to fatty acid metabolism

Apolipoprotein E (apoE protein; *APOE* gene) plays a central role in lipid metabolism as ligand for two cell-surface lipoprotein vectors mediating cellular uptake of specific lipoproteins, intermediate-density lipoprotein (IDL) and chylomicron remnants. Three common alleles *E*2*, *E*3*, and *E*4* have quantitative effects on lipid and lipoprotein levels, that are risk determinants in cardiovascular diseases. The *APOE*2* allele is associated with lower total cholesterol and low-density lipoproteins (LDL), but higher HDL levels. In contrast, the *APOE*4* allele is linked to opposite effects and has been associated with Alzheimer disease in several populations (reviewed by Demarchi et al., 2005). *APOE* polymorphism was reported for several populations living at subtropical latitudes such as indigenous Americans of Argentina, Brazil and Paraguay, and indigenous populations from South America, North America, Greenland and Siberia. The incidence of the most common *APOE*3* allele ranged from 0.78 to 0.98 (mean for all Inuit 0.78), and the incidence of the *APOE*4* allele ranged from 0.00 to 0.17 (mean for all Inuit 0.21). The rare allele *APOE*2* was found in 18 out of 52 study groups investigated, with allele frequency ranging from 0.00 to 0.05, and found in four out of five studied Inuit groups with a mean frequency of 0.012. The *APOE*2* allele increased its frequency with latitude in South America, and a random distribution in the northern hemisphere with some indication of higher frequency in Inuit and Asians suggesting the possibility of selection. The *APOE*3* and *APOE*4* allele frequencies, respectively, present positive and negative associations with latitude, although were most pronounced in the northern hemisphere (Demarchi et al., 2005).

A study of 42 female and 56 male Greenlandic Inuit showed that the apoE, derived from the observed frequencies of the six common apolipoprotein E genotypes, are *E2*: 0.015 ± 0.009; *E3*: 0.776 ± 0.030; and *E4*: 0.209 ± 0.029. *E2* alleles are very rare (0.015), and *E4* alleles (0.21) are slightly more frequent in the Greenlandic Inuit population than in other populations. No significant associations were found between *apoE* genotypes and the extent of atherosclerotic lesions, nor was any strong evidence found for an association between serum lipids, glycohemoglobin levels or adiposity measurements and *apoE* genotype in Greenlandic Inuit (Boudreau et al., 1999).

The paraoxonase gene family consists of three genes, *PON1, PON2* and *PON3*, where the gene product of *PON1* serum paraoxonase is associated with HDL particles, probably via Apo Al. In serum it functions as esterase towards organophosphate insecticides and *in vitro* as an antioxidant that can destroy oxidized LDL that can participate in arthrosclerosis. Moreover, arachidonic acid derivatives at LDL phospholipids are substrates for paraoxonase. In contrast, the products of *PON2* and *PON3* are unknown (reviewed by Fanella et al., 2000). A common variation in the *PON1* gene (at codons M55 and M192) is linked to atherosclerosis and lipoprotein metabolism. In two Canadian aboriginal populations, Oji-Cree and Inuit, the following was observed for *PON1 M55* carriers vs. non-carriers: diabetic Oji-Cree had higher plasma triglyceride concentrations than non-carriers, whereas for non-diabetic Oji-Cree and Inuit higher total and LDL cholesterol, and for the former also apo B, were found for carriers. The results suggest that the common *PON1 M55* variation is associated with traits in plasma lipoprotein metabolism in aboriginal Canadians (Hansen and Gilman, 2005), and a link to methyl mercury has been shown (see also Chapter 7).

The carnitine palmitoyltransferase 1A (CPT1A) protein catalyses the transversion of long-chain acyl-CoA into acylcarnitines and enables the transport of long-chain fatty acids from the cytosol to the inner mitochondria for β-oxidation. Genetic deficiency of *CPT1A* is rare and less than 30 clinically identified

cases of *CPT1A* have been reported. The CPT1A deficiency, occurring early in life, has hypoglycemia and no end-product of hepatic fatty-acid oxidation, ketones, in the urine. The *CPT1A 1436(C-T)* mutation was first determined in an Inuit male and later in 13 other cases in Canadian First Nations and Inuit populations. This mutation has been demonstrated to be resistant to malonyl-CoA inhibition and might result in unregulated fatty acid oxidation (Park et al., 2006). Several haplotypes of an *Alu* insertion in the 3'untranslated region of the LDL-receptor gene have been determined (Heller et al., 2004). Almost all (93%) the variability occurs at the intra-population level, but the greatest intra-group differentiation (6% to 8%) was found in grouped Native Americans plus Siberian Inuit and Chukchi, compared to Asians. This result is compatible with earlier mtDNA and Y-chromosome suggestions of a single origin for the first colonizers of the American continent.

6.10.1. Genetic determinants of cardiovascular diseases and diabetes and risk factors

Ischemic stroke in persons of European decent has a genetic basis. A systematic literature-based review (500 manuscripts, 12 883 cases, 19 548 controls) to evaluate whether the stroke susceptibility genes are the same in non-Europeans (Chinese, Japanese and Koreans) was performed by comparative genetic analyses across different ethnic groups (Ariyaratnam et al., 2007). Of the eight candidate genes three were associated with ischemic stroke: the angiotensin I converting enzymes (ACE) insertion/deletion polymorphism, the *ACE- C677T* variant of 5,10-methylenetetrahydrofolate reductase (MTHFR), and the *APOE* gene. Comparing the Asian groups with the individuals of European descent suggested that genetic associations studied to date for ischemic stroke are similar for Europeans and non-Europeans. However, due to the limited number of gene variants studies and fewer individuals in the non-European group the existence of differential effects by ethnicity cannot be excluded (Ariyaratnam et al., 2007).

Risks of cardiovascular disease for Greenlandic Inuit are low from a genetic point of view. The potentially high risk alleles of apolipoproteins, fibrinogen, factor V, glycoprotein IIIa and factor VII (FVII) have different frequencies in Inuit compared to Caucasian populations. Analyses of genetic polymorphism of tissue-type plasminogen activator (*t-PA*), plasminogen activator inhibitor-1 (*PAI-1*), angiotensin-converting enzyme (*ACE*), and angiotensinogen showed that the polymorphism frequencies were significantly different to those for Caucasians, and were in accordance with a low risk of cardiovascular disease in Inuit. In contrast, the levels of plasma fibrinogen and D-Dimer were higher in Inuit than Danes, PAI-1 was lower and FVII, t- PA and CRP levels were comparable (de Maat et al., 1999). Thus, genetic background and risk factors clearly differ between Inuit and Danes (Caucasians).

Box 6.10. PPAR vs AHR

TCDD (mediated via the AhR) strongly inhibits adipogenesis. In mammals, TCDD causes a redistribution of triglycerides from adipose tissue to the liver and diabetic characteristics including reduced glucose uptake. In adipose tissue, TCDD lowers the activity of a series of adipogenic genes (Potter et al., 1986; Brodie et al., 1996). Primary and immortalized mouse embryo fibroblasts both require PPARγ agonists to induce adipogenesis and this response is suppressed by TCDD. These findings implicate the AhR as a constitutive inhibitor of triglyceride synthesis, and as an early regulator of adipocyte differentiation. AhR interference with cell-cycle arrest in differentiation may be linked to the increased rate of senescence (Alexander et al., 1998).

6.10.1.1. Gene polymorphism and risk of diabetes type II

Non-optimal fetal growth leading to small-for-gestation-age body size compensated after birth is associated with risk of diabetes type II. However, extensive research for underlying genetic factors has not succeeded and very little has been reported for Arctic populations.

The peroxisome proliferator-activated receptors (PPARs) are members of the nuclear-receptor super-family and include three family members, PPARα, PPARβ/δ, and PPARγ (see Chapter 7). Ligands for the PPAR family tend to be fatty acids or metabolites, including prostaglandins, and interaction with these receptors regulates the transcription of specific genes. Although expression of PPARs can be observed in a variety of cell types, PPARγ seems to have a more preferential expression, and in particular, is expressed in adipocytes and myeloid cells that include dendritic cells, macrophages, and eosinophils, as well as T cells. The identification of PPARγ receptors in several different cell types of the immune system has prompted the investigation of PPARγ as an immune-system regulator (Standiford et al., 2005). Studies in mice have indicated that adipogenesis requires PPARγ agonists and that this response is suppressed by TCDD, implicating the AhR as a constitutive inhibitor of triglyceride synthesis, and as an early regulator of adipocyte differentiation (Alexander et al., 1998) (Box 6.10).

A recent study of 15 846 individuals born in Helsinki (Finland) showed a polymorphism in the *PPAR-γ 2* gene (*Pro12Pro* and *Pro12Ala*) that depended on body size at birth. Individuals with small body size and the *Pro12Ala* genotype were protected against insulin resistance and type II diabetes later in life (Eriksson, 2007). These findings reflect gene-early environment interactions and can be attributed to the phenomenon of developmental plasticity.

6.11. Vitamin D polymorphism and genetic adaptation of Inuit children to a low-calcium diet

Allelic variation in the vitamin D receptor genotype was reported to influence bone turnover, where the *b* allele was associated with higher bone density (Morrison et al., 1994). In Chinese and Thai individuals the *bb* is a dominant genotype and is believed to be an adaptive event due to its association with more efficient intestinal calcium absorption to compensate for low calcium intake (Beaven et al., 1996; Ongphiphadhanakul et al., 1997), thus maintaining eucalcemia and mineralization of their bones. In a study of ten healthy Inuit children (5 to 17 years of age) the *bb vitamin D* genotype (8 out of 10) was predominant and dietary calcium absorption appeared to be more efficient in individuals with the *bb* genotype, with increased hypercalciuria. The authors suggested a genetic adaptation to dietary constraint, but wondered whether it might predispose to nephrolithiasis or nephrocalcinosis if standard nutritional guidelines are followed (Sellers et al., 2003).

In Greenlandic Inuit women there is some evidence that organochlorine exposure is related to osteoporosis, but whether exposure to dioxin-like compounds might be linked to decreased bone quality and osteoporosis merits further attention (Cote et al., 2006).

6.12. Allelic distribution of human sex hormone receptors and the AHR

6.12.1. Aryl hydrocarbon receptor gene

The aryl hydrocarbons (including dioxin-like compounds) mediate their biological effects via the AHR upon binding to the receptor, translocation from the cell cytoplasm into the nucleus, dimerization with the Ah-nuclear translocator protein and then binding to the AHR-responsive DNA sequences (AHREs or DRE) located in the 5'-flanking region of several genes, including genes responsive to dioxin-like compounds (Kawajiri and Fujii-Kuriyama, 2007). Relative to the rodent counterpart (*AhR*), the human *AHR* gene appears to be highly conserved. Four variations in the coding sequence of the human *AHR* were found (Box 6.11). Whether the different combinations of *AHR* polymorphisms might affect susceptibility to carcinogens needs further research. Ethnic variability in the *AHR* gene (Table 6.9) indicates that Caucasians and Inuit have similar *AHR* polymorphism and differ relative to Japanese and African populations.

Box 6·11. *AHR* gene variation in humans

Four variations in the coding sequence of the human *AHR* were found: one in exon 2 being silent and the others in exon 10 in codon 554 changing arginine (Arg_{554}) to lysine (Lys_{554}) (Wong et al., 2001a), in codon 570 ($valine_{570}$ to $isoleucine_{570}$) and in codon 571 ($proline_{571}$ to $serine_{571}$) (Wong et al., 2001b). Controversial data for the aryl hydrocarbon hydroxylase (AHH) inducibility in lymphocytes was found for the Arg_{554} to Lys_{554} variation; Kawajiri et al., 1995 found no effect, whereas Daly et al., 1998 reported significant increased capacity for *CYP1A1* induction. However, when combining the Ile570 + Lys554 this variant failed to support TCDD-dependent induction of *CYP1A1* expression in cell culture (Wong et al., 2001b). These polymorphisms seem not to be related to any phenotypic toxicity if they occur independently.

6.12.2. The estrogen receptor and the androgen receptor

The endocrine axis comprises the hypothalamic gonadotropin-releasing hormone (GnRH), pituitary gonadotropins, and gonadal steroid hormones. The gonadotropins act at the gonads, the ovaries in females and testes in male, stimulating gonadal maturation, gametogenesis and steroidogenesis (Dickerson and Gore, 2007). The sex steroid receptors such as the estrogen receptor α (ERα) and ERβ and the androgen receptor (AR) belong to the nuclear receptor family and are generally ligand-dependent transcription factors (Fu et al., 2003; Verrijdt et al., 2003; Schwabe

Table 6·9. Allele frequencies of human *AHR* in different ethnic populations. Source: adapted from Wong et al. (2001a,b).

Population	n	Arg_{554}	Lys_{554}	n	Val_{570}	Ile_{570}	Pro_{517}	Ser_{517}
Japanese	227	0.57	0.43	-	-	-	-	-
Ivory Coast Africans	58	0.43	0.57	58	0.93	0.07	0.965	0.035
Mixed African	20	0.47	0.53	20	0.93	0.07	0.95	0.05
Caribbean African	55	0.61	0.39	55	0.97	0.03	1.00	0
North American (mixed)	45	0.89	0.11	45	0.99	0.01	-	-
Canadian Chinese	41	0.68	0.32	41	1.00	0	-	-
Canadian Inuit	22	0.91	0.09	22	1.00	0	-	-
Canadian French	20	0.88	0.12	20	1.00	0	-	-
German	78	0.93	0.07	78	1.00	0	-	-
Native Indian	47	0.86	0.14	-	-	-	-	-

and Teichmann, 2004; Bjornstrom and Sjoberg, 2005). Their genomic-mediated pathways include steps such as binding of ligand to receptor, translocation into nucleus, and binding of the receptor-ligand complex to a specific DNA response element causing a gene response. Androgens and estrogens are not male or female hormones only. Both hormones are important in both sexes and essential for reproductive development, including male fertility (Hess, 2003). The steroid androgen hormones, testosterone and dihydrotestosterone, are necessary for the normal male phenotype and the presence of ERα and ERβ in human fetal testis and epididymis cells indicates that estrogens play a physiological role in regulating spermatogenesis in mammals (Couse et al., 2001; Carreau, 2003; Shapiro et al., 2005). The receptors of testosterone (AR) and estradiol, (ER) are polymorphic.

6.12.3. **The androgen receptor**

The basis for hormonal contraception is the negative feedback that testosterone and its metabolite estradiol (E2) exert on the gonatropins, luteinising hormone-releasing and follicle-stimulating hormone, secretion and thus spermatogenesis. The androgen receptor (*AR*) gene carries a common polyglutamine stretch (CAG repeat) in the peptide coding region exon 1, affecting its function as a transcription factor in activating responsive genes. Androgens play a critical role in prostate development, and polymorphisms to high metabolism and/or response in the 5α-reductase type 2 (*SRD5A2*) and the genetic CAG variation (length) of *AR* has been linked to the risk of prostate cancer (Freedman et al., 2005).

Ethnic differences worldwide in prostate cancer have been observed, the highest rates among the United States, Canada and Scandinavia, and the lowest in China and other parts of Asia (Crawford, 2003). Prostate cancer incidence in Greenland is extremely low (Prener et al., 1996; Dewailly et al., 2003). A study to evaluate a possible link between the low incidence of prostate cancer and the genetic status of the Inuit, compared Greenlandic Inuit and Swedish military conscripts. Results showed that the Greenlanders in addition to having longer CAG repeats also showed a lower and higher frequency of high-activity and low-activity *SRD5A2* genotype, respectively. Thus, being genetically related to Asians in several loci, Greenlanders also seem to have an androgenic genotype partly protecting them from prostate cancer compared to the high risk Swedish men (Giwercman et al., 2008). Further studies among healthy European and Greenlandic men showed that men with a short *AR* CAG repeat length and a high level of CB153 had significant risk for low sperm counts. Thus, the longer *AR-CAG* repeats in Greenlandic Inuit might protect them against adverse effects of POPs on sperm count and prostate cancer (Giwercman et al., 2007, 2008).

6.12.4. **Estrogen receptor α and estrogen receptor β**

Different polymorphisms have been described in both the estrogen receptor α (*ERα*) and estrogen receptor β (*ERβ*) genes. Although a large number of association studies have been performed, the individual contribution of these polymorphisms to the pathogenesis of, for example, osteoporosis remains to be universally confirmed (Gennari et al., 2004).

ERα and ERβ have distinct cellular and tissue distributions (Enmark et al., 1997; Kuiper and Gustafsson, 1997; Nilsson and Gustafsson, 2000), and regulate separate sets of genes (Palmieri et al., 2002; Frasor et al., 2003a,b; Harrington et al., 2003). The expression level of *ERβ* in, for example, mammary cancer fibroblast cells (MCF-7BUS cells) is approximately 100 times lower than for ERα (Vienonen et al., 2003; Grunfeld and Bonefeld-Jorgensen, 2004). It is suggested that ERβ modulates the effects mediated by ERα, and that ERβ has an inhibiting effect on cell proliferation (Dickerson et al., 1999; Pettersson et al., 2000; Lazennec et al., 2001; Cappelletti et al., 2003). However, although many functions of ERβ have been suggested, its role is still controversial (Grunfeld and Bonefeld-Jorgensen, 2004). In particular, ERβ can have opposing effects to ERα in mediating estrogenic action and for some genes, particularly those involved in proliferation, the proliferative response to estradiol is the result of a balance between ERα and ERβ. Functional ERs are usually homodimers, but ERα/ERβ heterodimers have also been described. Importantly, ERβ can inhibit transcriptional activation of *ERα* through formation of these heterodimers, as shown by different *in vitro* and *in vivo* experimental studies. However, in the absence of ERα, ERβ is able to replace some of its activity (Matthews and Gustafsson, 2003; Heldring et al., 2007).

The estrogens are ubiquitous and found in almost all tissues in females and males. They are important factors from the start of life, during fetal development, during sexual development in puberty, and in many physiological and metabolic aspects during adult life. Thus, being multi-functional the estrogens are also critical for possible adverse effects on disturbance of homeostasis, for example by genetic polymorphisms and/or environmental contaminants, the latter often termed 'endocrine disrupters'.

Polymorphisms in the *ER-α* gene have been studied with respect to several diseases, such as breast cancer, dementia, and the effects of estrogen replacement on HDL-cholesterol level in women with coronary diseases and low bone mineral density.

Ethnicity plays a role in risk of breast cancer with the lowest and highest incidence in Asian and Caucasian populations, respectively (Brinton et al., 1997; Lacey et al., 2002). The human *ER-α* exhibits low mutational frequency in breast cancer (Roodi et al., 1995), but allelic variants have been associated with breast cancer in Caucasians and Asians, although at different frequencies (Hsiao et al., 2004). Moreover, ethnic allelic

Box 6·12. Polymorphism in the estrogen receptor *ER-α* gene

Analyses of ER polymorphisms in ER-positive and ER-negative breast cancer patients of the entire coding region for point mutations and deletions/insertions, showed several neutral polymorphisms in the nucleotide codons 10, 87, 243, 325, and 594. No correlations were observed between any of the polymorphic alleles and ER phenotype or clinicopathological parameters, whereas the controversial polymorphism in codon 325 had a strong association with a family history of breast cancer. This implies that mutation in the regulatory sequences influencing the expression of the gene rather than in the coding region of *ER* might play a role in the development of breast cancer (Roodi et al., 1995). Murphy et al. (1997) supported this work by showing the existence of large numbers of ER mRNA variants and mutant ER proteins.

Two polymorphic loci of the *ER-α* gene (the *Pvu II* and *Xba I* locus, 50 bp apart in the non-coding region intron 1) can influence the expression of the gene. Lin et al. (2003) reported that the *ER-α* gene polymorphism was significantly different among Chinese populations and some other ethnic populations including Japanese, and in Caucasians such as Swedes, Italians, and Americans. Moreover, the mutant frequencies of the *ER-α* gene were linked to risk of dementia, especially in females. Differences in the distribution frequency between Asian and Caucasian females were found both at the *Pvu II* and the *Xba I* locus. The Italian and Asian females also differed for the combined genotype. In Chinese women the *PvuII* polymorphism had a very weak association with femoral neck bone mass index whereas *XbaI* polymorphism was unlikely to be a predictor of the femoral neck or spine bone mass index (Wang et al., 2007).

Even though results are still conflicting and the molecular mechanisms by which these polymorphisms influence ER activity remain, in part, to be investigated. Recent studies have linked polymorphism in the *ER-α* gene with estrogen metabolism-related genes:

- beneficial effects of HRT for carriers of the *ER-α Pvu II* polymorphism eliciting osteoprotection and blood lipid changes, and the ER-*α IVS1-401 C/C* genotype have an augmented response to HDL cholesterol upon HRT;
- polymorphism in catechol-O-methyltransferase (*COMT*), *ER-α* , *GST* and *NAT-2* being susceptibility markers in clinical courses of endometriosis risk (Tempfer et al., 2004); and
- for breast cancer ER-/PR-tumors an inverse risk was found for the *CYP1A2*F* allele (Le Marchand et al., 2005), and the combination of *CYP19 (TTTA)7(-3bp)* and *CYP1A1 6235C/T* polymorphisms is associated with an ER-positive, but not an ER-negative, breast cancer risk (Miyoshi et al., 2003).

differences in *ER* have been linked to other changes/diseases such as risk of dementia, femoral neck bone mass index, osteoprotection and blood lipid changes, augmented responses to HDL cholesterol upon hormone replacement therapy (HRT) (Box 6.12).

No reports were found on human studies to evaluate the effect of environmental contaminants on wild-type and variant forms of ERα. However, *in vitro* studies showed for an array of synthetic compounds (e.g., hydroxyl-PCBs, bisphenol-A, p-nonylphenol) and often used estrogenic compounds (e.g., E2, tamoxifen, IC 182,780), that the estrogenic and antiestrogenic activity of structurally diverse synthetic and natural estrogenic compounds is complex, and that this is consistent with published data that often give contradictory results for these compounds (Yoon et al., 2001).

Several polymorphisms of the *ERβ* have been characterized. The functional importance of these variants has not yet been reported (Gennari et al., 2005). Few specific gene-environment interactions have been described for the *ERβ* polymorphisms. *In vitro* studies have linked environmental exposures to effects on both ERα and ERβ. In human breast cancer cells ERα regulated the expression of its heterodimer partner *ERβ*, and the antiestrogen TCDD was shown to inhibit the ERα-mediated induction of *ERβ* (Kietz et al., 2004). Another study showed that dioxin inhibited ERα more than ERβ (Ruegg et al., 2008). A PCB mixture (Arochlor 1221) was reported to decrease the ERβ cells positive cell number in the anteroventral periventral nucleus of the rat brain. Moreover, an array of currently used pesticides showed *in vitro* to counteract the expression of estradiol-induced *ERα* gene expression, whereas several of the pesticides increased the gene expression of *ERβ* (Grunfeld and Bonefeld-Jorgensen, 2004). Also, the metabolite of the methoxychlor pesticides acted oppositely on the two ERs, as agonist and antagonist on ERα and ERβ, respectively (Gaido et al., 2000).

6.13. Conclusions

Selected diversity, diversity not being neutral, can be a consequence of random mutation and natural selection such as adaptations to past environments. Changes in the environment such as chemical contamination or changes in diet might cause health problems for a population. Chemical contamination can cause population reduction via heritable genetic somatic and germ-line mutations initiating a cascade of responses on, for example, reproduction and population genetics. Based on human data and animal studies it can be hypothesized that mutagenic and non-mutagenic (e.g., endocrine disrupting) chemicals can affect the reproductive success of a population and ultimately lead to decreased genetic diversity, extirpation and/or adaptation to a contaminated environment that might be permanent since a population cannot recover to what it was prior to the environmental impact (assuming the absence of gene flow from other populations) – unless the population survives for a very long time.

External influences on the Inuit lifestyle have caused changes in diet and an increase in smoking and alcohol consumption. It might be assumed that traditional food is/was an adaption to life in the Arctic contributing advantages and maybe also to some extent disadvantages with respect to exposure to chemical contaminants and lifestyle changes. Relatively few genetic data are available for indigenous peoples in the Arctic other than the Inuit. Future studies are needed to compare and elucidate the genetic background of other ethnic populations.

Traditional culture and diet have a big impact on the health of Arctic populations, however too little is known about the genetics of these populations to elucidate the implications of contaminant-genetic interactions on health. Because the genetic background of the Inuit differs in some respects compared with Caucasians these genetic differences must be taken into consideration in advice concerning changes in diet and lifestyle.

Genetic studies are a sensitive issue; however, to understand gene-environment interactions in the Arctic this must become a part of future studies on Arctic populations because the genotype may be fundamental to the effects of exposure to environmental contaminants. Therefore, it is important to elucidate genetic polymorphism and possible genetic susceptibility among Arctic peoples. Including genetics in studies which examine lifestyle and contaminant interactions will provide better insight into individual and population vulnerability to contaminants.

Chapter 7

Interactions between Contaminants and Nutrients

Jens C. Hansen, Markku Savolainen, Arja Rautio

Summary

Over the last five decades, increases in the prevalence of obesity and subsequent health problems – metabolic syndrome, diabetes type II, and cardiovascular diseases – have been observed world-wide, including within populations living in the Arctic. These conditions have been regarded as lifestyle-related metabolic disturbances caused by hypercaloric- and misbalanced diets in combination with a sedentary lifestyle. However, it has recently been suggested that exposure to contaminants might also play a role.

The first part of this chapter describes metabolic disturbances in relation to nutritional factors and changes in diet, while the second part describes the degree to which contaminants might interfere with metabolic processes within the body.

Disturbances related to both lifestyle and contaminants are basically mediated by the overproduction of reactive oxygen species, causing oxidative stress within the cells, which is probably the main reason for the interactions observed within the body. It is concluded that contaminants, even at a relatively low exposure level might aggravate lifestyle-induced metabolic disturbances.

As a consequence, it is recommended that future studies on diet and environmental health, include both aspects as integrated and interrelated health determinants. There is also a need for better understanding of the interactions between nutrients and xenobiotic compounds, and the risks should be evaluated to improve the health status of populations living within the Arctic.

7.1. Introduction

This chapter examines the concept that nutrition may modulate the toxicity of environmental pollutants, and vice versa, and is based on the recent review by Hansen et al. (2008). To limit the size of the chapter critical evaluations of the studies quoted have not been included. To the best of knowledge, the most relevant publications have been chosen from the recent literature.

Because the idea that nutrients and contaminants may interact is relatively new, few studies on this topic have been undertaken to date, particularly in the Arctic. However, the unique characteristics of many Arctic diets, which provide both essential nutrients and potentially harmful contaminants ('The Arctic Dilemma'), make the Arctic highly relevant for such studies. Social change and modernization have also increased the prevalence of chronic diseases, such as cardiovascular diseases and diabetes (Bjerregaard and Young, 1998) (for further information see Chapter 3, section 3.1.5). Studies on the interactions between nutrients and contaminants are thus urgently required, and should be able to provide important information about the increasing number of lifestyle-related diseases being reported world-wide, including in the Arctic.

This chapter examines the degree to which environmental contaminants are likely to interact with nutrients and influence the development of metabolic disturbances (for definitions and prevalences of metabolic disturbances see Desroches and Lamarche, 2007), such as obesity, and metabolic syndrome and its co-morbidities: diabetes type II and cardiovascular diseases. These conditions are usually thought to be mainly lifestyle-related; and including an unbalanced diet and lack of physical activity. However, a condition of latent disease may be aggravated by exposure to contaminants. This might occur even at an exposure level which does not in itself give rise to signs of negative effects, but for which the contaminants may in combination with lifestyle-related metabolic disorders act additively and cause a state of clinical disease. Genetic background is also an important factor for the development of obesity and metabolic syndrome (Groop, 2007; Frayling et al., 2007). Figure 7.1 shows the possible interactions between genes, nutrition, and xenobiotic compounds.

The health status of people living in many Arctic regions has changed significantly over the past few decades, and the climate, weather, and environment have played a significant role. Some recent studies have reported possible connections between global pollution and the development of metabolic disorders. For example, Longnecker and Daniels (2001) suggested that the levels of polychlorinated biphenyls (PCBs) in blood and the existence of diabetes might be causally related in pregnant women. They found the mean concentration of PCBs in serum to be 30% higher in diabetics than in non-diabetic

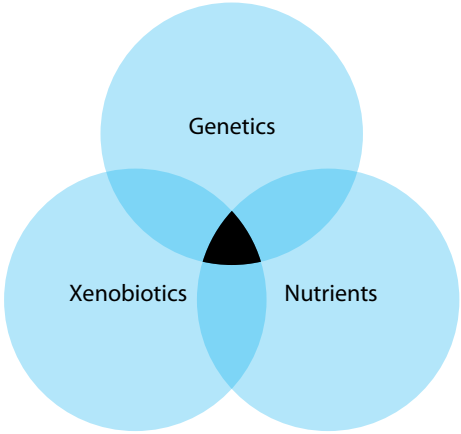


Figure 7.1. Genes, macronutrients, and contaminants may have synergistic effects on the development of diseases. The probability for illness is increased when several pre-disposing factors are simultaneously present in the same individual.

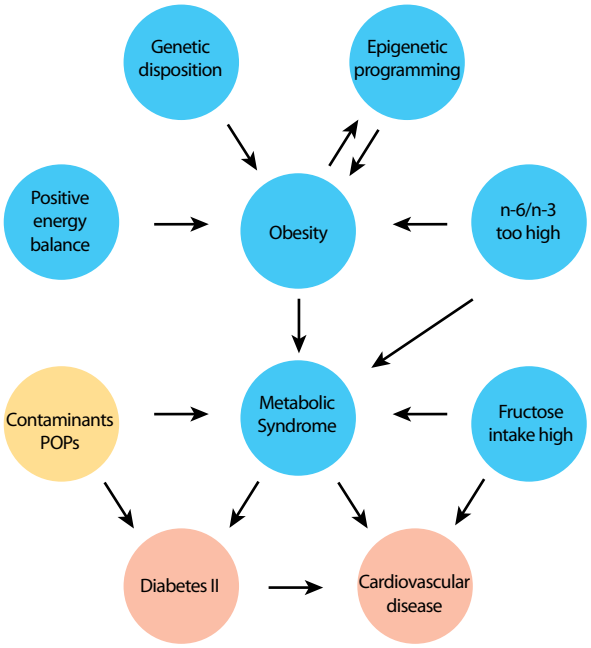


Figure 7.2. Genetic and environmental factors increase in concert the susceptibility of an individual for public health problems such as, type II diabetes and metabolic syndrome. All these conditions may have complications involving the cardiovascular system. Source: adapted from Hansen et al. (2008).

controls, and the correlation between concentrations of PCB in serum and the existence of diabetes to be linear. Another study found that the risk of diabetes seemed to be significantly increased in Belgian subjects in the top decile of adjusted plasma concentrations of dioxins (odds ratio 5.1; 95% confidence interval 1.1 – 21.8), co-planar PCBs (odds ratio 13.3), or Σ12 PCB markers (odds ratio 2.6) (Fierens et al., 2003). Differences were also found between women and men in the Michigan PBB (polybrominated biphenyl) cohort study; at high plasma levels of PCB (> 10 µg/L) an increased incidence of diabetes was found in women, but not in men (Vasiliu et al., 2006). Today, about 80% of the adult Greenlandic population has PCB concentrations in serum of over 10 µg/L, which according to the Michigan PBB cohort study was the limit value for a correlation of diabetes and contaminants. Diabetes is an increasing problem in Greenland (Martinsen et al., 2006). Recent data from Greenland generated under the AMAP human health program indicate a link between lifestyle-related obesity and contaminant levels and an increased risk for development of cardiovascular diseases (Hansen et al., 2008) (see Figure 7.2). There is also some epidemiological evidence for a connection between background exposure to dioxin-like compounds and diabetes (Everett et al., 2007).

7.2. Influence of nutrients

The macronutrients, such as fat, carbohydrates, and proteins serve as the fuel for energy production, but are also active regulators of metabolic processes. This section describes some of the biochemical reactions and actions of fat and carbohydrates in order to help an understanding of the basic mechanisms of their interaction with contaminants. For a more general discussion on macronutrients see Willet (2008).

There is emerging evidence that proteins may also be active in the process of gene expression, but too little is known about this, and there is no information about the possible mechanisms of interaction between proteins and contaminants. This is also the case for micronutrients, trace elements, and vitamins. Only possible interactions between selenium and mercury are discussed.

7.2.1. Fats

The average human fat intake is about 100 g per day in adults, and consists mainly of triglycerides (including glycerolipids). Each molecule of triglyceride contains three fatty acids and a molecule of phospholipids consists of two fatty acids. The molecular weights of each class of glycerolipids are not well-defined; their molecular weight and characteristics depend on the fatty acids. Therefore, it is essential to focus on the nature of fatty acids ingested.

There are three categories of fatty acids: saturated, monounsaturated, and polyunsaturated fatty acids (PUFA), and these each have different effects on the metabolic processes in man. The PUFAs of both fatty acid families (n-6 and n-3) are essential, because the precursor molecules for the long-chained metabolites, linoleic acid (18:2, n-6; LA) and α-linolenic acid (18:3, n-3; ALA) cannot be synthesized in the human body.

Linoleic acid and α-linolenic acid are enzymatically elongated and desaturated (Δ-6 and Δ-5 desaturases) in the human body and form the very long-chained PUFAs. Arachidonic acid (20:4, n-6) is formed from linoleic acid, and eicosapentaenoic acid (20:5, n-3) and docosahexaenoic acid (22:6, n-3) from α-linolenic acid (see Figure 7.3). Arachidonic acid and docosahexaenoic acid are both essential for the development of the central nervous system (see Table 7.1) and retina.

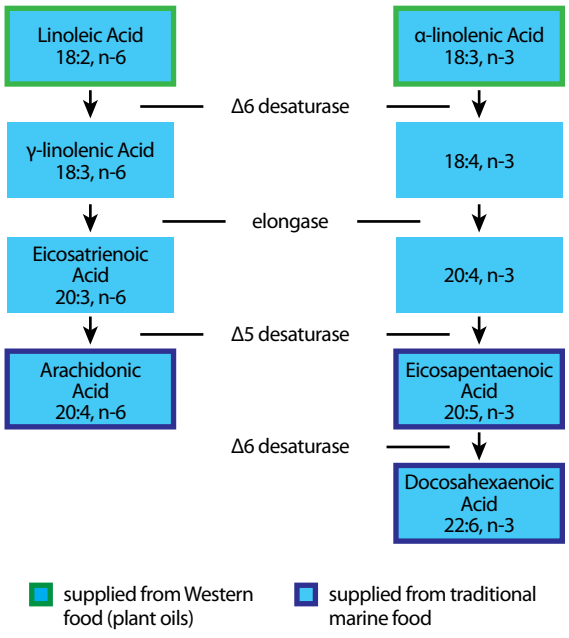


Figure 7.3. Metabolism of polyunsaturated fatty acids.

Table 7.1. Effects of different types of fatty acid.

Effect	PUFA		Saturated fatty acids	Monosaturated fatty acids
	n-6	n-3		
Essentiality [a]	+	+	–	–
Adipogenicity [b]	+	–	+	(+)?
Pro-inflamm.	+	–	+	–
Developments of the CNS	+ (AA)	+ (DHA)	–	–

CNS: central nervous system; AA: arachidonic acid; DHA: docosahexaenoic acid.

[a] essential means that the nutrient must be supplied through the diet; [b] adipogenicity means that the nutrient favors deposition of fat.

Box 7.1. The PPAR system

Peroxisome proliferator activated receptors (PPARs) belong to the superfamily of nuclear steroid hormone receptors. To date, three related PPAR iso-types have been identified: PPAR-α, PPAR-β/δ, and PPAR-γ. PPAR-α is highly expressed in the liver, heart, kidneys, and skeletal muscle, PPAR-γ is primarily expressed in adipose tissue, while PPAR-β/δ is expressed ubiquitously, however, in skeletal muscle to a higher degree than PPAR-α. Activation of all three types causes an anti-inflammatory effect (see Figure 7.4) in adipocytes and induces expression of TNF-α (tumor necrosis factor alpha) and IL-6 (interleukin- 6) (Ajuwon and Spurlock, 2005; Suganami et al., 2005). The balance between physiological levels of PUFAs with pro- and anti-inflammatory the type of fatty acids in diet is very important for their effects in body. Dietary intake of n-3 fatty acids decreases triglyceride concentrations in serum. The effects of n-3 fatty acids on PPAR-α have been studied in genetically modified obese mice (*ob/ob*) and wild-type mice. N-3 fatty acids induce mRNA (messenger ribonucleic acid) of PPAR-α in the wild-type and in *ob/ob* mice, and fish oil has a more potent effect on triglyceride concentrations in serum than eicosapentaenoic acid (20:5, n-3), and in *ob/ob* mice n-3 fatty acids ameliorate obesity-associated symptoms by activation of PPAR-α (Sekiya et al., 2003). Tanaka et al. (2003) have shown that activation of PPAR-β/δ induces β-oxidation of fatty acids in skeletal muscles.

Experimentally, both *in vitro* and *in vivo*, it has been shown that arachidonic acid, the precursor for prostacyclin, is adipogenic, whereas eicosapentaenoic acid and docosahexaenoic acid are not (Massiera et al., 2003, 2006). The effect of arachidonic acid is suggested to act through prostacyclin with a series of ligand-receptor reactions which lead to activation of PPAR-γ2, the master gene of terminal differentiation of preadipocytes to adipocytes (adipogenesis).

In animals, fructose-induced hypertriglyceridemia reduces the hepatic expression of PPAR-α which is down-regulated by the expression of fatty acid oxidation enzymes. This event leads to an up-regulation of sterol regulatory element binding protein, a key transcription factor of regulation fatty acid and cholesterol biosynthesis (Nagai et al., 2002; Yoshikawa et al., 2003). Also, in humans it is found that the significantly decreased levels of uric acid in serum activate synthetic ligands of both PPAR-α and PPAR-γ receptors. This suggests that in humans a high fructose consumption may lead to PPAR-α inhibition (Seber et al., 2006).

The long-chained PUFAs serve as substrates for the formation of a number of local hormones called eicosanoids. These eicosanoids consist of (1) prostaglandins, which are important factors in the regulation of blood coagulation and blood pressure, and (2) leucotrienes, which play an important role in the immune system by regulating pro- and anti-inflammatory processes in the body.

PUFAs and a subset of their eicosanoid metabolites are active in gene transcriptions and serve as ligands for key metabolic regulating systems, such as PPARs (peroxisome proliferator activated receptors). Thus, they play a central role in the balance between deposition and catabolic degradation of fats (for information about the PPAR system see Box 7.1). The effects of various types of fatty acids are shown in Table 7.1.

Adipose tissue is not only a depot of energy, but is also an endocrine organ which produces a number of metabolically active compounds, the so-called adipokines. Some adipokines have anti-inflammatory effects while some have pro-inflammatory effects. The balance between these various effects is influenced by the ratio between dietary intake of n-3 and n-6 fatty acids (see Box 7.2).

Box 7.2. Immunomodulating effects of fat

Several studies have shown that different types of fat have either pro- or anti-inflammatory immunomodulating effects (see Table 7.1). The saturated fatty acids, for example palmitate, but not laureate, activate pro-inflammatory pathways both in myotubes and adipocytes, biochemical markers of those have been described in the epidemiological study (n = 1123, aged 20 – 98 years) by Ferrucci et al. (2006). They concluded that both n-6 and n-3 fatty acids are independently associated with low levels of pro-inflammatory markers (IL-6, IL-IRa, TNF-α, and CRP (interleukin 6, Interleukin-I receptor antagonist, and C-reactive protein) and with high levels of anti-inflammatory markers (IL-10, and TGF-β [interleukin 10 and transforming growth factor beta]). The immunomodulatory effect of PUFAs is influenced by the n-6 : n-3 ratio, and there is a strong negative correlation between the n-6 : n-3 ratio and levels of IL-10, and TGF-β. The importance of the n-6 : n-3 ratio in *ex-vivo* studies shows that linoleic acid (18:2, n-6) can generate oxidative species which can trigger oxidative stress-sensitive pro-inflammatory signaling pathways, whereas n-3 fatty acids have anti-inflammatory effects (Hennig et al. 2002b).

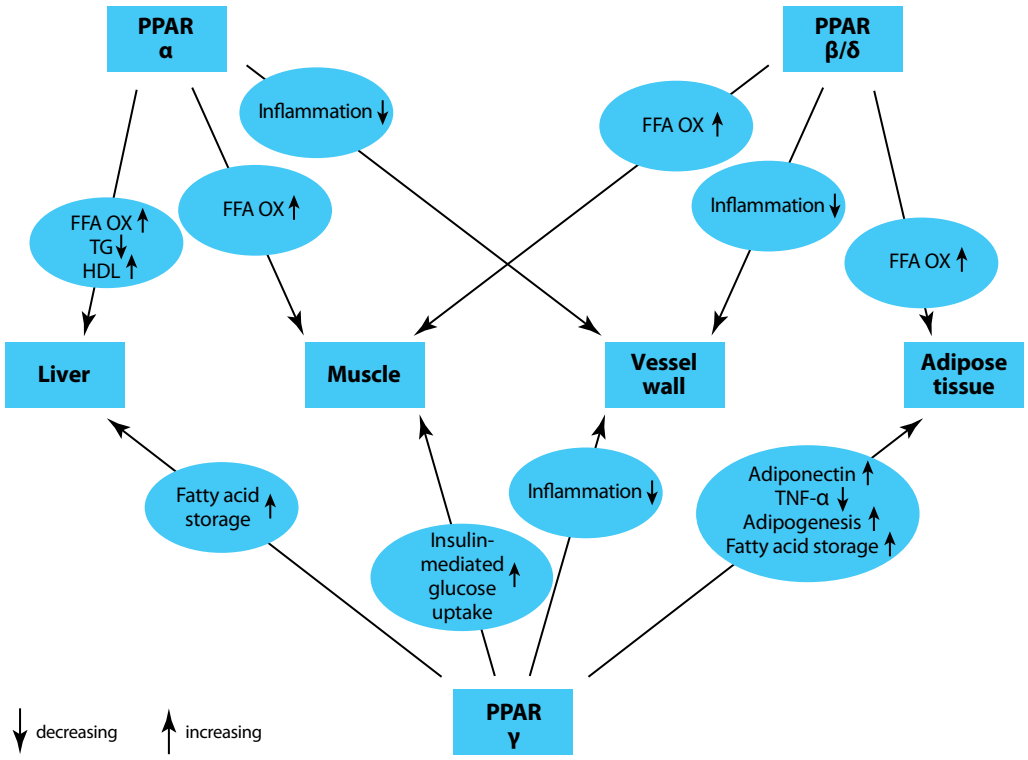


Figure 7·4. Effects of PPAR- α, PPAR-β/δ, and PPAR-γ in various tissues. Source: Hansen et al. (2008).

The dietary intake of n-3 and n-6 fatty acids has been found to be inversely associated with plasma levels of sTNF-α receptors 1 and 2 in men and women (Kang and Weylandt, 2008). These important observations show that physiological levels of fatty acids are able to modulate inflammation, and also that the composition of dietary fat can influence the pathological sequels of obesity (Pischon et al., 2003).

There is also evidence that the hormonal balance is influenced by PUFAs. It has been shown that one metabolite (eicosanoid, PGE2) of arachidonic acid stimulates the formation of estrogens by activating the aromatase (cytochrome-P450, CYP19) (Noble et al., 1997).

Recent studies demonstrate that very low-carbohydrate diets are equal to or even more efficient than low-fat diets in obtaining weight loss (Sondike et al., 2003; Samaha et al., 2003; Brehm et al., 2003). However, the type of dietary fat consumed has substantially different effects on the profile of lipoproteins. Serum cholesterol is raised by saturated fatty acids and the relative content of plasma saturated fatty acids is associated with features of the metabolic syndrome independent of body fat mass (Klein-Platat et al., 2005). In contrast, PUFAs and in particular n-3 PUFAs increase the levels of HDL (high density lipoprotein) cholesterol, decrease levels of triglycerides, and have favorable effects on insulin resistance and inflammation (Samaha, 2005). The linoleic acid (18:2, n-6) content of breast milk measured in the United States increased from 6% to 7% (of total fat in milk) in the early 1950s, to 15% to 16% in the mid-1990s (Ailhaud and Guesnet, 2004). The relative increase in dietary intake of n-6 may be an important causal factor for the globally-observed increasing childhood obesity (Massiera et al., 2003, 2006).

This also indicates that the quality of dietary fat is more important than the energy percentage of total dietary fat. It is recommended that less than 10% of the daily energy intake should be in the form of saturated fat, and 20% to 35% from total fat. The minimum amount of dietary fat for small children is 30% and for adults and children over four years the amount is 25%. This is an increase in the amount of total fat compared to previous recommendations.

7.2.2. Carbohydrates

To prevent metabolic disorders it is now recommended that the intake of refined carbohydrates with a high glycemic index (GI) is reduced by avoiding easily absorbed, high energy sugars, such as glucose. The glycemic index is a measure of individual nutrients that induce glucose load compared to glucose itself (GI for glucose = 100). The glycemic load is the GI multiplied by the amount of nutrients eaten daily.

There have been controversial results about the transformation of glucose to fat through *de novo* lipogenesis (DNL) in man, mainly because appropriate methods to measure DNL have been lacking. As a result, the DNL effect has been largely neglected until recently. Obese individuals with hyperinsulinemia have

significantly higher DNL than normoinsulinemic lean subjects on the same diet (Schwartz et al., 2003). On the other hand, lean subjects on a high carbohydrate diet have a significantly higher DNL than normoinsulinemic lean subjects on a high fat diet, mainly due to high contents of refined sugars on the high carbohydrate diet. Finally, when the refined sugars are below 40% of the total carbohydrate energy, the DNL is minimal (Schwartz et al., 2003).

Fatty acid synthase is the key enzyme of DNL (Wang et al., 2004) and its gene transcription is increased by insulin in humans (Claycombe et al., 1998). For this reason hyperinsulinemic subjects may have a higher activity of DNL than normoinsulinemic subjects. PUFAs, especially those of the n-3 family, attenuate fatty acid synthase expression and decrease lipogenesis (Kim et al., 2003).

In addition to glucose another simple sugar, fructose, is supplied through the diet. It originates from fresh fruit and from sucrose (a disaccharide consisting of one molecule of glucose and one molecule of fructose). Historically, the daily intake of fructose in United States has been estimated at 16 g to 20 g (Elliott et al., 2002). This physiological background intake seems to be advantageous for improving glucose homeostasis (Vaisman et al., 2006). Industrialization of food production during the 20th century has, however, resulted in significant increases, mainly from corn syrup which contains up to 90% fructose, leading to a typical daily consumption of 85 g to 100 g (Basciano et al., 2005).

The correlation between the consumption of refined carbohydrates and the prevalence of diabetes type II in the United States suggests that increasing intakes of refined sugar (corn syrup) together with decreasing intakes of fiber may contribute to the observed upward trend in the prevalence of type II diabetes (Gross et al., 2004). Moreover, a high fructose diet significantly increases fasting glucose (7 ± 2%), triglycerides (79 ± 22%), and DNL (six fold) in humans (Faeh et al., 2005), and thus the high fructose diet increases insulin resistance (McAuley and Mann, 2006). Unlike glucose, which is widely utilized by tissues throughout the body, the metabolism of fructose takes place primarily in the liver. Exposure to large quantities of fructose leads to stimulation of lipogenesis and accumulation of triglycerides, which in turn contributes to reduction of insulin sensitivity and increase of hepatic insulin resistance/glucose intolerance (Basciano et al., 2005). Fructose also increases serum uric acid levels. In human studies, increased serum uric acid has been linked to obesity, dyslipidemia, hypertension, and insulin resistance, all of which are related to cardiovascular diseases (Nakamura et al., 1994) (see Box 7.3).

Box 7.3. Specific effects of fructose

In an *in-vivo* study by Nakagawa et al. (2006) rats were treated with diets containing 60% glucose or 60% fructose. It was found that only the fructose-fed rats developed hyperuricemia, hypertriglyceridemia, and hyperinsulinemia. Treatment with allopurinol, a xanthine oxidase inhibitor which lowers uric acid concentrations in serum, both prevented and reversed features of metabolic syndrome in rats with a fructose-rich diet. These findings suggest a causal effect of increased levels of serum uric acid derived from fructose, resulting in metabolic syndrome in rats (Nakagawa et al., 2006).

Nyby et al. (2007) demonstrated *in vitro* in endothelial cells that the renin-angiotensin system is up-regulated in fructose-fed rats compared to controls. Angiotensin II activates the NADPH oxidase, which in turn activates the uric acid producing xanthine oxidase, both processes produce superoxide anions ($O2^{2-}$) (see Figure 7.5). This explains why fructose-fed rats develop the metabolic syndrome model characterized by hypertension, decreased glucose tolerance, hypertriglyceridemia, and hyperinsulinemia.

Matsubara et al. (2002) reported that leptin concentration in serum is an independent variable for values of uric acid in serum. Thus, the levels of leptin and uric acid in serum would be causally involved in the pathogenic process of metabolic syndrome. However, Bedir et al. (2003) suggested that leptin might be a regulator of serum uric acid in humans because the leptin levels in serum were independently associated with uric acid in both genders, but only in overweight or obese individuals. In contrast to the situation for leptin, there was a reverse relationship between adiponectin and uric acid in serum (Asayama et al., 2003; Böttner et al., 2004; Gilardini et al., 2006). Recently, Mukherjee et al. (2006) suggested that leptin could be a link between obesity and hypertension. However, these findings were not confirmed (Li et al., 2005b; Almeida-Pititto et al., 2006). These observations are all consistent with results reported by Pladevall et al. (2006) who, using confirmatory factor analysis, concluded that metabolic syndrome is likely to be a distinct entity, with evidence that leptin resistance and uric acid play a causative role. However, the authors stressed that further investigations were needed to determine whether the underlying factor is genetic or environmental.

There is a positive correlation between the levels of circulating C-reactive peptide in blood and insulin resistance and development of type II diabetes in healthy women (n = 1999) (Wu et al., 2004). There is also a significant difference between the highest quintile of energy-adjusted fructose intakers ($p = 0.01$) compared to those of the lowest quintile (Wu et al., 2004).

Increased levels of uric acid in serum have been found to be associated with lowered brachial-ankle pulse wave velocity, a surrogate marker of early atherosclerosis (Ishizaka et al., 2007) and increased carotid intima-media thickness, reduced brachial artery flow-mediated dilatation, and increased arterial stiffness in healthy subjects (Erdogan et al., 2005), thus indicating a risk factor for cardiovascular events. Corry and Tuck (2006) concluded in a recent review that there is increasing experimental and clinical evidence about the mechanistic role of uric acid in cardiovascular disease.

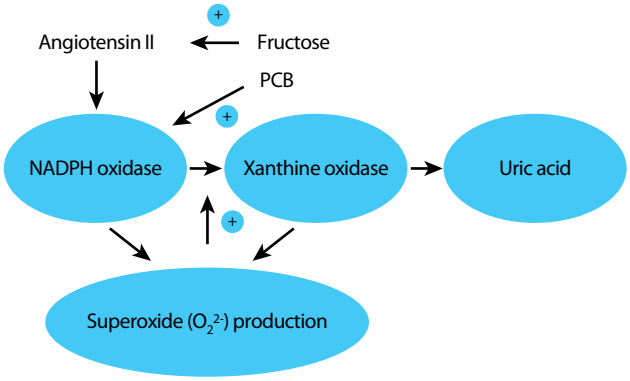


Figure 7-5. Interactions between the uric acid formation pathway and dietary and environmental factors.

7.3. Metabolic disorders and contaminants

The first observations of a possible influence of halogenated organic compounds on increased risk for cardiovascular disease were made at the beginning of the 1980s. Several human studies indicated positive and significant correlations between PCBs and triglyceride concentration in serum both in occupational (Chase et al., 1982; Smith et al., 1982; Hara, 1985) and environmental exposures from local highly polluted areas (Baker et al., 1980; Steinberg et al., 1986; Stehr-Green et al., 1986). Steinberg et al. (1986) found the same correlation between serum concentrations of DDE and triglyceride, and also, that only concentrations of the less-chlorinated PCBs (Aroclor 1242) correlate significantly and negatively with those of HDL-cholesterol. Elevated serum concentrations of triglyceride were also observed among the victims of the poisoning from rice oil contaminated with PCBs and furans that occurred in Japan in 1968 ('Yusho disease') (Hirota et al., 1993). The correlation between serum concentrations of triglyceride and PCBs persisted for 20 to 30 years, although they were relatively close to their normal or low concentrations (Hirota et al., 1993; Masuda, 2001). In these early studies, congener-specific information was not available, but it is known that the Yusho patients were exposed to a mixture of polychlorinated dibenzo-*p*-dioxin / polychlorinated dibenzofurans (PCDD/Fs) and PCBs. Other studies found increased mortality due to cardiovascular diseases in Swedish capacitor manufacturing workers exposed to PCBs for at least five years (Gustavsson and Högstedt, 1997) and in workers after exposure to phenoxy herbicides and PCBs from waste transformer oil (Hay and Tarrel, 1997). Occupational exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) has been related to hypertriglyceridemia (Pelclova et al., 2002). There is also evidence that co-planar PCBs affect thyroid function of newborns during *in utero* exposure (Wang et al., 2005), but the effect seems to be transient (ten Tusscher and Koppe, 2004). Perinatal exposure to background concentrations of dioxins in Europe and the United States was found to cause persistent effects in growth and development of children, including effects on IQ, behavior, hematopoiesis, and lung function (for review see ten Tusscher and Koppe, 2004).

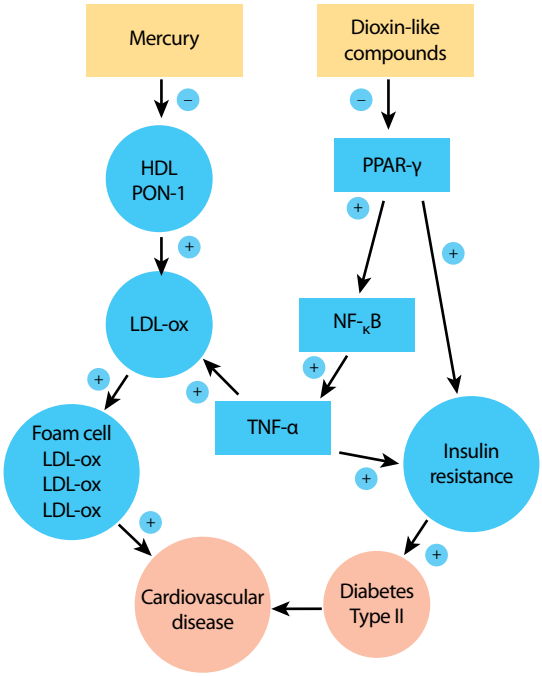


Figure 7-6. Effect of mercury and dioxin-like compounds on the pathogenesis of diabetes and its complications. Source: Hansen et al. (2008).

Cranmer et al. (2000) found that Vietnam veterans exposed to TCDD developed hyperinsulinemia, and later Fujiyoshi et al. (2006) described possible molecular and epidemiological evidence of a diabetogenic effect after TCDD exposure. They suggested that PCBs may lead the lipoprofile in plasma and tissues in an atherogenic direction via lipid metabolism and lipid-dependent cellular signaling pathways. These processes may result in obesity, the main risk factor for metabolic syndrome, type II diabetes, and cardiovascular disease (Hennig et al., 2005) (Figures 7.2 and 7.4). A possible link between dioxin-like compounds and diabetes is that the compounds, which act as AhR (aryl hydrocarbon receptor) agonists, increase the production of TNF-α, a pro-inflammatory cytokine, which in turn reduces the production of PPAR-γ and induces insulin resistance in the body (Remillard and Bunce, 2002) (see Figure 7.6).

7.3.1. Contaminant influence on metabolism

There are several processes related to the development of metabolic disorders where contaminants may play an aggravating role (Figure 7.6). These include, among others, formation of reactive oxygen species, oxidative stress and formation of pro-inflammatory cytokines; modulation of fatty acid metabolism; effects on nuclear receptors; and effects on steroidogenesis.

7.3.1.1. Pro-inflammatory effects

Several persistent contaminants have pro-oxidative properties and so act as pro-inflammatory substances. It has been shown *in vitro* in porcine endothelial cells that the co-planar PCBs 77, 126 and 169 produce oxidative

stress in a dose-dependent manner, where CB126 is the most effective with maximal response at 0.5 μM (Hennig et al., 2002a). This effect is suggested to be mediated through the agonistic action of AhR, and the intact AhR may be necessary for the observed effect of PCBs (Hennig et al., 2002b). Activation of the AhR can be an underlying mechanism of atherosclerosis mediated by certain environmental contaminants. Choi et al. (2003) reported that CB104 is also a potent stimulant of inflammatory mediators in human vascular endothelial cells, mediated through induction of the macrophage activating agent MCP-1 and adhesion molecules. The pro-oxidative action of co-planar PCBs was measured *in vivo* in rats and it was found that CB77 significantly reduced the level of glutathione-peroxydase, the selenium-containing antioxidative enzyme, while the higher halogenated PCBs were inactive (Twaroski et al., 2001).

The formation of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and activity of cyclooxygenase-2 (COX-2) have been suggested to be induced by CB153 in human leukemic mast cell lines (Kwon et al., 2002), however, Hennig et al. (2002a) did not find any effect. The expression of the cytokines is mediated by the activation of NF-κB (nuclear factor kappa-beta). Fadhel et al. (2002) reported that CB153 produces oxidative stress in rats, but suggested that there is a different mechanism of action for the co-planar PCBs. The pro-inflammatory effect of CB153 may, however, be indirect via different pathways. Zhou et al. (2006) demonstrated a mutual repression of both steroid and xenobiotic receptors and the NF-κB signaling pathway. Tabb et al. (2004) showed that the higher-chlorinated PCBs block the action of xenobiotic receptors, and consequently that the NF- κB will be up-regulated leading to the formation of pro-inflammatory cytokines. The authors concluded that there is a link between exposure to xenobiotic compounds and inflammation.

The pro-oxidative effects of co-planar PCBs have been shown *in vitro* and *in vivo*. Dietary flavonoids modulate the PCB-induced oxidative stress in cultures of endothelial cells (Ramadass et al., 2003) and *in vivo* it has been shown that the administration of vitamins E and C concomitantly with PCBs ameliorated the oxidative effects of PCBs (Murugesan et al., 2005).

The experimental evidence that several PCB congeners have pro-oxidative effects (especially the lower-halogenated co-planar compounds), and findings concerning their pro-inflammatory properties, are well supported. However, the evidence in human studies is not so clear. There was a decrease in the release of TNF-α after an addition of CB77 and CB126 in concentrations of 50 and 500 ng/mL in human blood (Ahne and Jarre, 2002). In agreement with these results, Bilrha et al. (2003) found an inverse correlation in cord blood between TNF-α secretion and concentrations of PCBs, *p,p'*-DDE and hexachlorobenzene (HCB) in *ex-vivo* phytohemoagglutinin stimulated cord-blood mononuclear cells. The samples were collected from the unexposed controls and from the population exposed to organochlorines and methylmercury via food. Bélanger et al. (2006) concluded in a study on adult Canadian Inuit that the contaminated traditional diet does not seem to have direct oxidative effects. Nevertheless, they reported that the levels of oxidized low-density lipoprotein (LDL) in plasma predict PCB concentrations ($p = 0.006$) even if the plasma levels of oxidized-LDL were low. This indicates that there is an oxidative load of PCBs which is partially counteracted by the n-3 fatty acids that were found to be positively correlated with the contaminant level in serum. There is no immediate explanation for the discrepancies between the data obtained in *in vitro* animal and human studies; they may partly be explained by differences in experimental study designs, methodologies, congeners tested (either individually or in mixtures), and exposure concentrations. Also, the concomitant intake of n-3 fatty acids could, through their antioxidative properties, counteract the contaminant effect.

A long lasting pro-oxidative effect of contaminants is seen in the Yusho victims (Shimizu et al., 2003). More than 30 years after the accidental poisoning, Shimizu et al. (2003) found lower serum concentrations of copper-zinc superoxide dismutase (SOD), and higher manganese-SOD in victims compared to concentrations measured in age-matched controls, indicating an imbalance of redox-regulation mechanisms.

While the immunotoxicity of the co-planar PCBs is well documented, the effects of the higher-chlorinated PCBs have received less attention. The non-coplanar PCBs 138, 153, and 180, but not 169, have been found to suppress leukocyte phagocytosis *in vitro* in human cells (Levin et al., 2005). The authors suggest an AhR-independent pathway through which the most abundant non-coplanar PCBs modulate phagocytosis, the immune system's first line of defense, and thus possibly will increase susceptibility to infectious diseases. They also found that this effect could not be predicted by either the toxic-equivalence (TEQ) approach or a mouse model. This undermines the use of these traditional methods in risk assessments of mixtures containing non-coplanar congeners, because exposure to a mixture of compounds will always be the case in human exposure situations.

However, in recent studies reviewed by Fonnum et al. (2006) it has been shown that *ortho*-substituted PCBs and some brominated flame retardants stimulate elevation of intracellular calcium. Disruption of calcium homeostasis leads to formation of reactive oxygen species and activation of the nicotinamide adenine dinucleotide (NADPH oxidase) complex. NADPH oxidase catalyzes reduction of oxygen to the superoxide radical (O_2^{2-}), which may be converted to hydrogen peroxide (H_2O_2) and peroxynitrite ($OONO^-$). These powerful oxidants will in turn activate xanthine oxidase, which catalyzes the formation of uric acid (Figure 7.5). Dieldrin has been shown to have the same effects in murine microglia cells (Mao et al., 2007). These findings shed new light on the observations made by Levin et al. (2005). The authors found that the *ortho*-substituted PCBs act in another, non-AhR dependent way compared to the co-planar congeners. It was also suggested that the *ortho*-substituted congeners modify phagocytosis by inducing respiratory

burst in human granulocytes (Voie et al., 1998), because the effect of chronic oxidative stress on phagocytic cells generally means that the cells are less active in killing micro-organisms (Fonnum et al., 2006).

It has also been shown that angiotensin II activates NADPH oxidase (Landmesser et al., 2007). In the patients with coronary disease treated with losartan (an AT1 blocker) the endothelium-bound xanthine oxidase was found to be reduced. Thus, there is a theoretical link between exposure to persistent organic pollutants (POPs) and elevated serum uric acid concentrations in humans (see also section 7.3.1.5 and Figure 7.5).

Methylmercury has also been suggested to have pro-oxidative properties involving calcium homeostasis (Hansen and Danscher, 1997). This has been supported experimentally by Gassó et al. (2001) who found, in cultured rat cerebellar granule cells, that disruption of redox equilibrium and Ca^{2+} homeostasis contribute equally to $HgCl_2$ toxicity, whereas oxidative stress is the main cause of methylmercury neurotoxicity. Because PCBs and methylmercury originate from the same dietary sources, they may have an additive effect (supported in studies by Bemis and Seegal, 1999; Voie and Fonnum, 2000; and Roegge and Schantz, 2006).

Because nutrient imbalances (e.g., a high n-6 : n-3 ratio) and xenobiotic compounds exert pro-inflammatory effects in a combined intake, as is characteristic for a Western diet, an additive effect can be anticipated (Figure 7.6).

7.3.1.2. **Effects on fat metabolism**

There seems to be ample epidemiological evidence that PCBs, especially the co-planar congeners, modulate fatty acid metabolism resulting in increased serum levels of triglyceride (reviewed by Hansen et al., 2008). The exact mechanisms are not yet known, but one suggestion is that PCBs inhibit Δ-6, and Δ-5 desaturases (Matasusue et al., 1999). As a consequence, the conversion of linoleic acid (18:2; n-6) to arachidonic acid (20:4; n-6) will be inhibited and linoleic acid will be allowed to accumulate. This is supported by Grandjean and Weihe (2003) who found in the Faroese birth cohort that increased PCB exposure is associated with a modest decrease in the concentrations of arachidonic acid, both in maternal and cord serum. In a cohort from Greenland (n = 353) the linoleic acid : arachidonic acid ratio was found to be negatively associated with serum PCB concentrations. The dietary intake of linoleic acid originates from the Western part of the diet while arachidonic acid is supplied through the traditional part of the diet, mainly through meat from marine mammals (see Figure 7.3). Thus the serum arachidonic acid concentration is positively correlated to the concentration of PCBs. As a consequence, both a low linoleic acid : arachidonic acid ratio and a high PCB concentration in serum are positively related to the amount of traditional food regularly consumed, and the correlation does not provide information on a possible effect on the desaturases. However, when the linoleic acid : eicosatrienoic acid ratio is used there is a significant positive correlation with PCB exposure, which indicates an inhibition of Δ6 desaturase (see Figure 7.3) (Deutch, B., pers. comm., 2008). Eicosatrienoic acid (20:3; n-6) is a metabolite of linoleic acid after elongation and Δ-6 desaturation and for that reason is related to the intake of linoleic acid and not to the proportion of traditional food eaten.

Hennig et al. (2002a) have shown experimentally that both linoleic acid and CB77 – and more markedly when applied in combination – can generate reactive oxidative species which trigger pro-inflammatory signaling pathways under formation of pro-inflammatory cytokines, which in turn promote the formation of triglycerides. The authors suggest an inhibitory effect of PCBs on PPAR-α; if this can be confirmed it would explain the pro-inflammatory effects as well as the triglyceride-increasing effect of PCBs (Hennig et al., 2005). In conclusion, a clear interaction seems to exist between diet, especially fat, and cellular functions of cytokines induced by PCBs.

7.3.1.3. **Influence on nuclear receptors**

AhR is a ligand-activated transcription factor that mediates a spectrum of toxic and biological effects of dioxins and dioxin-like compounds. Activation of AhR inhibits PPAR-γ (Alexander et al., 1998), leading to decreases in adipocyte differentiation and regulation of glucose homeostasis. Exposure to dioxin and dioxin-like compounds has thus been linked to development of diabetes type II. Experimentally, it has been demonstrated that dioxin, in an AhR-dependent manner, induces insulin growth factor binding protein in human hepatocytes and this may contribute to the disruptive effects of dioxin on glucose homeostasis (Marchand et al., 2005). Due to a lack of longitudinal studies it is still unclear whether background exposures to dioxin-like compounds are associated with increased risk of diabetes (Arisawa et al., 2005).

As well as inhibition of PPAR-γ and activation of AhR, dioxin-like compounds also have an inhibitory effect on PPAR-α (Shaban et al., 2004). AhR agonists down-regulate the PPAR-α induced expression of CYP2B and CYP3A, while both activated receptors down-regulate expression of CYP2C11 in an additive way (Shaban et al., 2005). CYP2B, CYP3A, and CYP2C11 act as testosterone hydrolases (You, 2004). Thus, dioxin-like compounds may also have an effect on sex hormone balance beside the negative interaction with the estrogen receptor (see also Chapter 8, section 8.3 and Box 7.4).

In rodents, both CYP2B and CYP3A are, via the constitutive androstane receptor and the pregnane-X-receptor, readily induced by a variety of environmental contaminants such as DDE, some PCBs (You et al., 1999) and polybrominated diphenylethers (PBDEs) (Sanders et al., 2005). Beside the induction of CYP enzymes, the constitutive androstane receptor and the pregnane-X-receptor also induce detoxification enzymes and will in this way play a role in protection against toxic effects of contaminants. Tabb et al. (2004) demonstrated that in humans, contrary to rodents, the higher-chlorinated PCBs inhibit the steroid and xenobiotic receptor (the human ortholog to the rodent pregnane-X-receptor) and

Box 7·4. CYP enzymes

The cytochromes P450 (CYP enzymes) are a superfamily of heme-containing mono-oxygenase enzymes, of which over 2700 individual members are currently known to exist in nature (Lewis, 2004). Human CYPs are located intracellular in the endoplasmic reticulum (microsomes) in almost all tissues. However, the most important tissues for the metabolism of xenobiotic compounds (e.g., drugs and chemicals) are the liver and intestine. CYPs are divided into families according to their degree of similarity in the amino acid sequence (> 40% identical, e.g., CYP1 family), subfamilies (> 55% identical, e.g., CYP1A subfamily), and individual enzymes with unique sequence (e.g., CYP1A1 enzyme). Currently there are 18 known CYP-families and 42 subfamilies in humans covering 57 CYP genes and 58 pseudogenes. CYP families 1, 2 and 3 are mostly responsible for the metabolism of a wide variety of xenobiotics, while other families are mainly involved in physiological functions, such as the biosynthesis of fatty acids, steroid hormones, and bile acids.

Most of the CYP-catalyzed reactions lead to detoxification of xenobiotics, involving the formation of more polar metabolites which are conjugated and excreted into urine or bile. However, in some cases after CYP-mediated reactions the products can be more toxic and reactive than the parent compounds. The expression of most xenobiotic-metabolizing CYPs is complex and is affected by genetic, host, and environmental factors of individuals, as well as by certain pathophysiological conditions in the body. The CYP system is often a crucial step in the overall elimination of xenobiotics and therefore a change in the activities or amounts (e.g., inhibition, induction, polymorphism) of CYP enzymes often results in inter-individual alterations of the pharmaco/toxicokinetics of xenobiotics. There are also differences in the patterns and functions of CYP enzymes of different species, and thus, extrapolation between species is difficult.

thus also its target gene CYP3A. CYP3A metabolizes most of the non co-planar PCBs in mammals, so in humans the higher-chlorinated congeners seem to inhibit their own metabolism. These findings provide a caveat not to rely on rodent models when estimating risk of these compounds in humans. An extensive review of the effects of xenobiotic compounds on the constitutive androstane receptor and the pregnane-X-receptor was given by Kretschmer and Baldwin (2005).

7.3.1.4. **Effect on steroidogenesis**

Until now, most interest in contaminants has been devoted to their hormone-disrupting properties in relation to reproductive disorders. However, as recent research has documented that the sex-hormone balance is also important for the development of the metabolic syndrome this issue must be considered as a contributory risk factor. Several experimental studies on single compounds or groups of compounds have been carried out with respect to their effects on the individual steps in steroidogenesis (You et al., 2001; Augustowska et al., 2003; Younglai et al., 2004; Wójtowicz et al., 2005; Holloway et al., 2005).

From these single compound experimental studies it is not possible to draw conclusions with regard to the situation of human exposure. The resultant effect will depend on the concentration of exposure, but principally on the relative concentration of individual components in every exposure situation. As this will vary from one population to another, there is a need to study the combined effects on steroidogenesis of contaminant mixtures representative of the actual composition of contaminants in specific high concentrations of exposure. A more extensive review of the effect of POPs on steroidogenesis is given by Hansen et al. (2008).

Some epidemiological studies have used one or just a few compounds, for example, CB153 as the most abundant PCB congener and DDE as the most abundant pesticide metabolite, as proxies for the exposure situation of a population. This is not scientifically justified, however, because the PCB congeners differ greatly from each other. The relative occurrence of PCBs with hormone-disrupting effects, which are primarily associated with the lower-chlorinated and easily metabolized PCBs, may vary according to the exposure situation. The relative occurrence of the congeners with hormone activity will depend on distance to the sources and on the trophic level from where the food is obtained. In an Arctic Inuit population, living far from the primary sources and with the contaminants having originated from a very long passage though the marine food chain, the higher-chlorinated and slowly metabolized PCBs will dominate over the lower-chlorinated, more readily metabolized congeners with hormone activity. Thus, effects of a specific hormonal influence differ between the Inuit and populations exposed more directly via the contaminant sources, and so using PCB as a proxy for the exposure situation will not necessarily provide information on the hormone effect of the actual exposure. Pliskova et al. (2005) found in man that the lower-chlorinated PCBs have estrogenic effects, while the higher-chlorinated congeners act as antiestrogens. This is in accordance with results from Greenland where a lower estrogen : androgen ratio was found, compared to European populations (Bonefeld-Jorgensen, E., pers. comm., 2008).

Another, and possibly more serious caveat to the use of single compounds as proxies for the exposure situation of a population, is that the influence of industrial compounds such as phthalates and bisphenols are neglected. Phthalates belong to the peroxisome proliferators, which activate PPAR-α and so inhibit the activity of aromatase (CYP19 arom) and as such exhibit an antiestrogenic effect, while bisphenol, widely used in coatings for the inner surface of food and beverage cans, is reported to have a link with insulin resistance at doses much lower than the LOAEL (Lowest Observed Adverse Effect Level), currently 50 mg/kg/day (Alonso-Magdalena et al., 2006). Currently, it is not possible to draw conclusions about the actual exposure to environmental hormone-disrupting chemicals in terms of influence on the risk of developing metabolic syndrome. This may be the result of an exposure which will depend on the distribution between estrogenic and antiestrogenic/androgenic and

antiandrogenic compounds present in an actual exposure. The effect of xenobiotic compounds on steroidogenesis in relation to the effects of different metabolic disorders is important and needs further attention.

7.3.1.5. **Other possible effects**

Uric acid is increasingly being considered as a pivotal factor in the development of metabolic syndrome (Onat et al., 2006), hypertension (Mellen et al., 2006; Krishnan et al., 2006) and cardiovascular diseases (Corry and Tuck, 2006). This has been related to the increasing dietary intake of fructose through industrialized food items. As described in section 7.3.1.1, fructose may increase the serum uric acid level through activation of the renin-angiotensin-system, which is also influenced by *ortho*-substituted PCBs and other POPs (Figure 7.5). A study involving rats demonstrated that exposure to PCBs increased serum uric acid concentrations, regardless of their degree of chlorination (Kutlu et al., 2007). In a human study, Kitamura et al. (2000) found a positive correlation between serum uric acid concentration and the body burden of PCDD/PCDF TEQ, for co-planar-PCB TEQ in workers occupied with waste incineration, however, the significance of the correlation disappeared after corrections for age, smoking, and alcohol consumption. The study by Kitamura et al. (2000) did not include the *ortho*-substituted PCB congeners. As previously described, *ortho*-substituted PCB congeners may influence the formation of uric acid and increase the production of reactive oxygen species. If this is also the case for humans it might indicate that PCB exposure can be an aggravating factor that adds to the negative influence of the increasing dietary fructose intake through industrialized food production. Epidemiological studies are required to confirm this hypothesis.

7.3.2. **Does selenium protect against effects from methylmercury?**

Because selenium binds very firmly to the mercuric ion in the formation of a complex of mercuric selenide units, it has been hypothesized that selenium will protect against the negative effects of mercury. Experimentally this has been known for four decades. The question is whether this is also the case for methylmercury, the main mercury species with regard to human dietary exposure. Methylmercury is slowly demethylated, after which the binding of mercury to selenium takes place. This happens primarily in the liver and lymphatic tissues. Therefore, it seems likely that selenium acts in these organs as a scavenger of mercuric ions and makes them biologically inert. This protective mechanism has been demonstrated in autometallographic studies, where it was shown that mercury is deposited in the lysosomes (Hansen and Danscher, 1997). However, in the case of continued chronic exposure to methylmercury, as in Arctic populations, there does not seem to be any protection despite selenium occurring in molar excess to mercury.

In a study on Inuit pre-school children in Nunavik, Saint-Amour et al. (2006) investigated possible protective effects of selenium and n-3 fatty acids on methylmercury and PCB neurotoxicity. However, the interactions between contaminants and nutrients were not found to be significant. Pedersen et al. (2005) showed that blood mercury concentrations in Greenlanders were significantly and positively correlated with pulse pressure, an indicator of cardiovascular disease risk, and this observation was later confirmed in the human health study from Greenland (Deutch, B., pers. comm., unpubl. data, 2008). These studies support the hypothesis that mercury intake from marine food is involved in cardiovascular diseases. However, they do not support the notion that there is a protective effect of selenium at a chronic dietary intake of methylmercury (see also Chapter 8, section 8.4.4.1).

7.4. **Discussion and conclusions**

The origin of obesity and its health consequences is rooted in a complicated causal web where genetic, epigenetic, environmental, and lifestyle factors all play pivotal roles (see Figure 7.2).

The concept that a hypercaloric, unbalanced diet will result in obesity is well established, with the energy balance as a central question beyond discussion. The efficiency of low-fat or low-carbohydrate diets has been discussed. Recent research tends to conclude that as long as the diet is hypo- or eucaloric, the relative amounts of the macro-nutrients are of minor importance. Raatz et al. (2005) compared obese subjects on three different hypo- and isocaloric diets (high-glycemic index diet, low-glycemic index diet and high-fat diet). After 12 weeks the weight losses and improvement in insulin sensitivity were significant in all groups, but there were no differences between groups. This emphasizes that energy restriction is an essential condition in weight control.

Maintenance of good metabolic health goes, however, beyond weight control. In this connection the quality of the macro-nutrients plays a pivotal role. The dietary fat composition is especially important. Some of the saturated fatty acids, for example palmitate, induce inflammation in adipocytes and will thus promote and exacerbate obesity and insulin resistance (Ajuwon and Spurlock, 2005). PUFAs, both the n-6 and n-3 families, are essential. The two interact in the regulation of pro- and anti-inflammatory processes (see Table 7.1), and for this reason a balanced dietary intake of n-6 and n-3 fatty acids is very important.

A high n-6 : n-3 ratio will tend to be pro-inflammatory, while a very low ratio will induce immuno-suppression. Furthermore, there is evidence that n-6, but not n-3, fatty acids act in a lipogenic manner (see Table 7.1). The optimal ratio is still under debate. The pre-colonial traditional Inuit diet provided a PUFA ratio of around 1, while a present-day westernized fast-food diet provides a ratio of 10 to 20. In relation to cardiovascular health, a ratio of ~6 : 1 has been recommended (Wijendran and Hayes, 2004).

Carbohydrate quality does not seem to play as important a role as does PUFAs, because carbohydrates do not interfere with gene expression of metabolic regulating enzymes. Carbohydrates serve as an energy source, and as long as the total energy supply is eucaloric, even the glycemic index value seems to be of minor importance. An exception is the high intake of fructose prevalent today as a result of the increasing industrialization of food production. Existing literature provides convincing evidence for this to be a major contributor to the increasing prevalence of obesity and metabolic syndrome on a global scale.

A common feature for dietary-induced obesity and metabolic syndrome is induction of oxidative stress at a cellular level, and thus development of inflammation. This is also a characteristic effect of environmental xenobiotic exposure through the diet.

As a consequence, it is reasonable to speculate on an interaction between an unbalanced diet and concomitant exposure to xenobiotic compounds, where the contaminants may play a role as aggravating factors. Early findings from studies in the 1980s of a PCB-related and persistent increase in serum triglyceride concentrations clearly support a connection to xenobiotic exposure (see section 7.3). Similarly, recent findings from Greenland were that the risk factor for cardiovascular diseases (TG/HDL ratio) increased with increasing body mass index, as expected, but that there was an additional increase in the TG/HDL ratio related to the POPs exposure concentration (Hansen et al., 2008). This indicates that in relation to obesity and metabolic syndrome, neither dietary imbalances nor exposure to contaminants should be evaluated separately, but should be addressed as a single entity.

Except for some Inuit populations, the general exposure level in the Arctic is below the guidelines for safe exposure to contaminants (AMAP, 2003). The question is whether these relatively low exposures can have an influence on metabolic disorders. From the existing literature it seems reasonable to speculate that in an organism already susceptible to developing a state of metabolic disorder, a concomitant exposure to dietary contaminants will, even at a relatively low level, be able to accelerate the processes, in an additive manner. At the moment there is not much epidemiological evidence for this, however, experimental evidence indicates that this potential interaction is a public health issue that should be accounted for in future studies.

Divergent scientific and regulatory agency perspectives on contaminants in food have lead to contradictory advice and often to confusing public messages (Brustad et al., 2008b). It is, however, widely recognized that owing to the multifactorial character of the problems 'cancer and non-cancer health impacts associated with environmental exposures generally cannot be directly isolated and measured', for this reason the discipline of risk assessment was established (see http://www.epa.gov/oswer/riskassessment/basicinfo.htm). A risk assessment approach using the formal tools established for this purpose is likely to be the most helpful approach for establishing risk and facilitating suitable risk management strategies (including dietary advice) (Brustad et al., 2008b).

The concept that nutrition can modulate the toxicity of environmental pollutants, and vice versa, is a new way of thinking in the area of environmental health. Nutritional awareness in environmental toxicology is critical because of the opportunities to develop guidelines which specifically target exposed populations. In this way, nutrition may provide the most sensible means to develop primary prevention strategies for diseases associated with environmental toxicology (Hennig et al., 2004).

To improve understanding of the health effects associated with exposure to contaminants in the Arctic, it is recommended that circumpolar studies, including both nutritional and toxicological aspects, should be implemented on a large scale. Methylmercury- and POPs-related effects are still the key issues. However, the role of newly discovered contaminants such as PBDEs, polychlorinated naphthalenes, phthalates, and bisphenyls, should also be investigated. For exposure estimates, mixtures of contaminants and nutritional benefits of foods should be incorporated in risk-assessment profiles. There is a need for better understanding of the interactions between nutrients and xenobiotic compounds, and risks should be evaluated in accordance with this interaction. Figure 7.7 provides a schematic representation of the relationship between nutrition and toxicology in the development of disease prevention strategies targeted at specific exposure populations.

It is essential that a better understanding is achieved of the health consequences of the dietary (and thus, nutritional) transition taking place within indigenous populations and the nutrient/contaminant interaction in Arctic populations, and that this information is communicated to the Arctic populations in a correct and understandable manner.

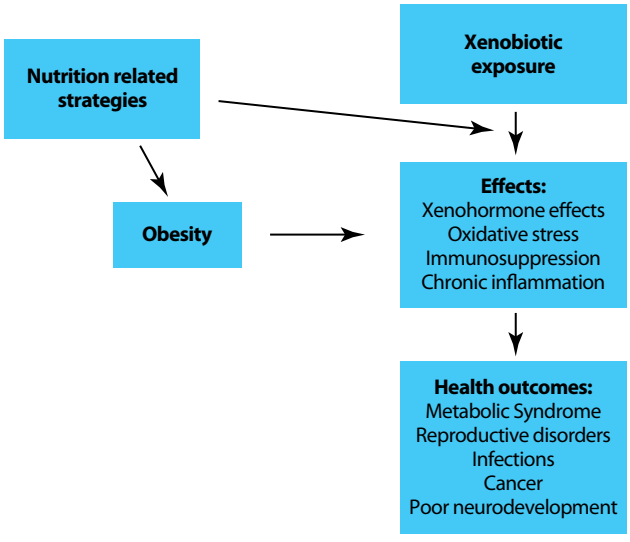


Figure 7.7. Potential methods for improving public health. Source: Hansen et al. (2008).

Chapter 8

Public Health and the Effects of Contaminants

Andrew Gilman, Pierre Ayotte, James Berner, Eric Dewailly, Aleksej A. Dudarev, Eva C. Bonefeld-Jorgensen, Gina Muckle, Jon Øyvind Odland, Constantine Tikhonov

Summary

Human populations in the Arctic, especially indigenous populations, have comparatively poorer health status than populations from non-Arctic regions of the same eight circumpolar countries. Although infant death rates are lower and population longevity has improved, rates of several chronic diseases have been increasing. These changes are not uniform across the Arctic and are influenced by a number of determinants of health related to socio-economic, dietary and cultural influences. One factor of concern to public health officials relates to exposure of indigenous populations to an array of contaminants, primarily through traditional food consumption. Exposure to several persistent contaminants (organic chemicals and metals) has the potential to contribute to the disease burden in populations already at a lower state of general health. Stronger evidence is now available for the adverse effects of persistent substances and metals on human health based on animal exposure studies involving individual substances and mixtures of substances found in the Arctic environment. Recent epidemiology findings appear to confirm some of the toxicology findings although some contaminant-health relationships are difficult to establish for methodological reasons and because of confounding factors related to lifestyle, general health status and genetic factors. Studies with laboratory animals confirm the effects of environmentally-relevant mixtures of chemicals on the immune system, reproduction, behavior, development of newborns, and possibly metabolic disorders. New animal and human data indicate that persistent organic pollutants (POPs) may be involved in adverse changes in bone density. The effects of polychlorinated biphenyls (PCBs) and mercury (Hg) on neurobehavioral health and of Hg on cardiovascular parameters are a significant cause of concern as these effects occur at very low levels of exposure. Specific effects of POPs and metals at current concentrations on reproductive health are still unclear although several indications point to some adverse outcomes in populations from some regions of the Arctic. In contrast, the capacity for POPs and metals to adversely affect child development and the immune system is very clear. Studies involving biomarkers of effects have indicated that POPs exposure at current levels can induce genetic alterations, decrease defense against oxidative stress, and disrupt endocrine systems. Although a traditional diet is the cause of exposure to contaminants, it provides excellent nutrition and may also be protective of some effects. Some polyunsaturated fats and selenium (Se) may reduce the toxic effects of dietary contaminants.

8.1. Introduction

Diet, water quality, disease prevention, genetic susceptibility, education, the economy, health care availability and use, cultural values, and lifestyle factors all play critical roles in any overall assessment of health. Other chapters in this assessment address some of these determinants of health in more detail. The focus of the AMAP Human Health Assessment Group remains on contaminants and how they interact with each other and with other factors to influence health.

Human exposure to contaminants in the Arctic is a reality primarily because of long-range transport of persistent contaminants into the region and because these contaminants build up in the food chains upon which many indigenous Arctic populations depend for sustenance. While concentrations of most contaminants are declining in many regions (especially PCBs, oxychlordane, Hg), some are still above acceptable levels in a proportion of the Arctic populations (e.g., PCBs and Hg) and concentrations of some 'emerging' substances are still increasing or only declining slowly (e.g., perflurooctane sulfonate and brominated flame retardants). Details are available in Chapter 5.

The aim of this chapter is to provide a summary of existing information with an emphasis on new data obtained since the last assessment (AMAP, 2003) on:

- the current health status and demographics of Arctic indigenous peoples;
- the toxicology of the legacy and emerging contaminants individually and as mixtures; and
- population studies which examine the effects of contaminants on indigenous peoples of the Arctic.

8.2. Demographics and health status of Arctic populations

8.2.1. Introduction

This section provides a short overview of cornerstone health outcome indicators for Arctic populations of the circumpolar countries. Detailed discussion of socio-economic determinants of health, and measures of health system performance and utilization are beyond the scope and purpose of this update report. This review updates some of the common health status indicators; it is not intended to be comprehensive. Recent sources of more comprehensive information on general health status are discussed below and provided throughout this chapter.

8.2.2. **Data sources**

In the period since the publication of the 2002 Human Health Assessment (AMAP, 2003), two major Arctic reports (ACIA, 2005; AHDR, 2004) and a book (Young and Bjerreggard, 2008) have included a review of population health indicators. The present section makes use of information from these sources as well as information from statistical agencies of circumpolar countries available on the internet, health statistics in the northern countries (NOMESCO, 2007), data available from the Alaska Bureau of Vital Statistics, and the ArcticStat Circumpolar Database (http://www.arcticstat.org/index.htm) maintained by Laval University.

8.2.3. **Population demographics**

Prior assessments have had new data on contaminant exposure in regions of Arctic Russia, but very little information on population health indicators at the sub-national level. This section provides the latest information on population age structure in the Russian Arctic. In addition to specific health status data, age structure can provide inferential information on possible population health problems, some of which can be associated with contaminant exposure. The age structures of the populations of circumpolar countries are shown in Figure 8.1.

Comparisons of the general population pyramids of some circumpolar countries with population

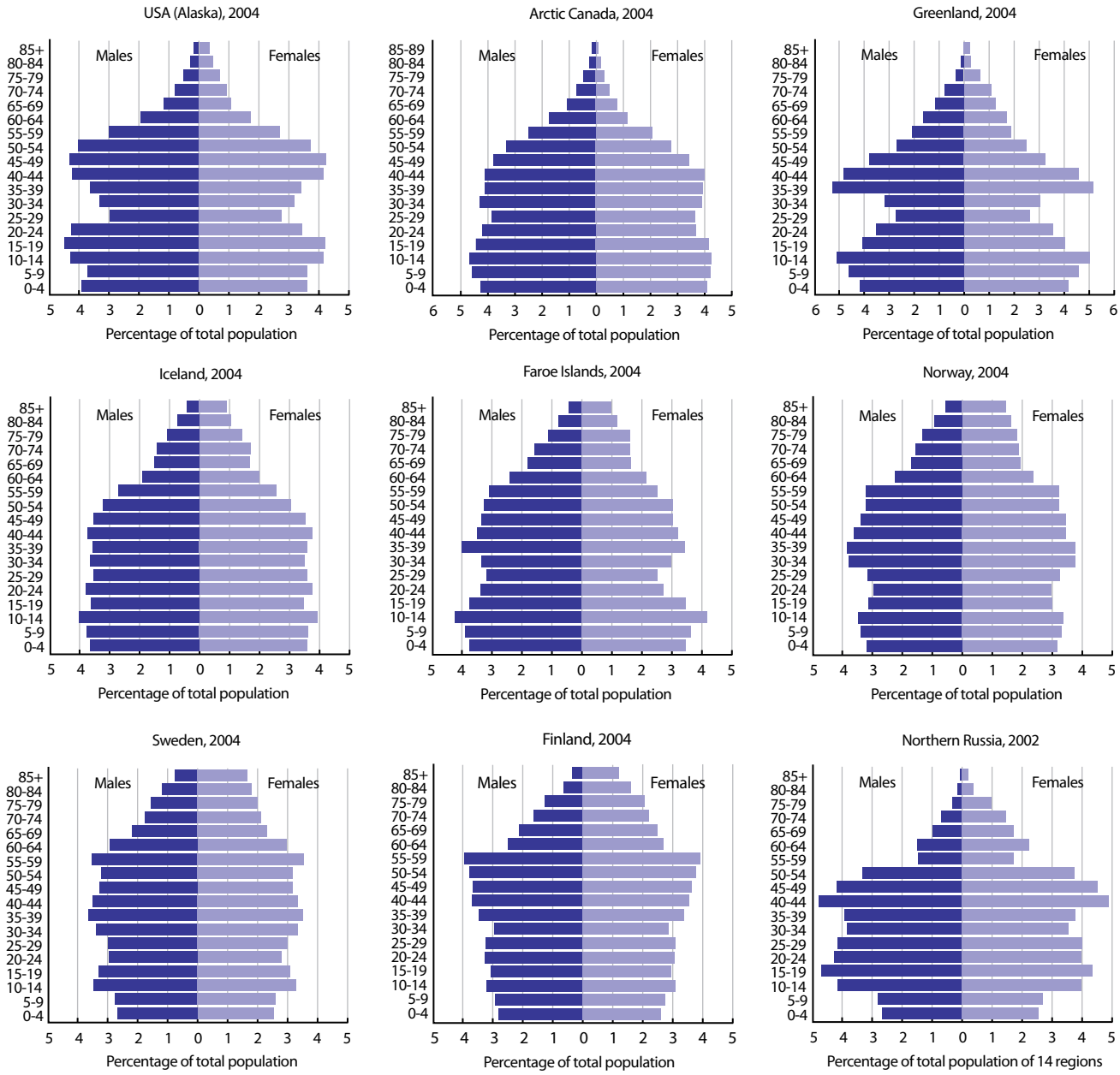


Figure 8.1. Age-gender population structure of Arctic countries and regions.

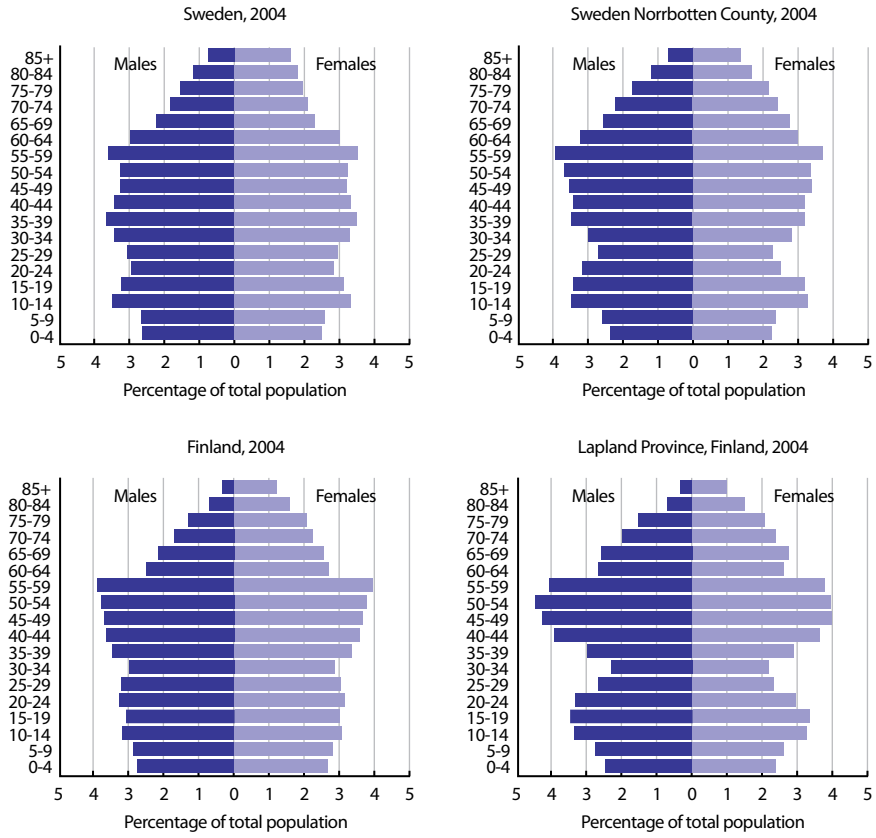


Figure 8·2. Age-gender population structure of Sweden and Finland in comparison to their Arctic regions.

structures of their most northern regions and counties (Figure 8.2) suggest that while the pillar-like structure of northern peoples population becomes less uniform, with slightly more pronounced variability of cohorts, the overall population structures of northern regions in Sweden and Finland are not too different from the general population, particularly in the older cohorts. The Icelandic population is also characterized by a very high survival rate of each infant cohort, a gradual loss of population members, and a very long life expectancy.

At the same time, some other Arctic countries (e.g., the Russian Federation and Canada) are characterized by rather noticeable differences in the structure of their general and northern populations (Figure 8.3). The composite population structure in the Russian Arctic regions indicates few births in the last ten years and few people surviving into old age. This may suggest voluntary limits on family size or poor reproductive success, high mortality in early adulthood, and a high mortality rate from communicable and chronic diseases, possibly due to lack of effective primary and secondary prevention. The age-sex pyramid of the Russian Arctic population is uneven with a dip at age 30–34. This reflects a very small number of children born to individuals who were born during the Second World War. Bogoyavlenskiy and Siggner (2004) refered to this as a 'second demographic echo of the war'. The 'suddenly' narrow base of the Russian pyramid reflects a dramatic fertility decline in the past decade, when the economic crisis of the 1990s and the 'second echo of the war' coincided (Bogoyavlenskiy and Siggner, 2004).

One of the notable characteristics of the population structures in Arctic North America, Greenland and Arctic Russia is a rather dramatic decline in the number of older people (above 60 years of age), in comparison to the general population of these countries. In North America and Greenland, one of the key contributary factors could be high infant mortality and premature mortality in the cohorts of people who are currently in their sixties and above. Furthermore, indigenous populations in the western hemisphere tend to have larger populations of children and smaller populations of elders, compared to populations in Scandinavia and Iceland.

Major migrations of Russians out of Arctic areas could also be a critical factor in the Russian demographic picture. In Arctic Russia, the past 15 years have seen the greatest out-migration of Arctic population recorded (Bogoyavlenskiy and Siggner, 2004). Between the census of Russian populations taken in 1989 and in 2002, the population in the Russian Arctic regions decreased by 1.4 million individuals. This constitutes a 12% overall decrease in the Russian population in the Arctic (RFCAN, 2006). The greatest population losses were in Chukotka, where nearly 70% of the 1989 population migrated out of the region. The Arctic part of the Republic of Sakha lost almost 50% of its population. Only the Yamalo-Nenets Autonomous Okgrug (AO) stands out with minimal losses of only 7% of the 1989 population (Bogoyavlenskiy and Siggner, 2004)

The current demographic situation in Russia continues to be characterised by negative migration

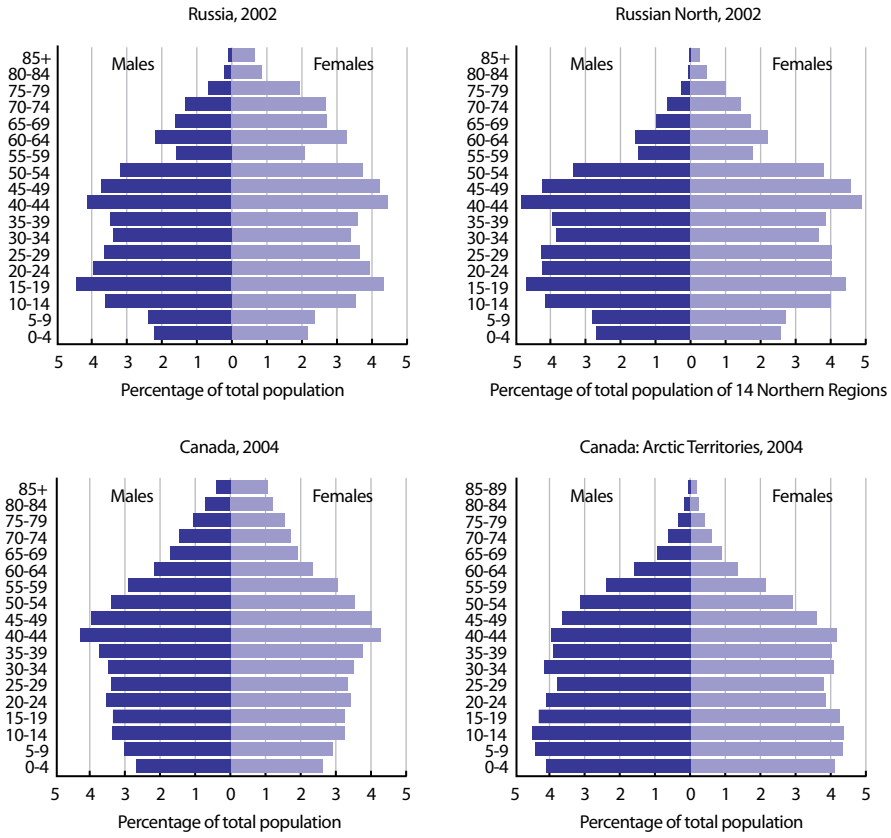


Figure 8·3. Age-gender population structure of Russia and Canada in comparison to their Arctic regions.

and birth statistics, coupled with significant decreases in life expectancy and increases in mortality rates. Contaminant-mediated health effects may be a contributor to the mortality rates observed. Adverse reproductive outcomes, fetal mortality, poor maternal-child health and infectious and chronic diseases are sometimes associated with contaminants and can be systematically investigated.

8.2.4. **Birth rate**

Compared to the rest of the world, current fertility in the Arctic cannot be characterized as high; the crude birth rates in circumpolar areas as a whole are below 20 (Bogoyavlenskiy and Siggner, 2004). Overall, in the Arctic region, crude birth rates in Nunavut (Canada), among Alaska Natives, in Greenland, and in the Northwest Territories (Canada) are among the highest in the Arctic (Table 8.1).

The overall Alaska 2000–2004 crude birth rate of 15.7 per 1000 population represents a 7.6% decrease from the crude birth rate of 17.0 per 1000 population recorded in 1995. The preliminary 2000–2004 crude birth rate for the United States was 14.1 live births per 1000 population, which is a slight decline from the rate of 14.8 in 1995 (Alaska Bureau of Vital Statistics, 2004).

A detailed analysis of general and total fertility rates is provided in the Arctic Human Development Report (ADHR, 2004).

8.2.5. **Key health outcomes indicators**

Evaluation of key indicators of health outcomes can provide a rough estimate of the overall health status of populations. Life expectancy, infant mortality rates, and data on causes of death in a given population are particularly useful. Box 8.1 provides definitions of some key indicators of health (Last, 2001).

Box 8·1. Definitions of some epidemiological indicators

Life Expectancy at birth is the average number of years a newborn baby can be expected to live if current mortality trends continue. Corresponds to the total number of years a given birth cohort is expected to live divided by the number of children in the cohort.

Crude Death Rate is an estimate of the portion of the population that dies during a specified period. The numerator is the number of persons dying during the period; the denominator is the number in the population, usually estimated as the mid-year population.

Infant Mortality is a measure of the yearly rate of deaths in children less than one year old. The denominator is the number of live births in the same year.

Birth Rate is a summary rate based on the number of live births in a population over a given period, usually one year. The denominator is the average of midyear population in the area in that year.

8.2.5.1. **Life expectancy**

Life expectancy is greatly influenced in most countries by a decrease in infant mortality. Table 8.1 provides an overview of life expectancy at birth for the total population in the AMAP area. It is clear from this overview that life expectancy is usually lower in the more remote northern regions of circumpolar countries, due to higher mortality in infancy and childhood. In the circumpolar parts of Norway and Sweden, the differences in life expectancy in their northern areas are due in part to greater male mortality (AHDR, 2004). The Russian Federation has the lowest life expectancy among circumpolar countries.

The pattern of higher life expectancy of females in comparison to males is consistent, although there are differences between the countries and northern regions in the extent to which this phenomenon is expressed. For example, in Russia, the difference in life expectancy between genders reaches 10 to 16 years, while in Arctic counties of Norway, life expectancy of males is about five to six years lower than for females and similar to Norway in general. Iceland has the highest life expectancy of circumpolar countries with the lowest gender difference in life expectancy.

Table 8·1. Circumpolar crude birth rates per 1000 population, life expectancy at birth, infant mortality per 1000 live births, and crude death rate per 1000 population; all data are for the period 2000-2004. Primary data source: Young (2008a). Other sources: ArcticStat Circumpolar database (http://www.arcticstat.org/searchregion.aspx), AHDR (2004), Statistics Canada, Russian Federal State Statistics Service, Alaska Bureau of Vital Statistics, NOMESKO.

	Circumpolar crude birth rates (2000–2004) per 1000 population	Circumpolar life expectancy at birth (2000–2004)		Circumpolar infant mortality (2000–2004) per 1000 live births	Circumpolar crude death rates (2000–2004) per 1000 population
		Males	Females		
USA	14.1	74.6	80.0	6.9	8.4
Alaska	15.7	74.5	80.1	6.8	4.7
Alaska Natives	22.8	68.1	75.4	10.8	6.3
Canada	10.6	77.2	82.2	5.3	7.1
Yukon	11.5	74.9	80.1	7.4	4.8
Northwest Territories	16.0	74.6	78.8	6.0	4.1
Nunavut	25.6	66.6	70.9	15.3	4.4
Greenland	16.1	64.6	70.4	12.7	7.8
Iceland	14.5	79.0	82.6	2.6	6.3
Faroe Islands	14.6	77.0	81.3	1.7	8.0
Norway	12.5	76.6	81.7	3.6	9.5
Nordland	11.3	76.7	82.0	3.9	10.3
Troms	12.4	76.5	81.5	4.0	8.9
Finmark	13.2	74.6	80.6	4.7	9.2
Sweden	10.7	77.8	82.3	3.3	10.4
Västerbotten	9.8	77.6	82.1	3.8	10.3
Norrbotten	9.3	76.6	81.6	4.6	11.0
Finland	10.9	74.8	81.6	3.3	9.4
Oulu	12.9	74.3	81.6	2.7	8.5
Lapland	9.6	73.7	81.1	3.8	9.5
Russian Federation	9.6	58.8	72.1	13.3	15.8
Murmansk Oblast	9.5	57.6	70.5	11.8	12.8
Kareliya Republic	9.8	55.1	69.6	10.8	18.2
Arkhangelsk Oblast	10.1	55.9	70.5	12.9	17.1
Nenets AO	14.5	53.8	69.0	20.3	13.2
Komi Republic	10.6	56.6	69.5	10.1	14.4
Yamalo-Nenets AO	13.1	61.8	72.2	13.8	5.8
Khanty-Mansi AO	13.0	61.3	73.0	8.4	6.9
Taymir AO	14.8	54.2	67.5	21.4	10.3
Evenky AO	14.9	53.6	64.6	22.0	12.6
Sakha Republic	14.5	57.9	70.4	15.3	10.1
Magadan Oblast	10.6	56.6	69.4	13.0	12.5
Koryak AO	11.9	49.9	61.7	21.9	16.5
Chukotka AO	12.9	53.6	63.7	28.9	11.2

8.2.5.2. **Infant mortality**

Infant mortality reflects not only the health of the population, but also highlight its living conditions, food security, possible aspects of domestic conflict, mental health, and overall socio-economic wellbeing of the communities. In respect to Inuit, infant mortality has decreased dramatically. Figure 8.4 indicates more than a ten-fold decrease in Inuit infant mortality in some Arctic regions over the past 40 years.

Despite significant improvements in infant mortality in the Arctic, there are noticeable differences in the infant mortality rates between Arctic regions. While Iceland, Sweden, Norway, and Finland are among the top ten countries in the world in terms of low rates of infant mortality (WHO, 2007), in several regions of Arctic Russia (Table 8.1) the average infant mortality in 2000 – 2004 exceeded 20 deaths per 1000 live births, reaching 28.9 deaths per 1000 live births in the Chukchi AO region. Nunavut (Canada), Greenland and Alaska Natives have infant mortality rates above 10 infant deaths per 1000 live births. In Canada, while the Northwest Territories' infant mortality is not far from the national average, the infant mortality in Nunavut is more than three times higher than in Canada as a whole. The general infant mortality rate in Alaska is about the same as for the general population of the United States and demonstrates how a larger proportion of the non-indigenous population (all-Alaska rate of 6.8 deaths per 1000) can hide a difference in a comparative infant mortality of a smaller indigenous population (Alaska Natives only rate of 10.8 per 1000) (Table 8.1).

Infant mortality can be separated (Figure 8.5) into neonatal (deaths under 28 days of life) and post-neonatal (deaths from day 28 to 364). The causes of death are generally different in these two categories and this has implications for public health and primary care practice. While neonatal deaths are generally thought to be associated with the quality of prenatal and perinatal health care provided, post-neonatal deaths are more affected by socio-economic conditions (NWT, 2005). Neonatal and post-neonatal mortality data need to be examined in all circumpolar countries, but particularly in Russia where they are not readily available.

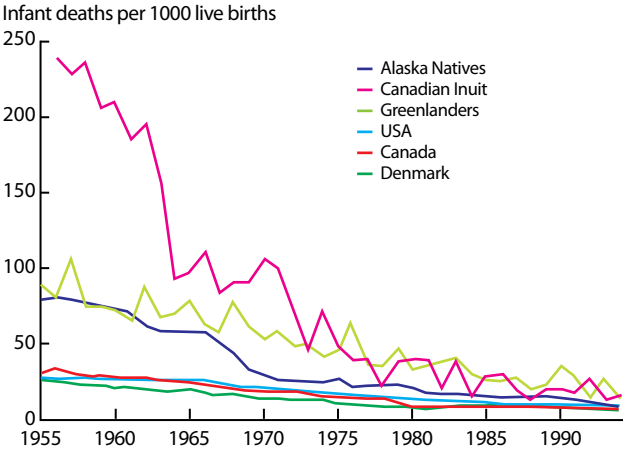


Figure 8·4. Trends in infant mortality rate among Inuit in different circumpolar regions in comparison with the general population of the respective countries. Source: adapted from Bjerregaard and Young (1998).

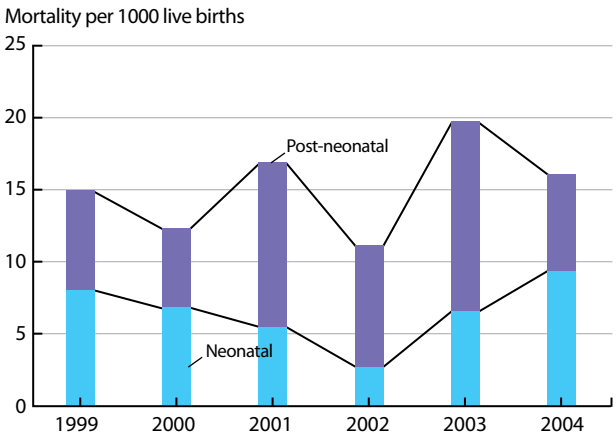


Figure 8·5. Infant mortality components in Nunavut 1999 – 2004. Source: based on Statistics Canada (2008b).

8.2.5.3. **Crude death rate**

Crude death rates presented in Table 8.1 suggest significant regional variations in crude mortality of Russian Arctic residents with differences reaching almost 13 deaths per 1000 population, when comparing the Yamalo-Nenets AO and the Kareliya Republic. About 15 000 indigenous people of the Russian Arctic lead a nomadic way of life, with the Yamalo-Nenets AO being home to the biggest nomadic group (Bogoyavlenskiy and Siggner, 2004). The extent to which a population is nomadic may cause some difficulties in the registration of all deaths.

Age-adjusted death rates enable a better comparison of death rates between populations of different countries and regions by compensating for differences in the age structures of these populations. Examination of the age-standardized mortality rates in Arctic regions (Figure 8.6) shows that the mortality from all causes is not very different in the northern regions of most Scandinavian countries from the total age-standardized mortality rates of each country as a whole. However, there are obvious differences between Greenland and Denmark, as well as between northern Canada and Canada, due to the large proportions of indigenous populations in Greenland and northern Canada. The age-standardized mortality of Alaska Natives is also much higher than the corresponding mortality rate in Alaska and the United States in general. Regions of Arctic Russia have the highest age-standardized mortality rates among all circumpolar regions and countries. There is a remarkable variation in mortality rates among different northern regions of the Russian Federation, which might be related to the variability of socio-economic conditions of the population, the accessibility of health care services, and the state of the public health infrastructure.

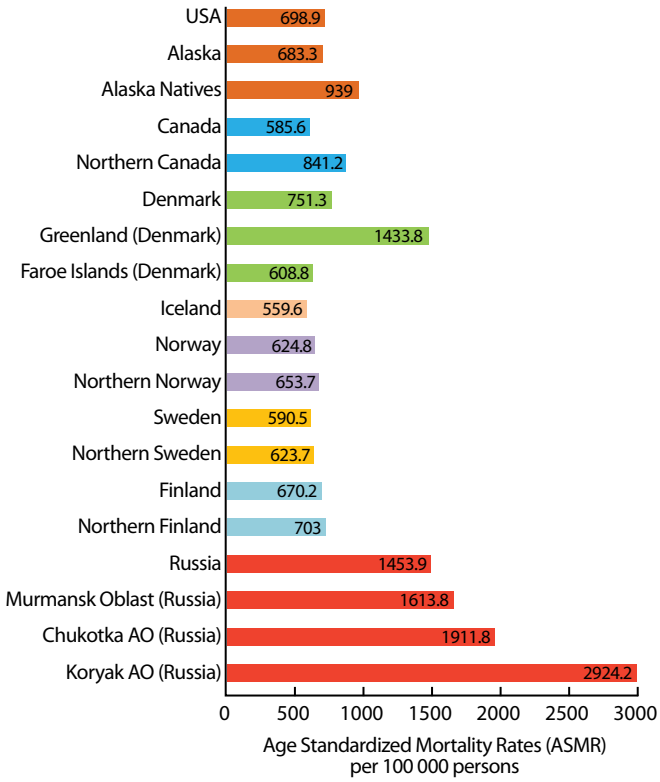


Figure 8·6. Circumpolar age-standardized mortality rates by cause per 100 000 persons; standardized to European Standard Population. Source: Young (2008a).

8.2.6. **Common causes of death**

There are differences among circumpolar countries in the leading causes of death, based on death certificate data (Berner and Furgal, 2005). Figure 8.7 compares mortality rates for a group of common causes of death in the Arctic regions of several circumpolar countries.

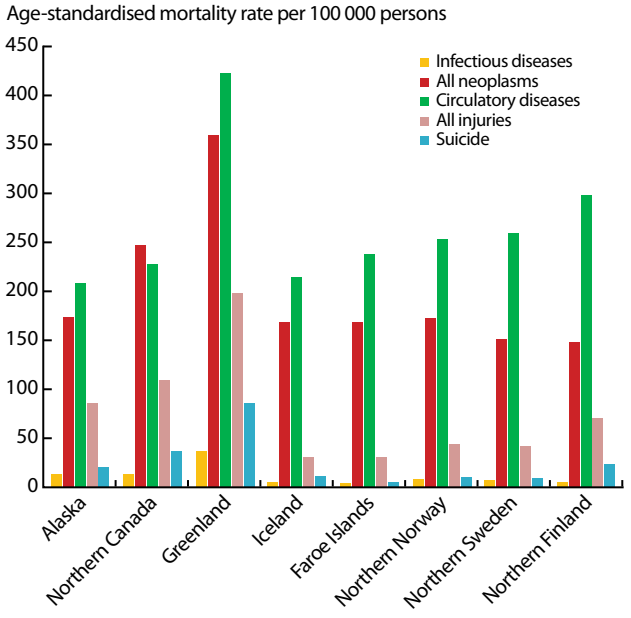


Figure 8·7. Common causes of death in some Arctic populations, 2000 – 2004. Source: Young (2008a).

It is clear that circulatory diseases and cancers are currently the leading causes of death in Arctic populations. At the same time, in several Arctic countries and regions with high proportion of indigenous people, taking Greenland (Denmark) and northern Canada as examples, there is also a pattern of high mortality due to suicide and injuries. Some Arctic regions seem to be experiencing a double burden of disease, i.e., facing higher rates of certain infections and injuries compared to non-Arctic populations, and at the same time a growing prevalence of chronic diseases more characteristic of the general (non-indigenous) population in their respective countries (Counil, 2007).

8.2.7. **Health status of indigenous Arctic residents**

Indigenous status has been associated with lower health outcomes in the past (Frohlich et al., 2006). The diversity of ethnic groups within the category of 'indigenous people' implies significant limitations to the analysis of health outcomes applicable to 'all indigenous people' of a circumpolar region. From an epidemiological point of view it would be more prudent to examine health status indicators specific to each indigenous ethnic group within the context of its particular spectrum of determinants of health. However, despite its limitations, the analysis of health indicators for the entirety of indigenous people could be predicated on the assumption that as an entity, all indigenous people have experienced a degree of marginalization within their respective countries. In addition, there is likely to be a certain commonality in shared experience of life among various circumpolar indigenous groups. Social and economic conditions of life are rather similar, as are the pressures on indigenous cultural adaptation, emanating from the profound changes imposed by the technologically advanced dominant cultures on traditional ways of life. This experience has not been all negative or all positive. Due to improved housing conditions, sanitation and food security in some regions, morbidity and mortality from infectious diseases has decreased. Yet, increased contact with the rest of the world has brought new infectious diseases to circumpolar residents, particularly sexually transmitted infections (Bjerregaard and Young, 1998, 2008).

In general, it appears that the health status of indigenous peoples of Greenland and the Arctic regions of the United States, Canada, and the Russian Federation is characterised, in comparison to non-indigenous populations of these countries, by lower life expectancy, higher infant mortality, higher rates of infectious diseases (particularly among children), and a much higher incidence of injuries and suicide. At the same time, higher prevalence of tobacco use, more widespread sedentary lifestyles, and ongoing nutritional transition to more calorie-rich and nutrient-poor store-bought foods among some indigenous populations in the Arctic have contributed to increasing burdens of chronic diseases (see Chapter 3). The health status disparities noticeable

among Sami, the indigenous people of Scandinavia, seem to differ from the above description and will be discussed separately.

8.2.7.1. **Alaska, USA**

There have been significant increases in the life expectancy of Alaska Natives. In the 1950s, life expectancy was 46 years; this was approximately 22 years below the all-USA life expectancy at that time. By the late 1990s this difference had narrowed to 7 years (Goldsmith et al., 2004).

Infant mortality also declined significantly in the second half of the 20th century, from 120 deaths in the first year of life per 1000 Native babies in 1945 to 24 per 1000 in 1975, and to 15 per 1000 by 1990 (Goldsmith et al., 2004). In the period 1998 to 2000, infant mortality among Alaska Natives was 9.5 per 1000; much closer to, but still above the 7.0 per 1000 for the entire United States population (Goldsmith et al., 2004).

According to the Status of Alaska Natives Report, 2004 (Goldsmith et al., 2004), the age-standardised death rates from heart disease among Alaska Natives in 1999–2001 were 218.6 per 100 000, compared to 209.9 per 100 000 among non-indigenous white Alaskans and 270.3 among black residents of the state. In 2003–2004, the age-standardised mortality rate for heart disease among Alaska Natives decreased to 199.8 per 100 000, compared to 175.2 per 100 000 for all Alaskans (Berner, 2008).

At the same time, cancer mortality has continued to increase. Cancer-related age-adjusted death rates in 1999–2001 were 239.5 per 100 000 for Alaska Natives, 193.5 per 100 000 for white residents of Alaska, and 166.7 per 100 000 for black Alaskans (Goldsmith et al., 2004). These rates reached 247.4 per 100 000 in 2003–2004 for the Alaska Native population, compared to 186 per 100 000 for the all-Alaska population (Berner, 2008).

Lanier et al. (2001) observed that the incidence of most 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 occurred in lung and breast cancer (Lanier et al., 2001).

Table 8.2 presents age-standardized mortality rates for selected causes and illustrates continued differences in disease mortality between Alaska Natives and the all-Alaska population.

Some of the determinants of health and risk factors of disease differ between Alaska Natives and non-indigenous Alaskans. For example, prevalence of obesity and being overweight in Alaska is increasing and for men was about the same between indigenous and non-indigenous residents in 2001–2003. Among women, however, the prevalence of obesity and being overweight was 62% for Alaska Natives compared with 51% for non-Natives (Berner, 2008).

The increase in lung cancer among Alaska Natives could be related to tobacco use. Up to 45% of Alaskan Natives smoke tobacco, although there was a slight decrease to 42% between 1991 and 2000. The rate of smokeless tobacco use among Alaska Native women (10%) is particularly high in comparison to the 0.5% rate among non-Native women (Berner, 2008).

Table 8.2. Age-standardized mortality rates for selected causes: Alaska Natives and Alaska. Source: based on Berner (2008), National Centre for Health Statistics, National Vital Statistics Reports, Alaska Department of Health and Social services (various years), and Alaska Bureau of Vital Statistics (various years).

Cause	Alaska Native	Alaska
Cancer	247.4	186.0
Diabetes-related (underlying cause)	20.0	25.1
Heart disease	199.8	175.2
Stroke	76.7	56.1
Influenza and pneumonia	38.2	17.3
Chronic lower respiratory tract diseases	54.0	43.1
Chronic liver disease and cirrhosis	22.7	9.3
Unintentional injuries	84.6	55.1
Suicide	42.8	22.1
Homicide	12.3	6.6
All causes	1079.6	790.7

Alcohol abuse continues to be a significant health risk factor in Alaska, particularly among indigenous Alaskans, contributing to high rates of domestic violence, child abuse, and violent death in Native communities. Concerns about alcohol use have led two-thirds of small villages to impose local controls on alcohol (Bashshur and Quick, 1990; Goldsmith et al, 2004).

8.2.7.2. **Canada**

Arctic Canada's population includes three groups of indigenous people: Inuit, First Nations, and Métis.

Geographically speaking, the proportion of indigenous people living in the three Arctic territories increases from west to east. According to the demographic profile of the Aboriginal People of Canada obtained from the 2001 Census (Statistics Canada, 2003), the 22 720 indigenous people in Nunavut represented 85% of the territory's total population, one of the highest proportions in the country. Indigenous people represented more than half (51%) of the population of the Northwest Territories, and almost a quarter (23%) of the Yukon population. According to the 2001 census, 91% of people living in Nunavik (northern Quebec) self-identified as Inuit. This increase in the proportion of the indigenous population is matched by a decreasing health status relative to the total Canadian population (Young, 2008b). Health statistics for Inuit, although available in some territories, are generally not provided as ethnically-specific analysis. However, regional data for Nunavut (85% Inuit) and the Nunavik region of northern Quebec (91% Inuit) can essentially be interpreted as Inuit data (Young, 2008b).

Although there are differences between health status indicators of various indigenous groups, this short overview of Arctic indigenous health status in Canada

will focus on highlighting selected data from Nunavut and Nunavik, as a recent in-depth analysis is already available (Young, 2008b).

Life expectancy at birth for residents of Nunavut (70.4 years) is ten years lower than in Canada (80.2 years) and has not improved significantly between 1999 and 2004. This is particularly notable for males (NRCHI, 2004; Statistics Canada, 2007a). The life expectancy indicator in Nunavik was 63.3 years in 2000–2003, considerably lower than in the rest of Quebec (79.4 years) (Counil, 2007).

According to the Nunavut Report on Comparable Health Indicators (NRCHI, 2004), the rate of infant deaths in Nunavut has steadily declined since 1991. The decline was presumed to be associated with increased early and regular prenatal care, obstetric care during labor and delivery, as well as postpartum care and maternal education. When averaged over the six years between 1999 and 2004, infant mortality in Nunavut (15.2 per 1000 live births) was nearly three times higher than it was for Canada (5.3 per 1000 live births) during the same period (Statistics Canada, 2007b).

In Nunavut (2000–2004), cancers were the leading cause of death (age-standardised rates), followed by circulatory diseases, respiratory diseases, and injuries, including suicide (Young, 2008a). In Nunavik, between 2000 and 2003 the leading causes of death were, in descending order: cardiovascular disease, cancers, respiratory diseases, suicide, and unintentional injuries/accidents (Counil, 2007).

In Nunavut, the age-standardized mortality rates in 2000–2002 for suicide (80.2 per 100 000) and unintentional injury (62.4 per 100 000) were much higher than in Canada (11.3 per 100 000 and 25.6 per 100 000, respectively) and other northern territories (Young, 2008b).

Although there has been progress in reducing the incidence of tuberculosis in the North, the current rate in Nunavut of 108 per 100 000 population (based on a mean for 2000–2004; Young, 2008a) is much higher than the national incidence rate of 5.1 per 100 000 population (PHAC, 2005). In Nunavik, the incidence rate of tuberculosis is also very high, 52 per 100 000 population (2000–2004) compared to 3.6 per 100 000 population in the rest of Quebec (Counil, 2007).

8.2.7.3. **Greenland**

In Greenland, residents 'born in Greenland' make up approximately 90% of the population. 'Born in Greenland' is usually used to represent Greenland Inuit (Bjerregaard et al., 2004b) although there are non-Inuit born in Greenland.

Infant mortality has been gradually decreasing for at least fifty years from almost 120 per 1000 in 1950 to around 16.9 per 1000 in 2001–2005 (NOMESCO, 2007). The Greenlandic rate is still quite high and well above the 4.7 per 1000 in Denmark (Bjerregaard and Stensgaard, 2008).

Since the 1950s, the importance of tuberculosis and acute infectious diseases as leading causes of mortality has decreased, while new causes of death have gained prominence (Bjerregaard and Stensgaard, 2008). Chronic diseases, especially cancer and cardiovascular disease became more visible. Accidents stayed at a high level and the suicide rate somewhat increased (Moesgaard Iburg et al., 2001).

Major causes of death responsible for most premature mortality are suicide and tobacco-related diseases. If these were removed as causes of death, life expectancy in Greenland would increase from 63 to 71 years for men and from 68 to 74 years for women (Bjerregaard and Stensgaard, 2008).

8.2.7.4. **Scandinavia (Sami)**

It is very difficult to estimate the population of Sami (or Saami) in the Nordic countries. Estimates suggest a range of 60 000 to 110 000 in the three countries: 60 000 for Norway, 36 000 for Sweden, and 10 000 for Finland. In the 2002 Russian Census, 1991 inidividuals self-identifed as Sami. As Sami status is not identified in any of the health-reporting systems of the Nordic countries, the lack of Sami-specific health data prevents the development of an adequate picture of the health status of Sami (Hassler et al., 2008b).

However, recent work by Hassler (2005), Soininen and Pukkala (2008), Silviken et al. (2006), and Silviken and Kvernmo (2007) contributes to a better understanding of several key Sami health outcome indicators. A prospective cohort study of Sami in northern Finland investigated causes of mortality from 1979 to 2005 (Soininen and Pukkala, 2008). The study concluded that "Sami men had a lower disease mortality as compared with the Finnish population generally and their non-Sami neighbours, although their life habits would suggest a higher mortality rate. Reasons for their lower mortality may be related to their diet that is rich in reindeer meat and fish, their physically active way of life or their genetic background". Mortality from accidents and violence was high both among the Sami and non-Sami populations. Suicide mortality among the Sami men in Finland was significantly elevated, while that of the non-Sami men was not. In general, a low mortality from disease and high mortality from external causes of death among the Sami in Finland seemed to bring mortality rates into the same zone as those of non-Sami.

Suicide mortality was also examined between 1970 and 1998 in a large cohort of indigenous Sami in northern Norway (Silviken et al., 2006). There was a significant and moderate increased risk for suicide among indigenous Sami. Significant increased suicide mortality was found for young Sami aged 15–24 years for both males and females. In general, however, the mental health of Sami children and adolescents in northern Norway did not seem to be much different to that of non-Sami children (Hassler, 2005). There were no significant ethnic differences in prevalence of suicide attempts between Sami adolescents and 'majority adolescents' (Silviken and Kvernmo, 2007).

Cancer risk among the Sami in 1961–1997 was lower than in the general population (except for increased

risk of stomach cancer) and the non-Sami population of the northern region of Sweden (Hassler et al., 2001). The lowest relative cancer risk was found among the reindeer-herding Sami men, while the highest was observed among non-reindeer herding Sami women (Hassler et al., 2008a).

Neither cardiovascular nor cerebrovascular disease mortality was different between Finnish Sami and the general population (Soininen and Pukkala, 2008). Earlier studies observed a lower risk for cardiovascular disease among Sami in Norway and Finland (Hassler, 2005). Among Swedish Sami, the mortality risk associated with acute myocardial infarction was increased for women, but not men (Hassler et al., 2008b). For subarachnoid hemorrhage, a subtype of stroke, the mortality was 50% to 60% higher among Sami than non-Sami, while the overall risk of dying from stroke was similar between the two groups (Hassler et al., 2008b).

The prevalence of infectious diseases appears to be low among the Sami compared to other indigenous peoples (Hassler, 2005). The incidence of asthma and allergies seem to be high among Sami school children (Selnes et al., 1999; Hassler, 2005).

It is possible that gradual integration of traditional and modern lifestyles, high living standards compared to some other indigenous peoples in the Arctic, as well as high educational attainment among the Sami have helped to both preserve good health and to facilitate high levels of access to public health services (Hassler et al., 2008b).

8.2.7.5. **Russia**

The Russian Federation appears to apply the term 'indigenous peoples' only to 'numerically small peoples of the North, Siberia and the Far East' (Kozlov et al., 2007). According to the 1996 legislation, these are peoples 'living on the territories of traditional residence of their ancestors, adhering to their original way of life, and believing themselves to be independent ethnic entities; their total number in Russia is less than 50 thousand people.' The 2002 Census of the Russian Federation showed that the sum of all 40 recognised peoples of the North, Siberia and the Far East totalled 279 794 (Kozlov et al., 2007), among them approximately 90 000 are living in polar regions (Bogoyavlenskiy and Siggner, 2004). There are also other ethnic minorities in Arctic Russia which are not considered 'numerically small': they are the Komi (the total number in Russia is 293 406 people); the Komi-Permyaks (125 235), the Yakuts (443 852 in Russia) and the Buryats (445 175 people) (Kozlov et al., 2007). A detailed analysis of the demographics and health status of indigenous peoples of the Russian Arctic was reported by Miretsky and Dudarev (2004).

Life expectancy at birth among the 'numerically small peoples of the north' averaged 45 years in males and 55 years in females (Northern Practical Dictionary, 2004). When these numbers are compared with the all-Russia values, which in 2000–2004 were 58.8 years for males and 72.1 years for females (Young, 2008a), it is clear that there is a significant health disparity affecting indigenous peoples in the Russian Arctic.

Mortality rates as a result of accidents, homicide and suicide are very high in the northern parts of Russia and especially among the indigenous population. Violent deaths, injuries, poisonings and alcohol abuse strongly influence the shortened life expectancy in the North (Kozlov and Lisitsyn, 2008). In 1998–2001, almost 37% of all deaths among Khanty, Mansi, and Nenets in the north of western Siberia were due to injuries, compared to 14% for the Russian Federation (Kozlov and Lisitsyn, 2008).

It was estimated that the number of suicides among northern indigenous people of Russia is likely to exceed the national average (36 per 100 000) by three to four times. The highest rates of suicide are reported in the northern regions of Russia – the Komi Republic (110.3 per 100 000), the Koryak AO (133.5 per 100 000), and the Nenets AO (95.7 per 100 000). Between 24% and 55% of all suicides among indigenous northerners co-occur with alcoholic intoxication (Kozlov, 2006; Kozlov and Lisitsyn, 2008).

Among infectious and parasitic diseases, helminthiases appear to be endemic in the North (Kozlov and Vershubsky, 1999).

Since the collapse of the Soviet Union, there has been a notable reappearance of tuberculosis in Russia. In 2000–2004, the active tuberculosis incidence rate in northern Russia was 91.5 per 100 000 – only slightly higher than the incidence rate for the Russian Federation of 88.8 per 100 000 (Young, 2008a). In all other Arctic countries the 2000–2004 incidence rate of active tuberculosis was below 9 per 100 000 (Young, 2008a). However, it remained very high in Greenland (137.5 per 100 000) and in Nunavut (107.6 per 100 000) (Young, 2008a).

8.2.8. **Concluding comments**

Health status of indigenous people of Greenland and the Arctic regions of the United States, Canada, and the Russian Federation is characterised by disparities, including lower life expectancy, higher infant mortality, higher rates of infectious diseases (particularly among children) and much higher incidences of injuries and suicide. At the same time, higher prevalence of tobacco use, increasingly widespread sedentary lifestyles and ongoing nutritional transition to more calorie-rich and nutrient-poor store-bought foods among some indigenous populations in the Arctic have contributed to an increasing burden of chronic diseases.

It is essential for indigenous peoples' organisations and tribal governments to work with other levels of government in their respective countries to support the establishment and/or active utilisation of indigenous status identifiers for ethnic-specific public health surveillance. This approach would allow better monitoring and analysis of ethnic-specific health status indicators of various indigenous groups, which could form the basis for more appropriate health interventions and could assist in the improvement over time of these indicators.

Examination of a 'wide brushstroke' picture of differences between population groups, not only between indigenous and non-indigenous, but between different indigenous groups, seems to suggest that several intersecting factors are likely to play a pivotal role in assuring the wellness and good health of indigenous peoples and non-indigenous peoples alike. These factors include: education, economic wellbeing, cultural strength, community engagement in shaping its present and future, healthy lifestyle choices, genetic susceptibility and availability of public health services.

8.3. Toxicology

8.3.1. Introduction

Toxicology is an experimental science that aims at identifying deleterious effects which are induced by exposure to chemicals. Compounds are tested on laboratory animals under controlled conditions, such that only the treatment with the test chemical differs between experimental groups. In contrast, epidemiology is observational in nature and aims at identifying factors that are associated with a specific disease in carefully selected groups of human subjects. Evidence from toxicology and epidemiology are complementary in establishing a scientifically valid causal connection between a potential risk factor and a disease. Toxicological studies provide essential data to support the biological plausibility of associations between exposure to toxicants and adverse health effects reported in epidemiological studies. This section provides a limited description of the properties of two 'emerging' contaminants and their toxicological effects. It also describes the results of experimental studies published since the last AMAP human health assessment report (AMAP, 2003) of exposure to environmentally-relevant mixtures of contaminants. The hormonal properties of mixtures of contaminants extracted from plasma samples of Inuit people and associations with reproductive endpoints are described in section 8.4.4.

8.3.2. Toxicology of individual POPs and mixtures of POPs

8.3.2.1. Toxicology of individual compounds

While legacy POPs (organochlorines such as PCBs and chlorinated pesticides) and toxic metals (cadmium [Cd], lead [Pb], Hg) are still of concern for consumers of traditional food in Arctic countries, brominated flame retardants such as the polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDs) and perfluorochemicals are receiving increased attention from the research community. These compounds share several physico-chemical properties with organochlorines: they are extremely persistent in the environment, they resist degradation, they can be subject to long-range transportation processes, and they bioaccumulate in biota, including humans.

8.3.2.1.1. *Polybrominated diphenyl ethers*

PBDEs are structurally similar to PCBs and have been used world-wide as flame retardants in various consumer products (polyurethane furniture foam, plastics for consumer electronics, coatings for draperies and upholstery) since the 1960s (see Chapter 5 for more information on use of these compounds). Trend analyses of concentrations in archived samples of seabirds, beluga whales (*Delphinapterus leucas*) and ringed seals (*Phoca hispida*) collected from Canadian Arctic locations indicated increases since the early 1980s to the present (de Wit et al., 2006). For example, analysis of ringed seal blubber samples collected from Holman Island illustrated exponential increases in PBDE concentrations from 1981 to 2000 which were consistent with global production figures for the penta commercial PBDE mixture (Ikonomou et al., 2002). A similar positive trend has been seen with blubber samples collected from St. Lawrence Estuary beluga whales, but at PBDE concentrations almost 100-fold higher (Lebeuf et al., 2004). In contrast, temporal trend analysis of ringed seal blubber samples collected from East Greenland (1986–2004) did not reveal any significant increase in total PBDE levels (Riget et al., 2006).

Analyses of human milk samples collected in Nunavik have shown almost 10-fold increases in PBDE levels between 1990 and 2001 (mean PBDE concentration of 22 ng/g lipid in 2001). However, in comparison, human residue levels of PBDEs in southern Canadian populations tend to be higher (mean human milk concentration of 64 ng/g lipid), probably from a combination of dietary exposure, indoor air/dust and direct exposure from consumer products (Ryan et al., 2002). Based on a combination of measured and estimated PBDE concentrations in air, soil, dust and foods, it has been suggested that inadvertent ingestion of indoor house dust represents the major contributor to daily exposure for southern Canada urban dwellers (Jones-Otazo et al., 2005). These results have been confirmed in a recent U.S. study which suggested that up to 82% of daily exposure to PBDEs comes from indoor house dust (Lorber, 2008).

There are few to no definitive human data to suggest that current dietary exposures to PBDEs are associated with a health risk. Based on the paucity of human data, a number of experimental toxicology studies have been conducted with both PBDE commercial mixtures and major PBDE congeners usually detected in food and humans. The main effects seen to date include endocrine disruption (thyroid hormone perturbation), neurobehavioral effects (impairments in spontaneous exploration behavior in an open field test, learning and memory processing), liver toxicity and possible reproductive effects (fertility). While continued uncertainty exists as regards the relevance of certain endpoints to humans, a recent summary suggested that at least for the experimental effects involving thyroid hormone changes, there is apparently a fairly large margin of safety when based on internal dose metrics (Darnerud et al., 2007).

8.3.2.1.2. *Perfluorinated chemicals*

Perfluoroalkyl acids (PFAAs) are a family of fluorinated chemicals that consist of a backbone, typically four to fourteen carbons in length, and a charged functional moiety (primarily carboxylate, sulfonate or phosphonate). The two most widely known PFAAs contain an eight-carbon backbone and include perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS).

Owing to their chemical resistance and surfactant properties, perfluorinated chemicals have been used in a wide variety of industrial and consumer applications including adhesives, cosmetics, cleaning products, fire fighting foams, and water-, stain-, and oil-repellent coatings for fabrics and paper (e.g., Teflon®, Scotchgard™) for the last 50 years. However, North American production of PFOS was phased out in 2002 with global production dropping to 175 tonnes by 2003. In contrast, the global production of PFOA increased to 1200 tonnes per year by 2004 (Lau et al., 2007).

The widespread use of these compounds has resulted in their detection in environmental matrices all over the world. Consequently, there are various potential sources of human exposure to perfluorinated chemicals, such as water, food, dust and treated fabrics. Dietary surveys conducted with market-basket food samples collected in southern Canada suggest average dietary exposures to perfluorinated acids is in the range of approximately 250 ng/d, with only low ng/g levels being detected in a few foods (Tittlemier et al., 2007).

PFOS/PFOA and a variety of additional perfluorinated contaminants have also been found in wide range of Canadian Arctic biota. As with commercial foods, the dominant PFAA tends to be PFOS and, within biota, liver contains the highest concentrations (Martin et al., 2004). PFOS was also the perfluorinated chemical occurring in the highest concentration in ringed seal liver samples collected in Greenland, with an apparent positive temporal trend (estimated annual increase of 8.2% from 1986 to 2003) (Bossi et al., 2005a). While analyses of ringed seal liver samples collected from Resolute Bay and Arviat also confirmed a temporal increase in PFOS up to 2000, recent analysis suggests that for both locations, concentrations have begun to decrease with disappearance half-lives ranging from 3.2 to 4.6 years (Butt et al., 2007). This is hypothesized to be due to the production and use phase-out implemented for PFOS.

It has been shown that humans worldwide are exposed to PFOS and PFOA, which have been detected in serum samples from populations in North America, South America, Europe, Asia, and Australia. Olsen et al. (2007b) reported concentrations of PFOS and PFOA in American Red Cross blood donors in the United States. Among the 100 serum samples analyzed for PFOS, the geometric mean was 33.1 ng/mL (95% CI 29.8–36.7) in 2000 compared to 15.1 ng/mL (95% CI 13.3–17.1) in 2005 for the 40 donor plasma samples. The geometric mean concentration for PFOA was 4.5 ng/mL (95% CI 4.1–5.0) in 2000 compared to 2.2 ng/mL (95% CI 1.9–2.6) in 2005. In most cases, occupationally exposed workers have serum levels of both PFOA and PFOS approximately one order of magnitude higher than those reported in the general population. Other PFAAs detected in human tissue include perfluorooctane sulfonamide, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid, 2-(N-ethyl-perfluorooctane sulfonamido) acetic acid, perfluoroheptanoic acid, perfluorononanoate, perfluorodecanoic acid, perfluoroundecanoic acid, perfluorododecanoic acid, perfluoropentanoic acid and perfluorohexanoic acid.

The majority of experimental studies to date have focused on PFOS and PFOA. Research has indicated that they are both well absorbed orally, but poorly eliminated and not extensively metabolized. Both compounds are distributed mainly to the serum, kidney, and liver, with liver concentrations being several times higher than serum concentrations. Major effects that have been observed in experimental animals include histopathological changes in the liver and thyroid, thyroid hormone alterations and changes in serum chemistry parameters, which can occur at dietary intakes as low as 30 μg/kg body weight per day (Covance Laboratories Inc., 2002a,b). There is some evidence to suggest that chronic exposure to PFOS may be associated with an increased liver cancer risk. However, statistically significant increases in tumor incidence were observed only at doses greater than those that induced non-neoplastic effects. In a recent study by Health Canada, rats exposed to concentrations of PFOS ranging from 2 to 100 mg/kg in the diet for 28 days did not exhibit symptoms of immunosuppression (Lefebvre et al., 2008). Toxic effects similar to those induced by PFOS have generally been observed in experimental animals following exposure to PFOA, but at higher doses. For example, exposure of male rats to 0.6 mg/kg body weight per day of PFOA has caused liver effects (Butenhoff et al., 2004).

8.3.2.2. **Toxicology of complex mixtures of POPs**

While the majority of toxicology studies investigate properties of individual chemicals, people in the Arctic whose traditional diet comprises species from the marine food chain are exposed to complex mixtures of chemicals. These mixtures contain persistent organic pollutants and metabolites that are generated from the parent compounds by biotic and abiotic degradation processes; these metabolites can in certain instances be more toxic than the original chemicals.

A series of studies was conducted by researchers at Université Laval (Québec, Canada) to examine the toxicity of a complex mixture that was designed to approximate the mixture of environmental contaminants found in local seal blubber (Table 8.3). Bilrha et al. (2004) fed this mixture to female pigs from four months of age, through pregnancy and until weaning of their first litter. Following weaning, the piglets were assessed for a variety of developmental and immunological parameters at intervals until they reached eight months of age.

There were no signs of maternal toxicity although female pigs in the high-dose group received doses that exceeded tolerable daily intakes by up to two orders of magnitude. There was, however, a dose-dependent decrease in length-at-birth for female piglets (7% decrease at the highest mixture dose). Following contaminant assessment in the piglets at one month of age, immunological tests were conducted up to the age of eight months. Minimal effects were seen with respect to physical development, although there was a slight decrease in testis weight for all animals (not dose-dependent) and sperm motility for the high-dose animals (unpublished data). For immunological endpoints, the most significant finding was a reduction in antibody response to *Mycoplasma hypopneumoniae* vaccination seen in the piglets exposed perinatally to the highest dose from the age of five months onwards. At eight months of age, only 10% of piglets in the high-dose group had what would be considered as a positive response to this antigen, compared to 50% in the controls (Bilrha et al., 2004).

Additional findings included slightly enhanced proliferative responses of lymphocytes and enhanced phagocytic activity of leukocytes, mainly evident in the mid- and high-dose animals. Because the findings became more prevalent as the animals aged, it was suggested that innate or natural immune defense was less affected as compared to acquired immunity.

When assessed at delivery, the pigs showed a dose-dependent increase in plasma concentrations for most of the organochlorines found in the complex mixture. For example, low-, mid- and high-dose group plasma concentrations of PCBs (sum of 14 congeners: International Union for Pure and Applied Chemistry nos. 28, 52, 99, 101, 105, 118, 128, 138, 153, 156, 170, 180, 183, 187) were 153, 1425 and 11 485 μg/kg lipids, respectively (controls not detected). In comparison, the mean concentration of PCBs in plasma samples from Inuit mothers in Nunavik was 397 μg/kg lipids, with a range of up to 1951 μg/kg lipids, or only 6-fold lower than the mean concentration observed in the high-dose group animals (Muckle et al., 2001b).

Table 8·3. Composition of the organochlorine mixture found in seal blubber in Arctic Canada. Source: Bilrha et al. (2004).

Compound	CAS number	% weight of total mix
PCB mixture[a]		32.6
Technical chlordane	57-74-9	21.3
p,p′-DDE	72-55-9	19.3
p,p′-DDT	50-29-3	6.79
Technical toxaphene	8001-35-2	6.54
α-HCH	319-84-6	6.17
Aldrin	309-00-2	2.52
Dieldrin	60-57-1	2.09
1,2,4,5-Tetrachlorobenzene	95-94-3	0.86
p,p′-DDD	72-54-8	0.49
β-HCH	319-85-7	0.46
Hexachlorobenzene	118-74-1	0.35
Mirex	2385-85-5	0.23
γ-HCH	58-89-9	0.20
Pentachlorobenzene	608-93-5	0.18

[a] Mixture containing 2,4,4′-trichlorobiphenyl (320 mg), 2,2′,4,4′-tetrachlorobiphenyl (256 mg), 3,3′,4,4′-tetrachlorobiphenyl (1.4 mg), 3,3′,4,4′,5-pentachlorobiphenyl (6.7 mg), Aroclor 1254 (12.8 g) and Aroclor 1260 (19.2 g).

In a similar study design, Anas and colleagues investigated whether *in utero* and lactational exposure of male rats to the same organochlorine mixture alters reproductive development and function. Female rats were gavaged with either corn oil (controls) or the organochlorine mixture in increasing doses (low, medium, and high) for five weeks before mating and through gestation (Anas et al., 2005). Developmental effects were monitored in the male offspring from Postnatal Day (PND) 2 until PND 90. The high-dose mixture reduced the number of pups per litter, percentage of live offspring, and pup weight. Because only three rats from the high-dose treatment survived, data from this group beyond PND 2 were not included in the statistical analyses. Based on the time of preputial separation, puberty was delayed in the pups from treated dams. Testes weights in the medium-dose group were greater than those in controls on PND 21, whereas ventral prostate weights were lower for the medium-dose group on PND 60. On PND 90, weights of the epididymis, ventral prostate, and seminal vesicle of the medium-dose rats were reduced compared to those of controls. Also on PND 90, sperm motility parameters assessed by computer-assisted sperm analysis were altered in the low- and medium-dose groups. Testicular and epididymal morphology was severely affected in rats exposed to the high dose of the mixture. Serum testosterone, luteinizing hormone, *follicle-stimulating hormone*, prolactin, and total thyroxine levels were not modified by treatments. The authors concluded that *in utero* and lactational exposure to this environmentally relevant organochlorine mixture adversely affects the reproductive system of male rats, suggesting a possible reproductive health hazard for humans and other species (Anas et al., 2005). The adverse effects might be a net effect of all compounds found in this complex mixture or, as the authors hypothesized, might be mediated by antiandrogenic compounds such as *p,p′*-DDE and PCBs that are present in the mixture.

Campagna et al. (2001) tested the same complex mixture *in vitro* for its ability to affect oocyte maturation, fertilization, and subsequent embryo development. Cumulus-oocyte complexes from sows were cultured in *in vitro* maturation medium containing increasing concentrations of the organochlorine mixture. Organochlorines reduced the quality of cumulus expansion and the viability of cumulus cells in a dose-response manner. The mixture did not affect the rates of oocyte degeneration, sperm penetration, and development to morula. However, the mixture caused a concentration-dependent increase in the incidence of incompletely matured oocytes and a decrease in polyspermy rate. Blastocyst formation and number of

cells per blastocyst also diminished with organochlorine concentration. In supplementary experiments involving exposure of oocytes and sperm during fertilization (Campagna et al., 2002), the organochlorine mixture diminished oocyte penetration rates and polyspermy. The mixture did not affect rates of oocyte cleavage nor development to multicell embryos. However, rates of development to the blastocyst stage were lower at the highest concentration at which oocyte penetration was observed. Exposure of frozen-thawed pig sperm to the mixture resulted in an immediate decrease in sperm motility parameters, followed by diminished viability two hours later. Globally, these results suggest that exposing porcine oocytes and sperm to an environmentally pertinent organochlorine mixture *in vitro* adversely affects oocyte development, polyspermy and sperm fertility, and further embryonic development, again supporting recent concerns that such pollutants harm reproductive health in humans and other species.

The same group examined the effect of the metabolized organochlorine mixture on porcine cumulus-oocyte complexes (COCs) *in vitro* (Campagna et al., 2007). The metabolized mixture was extracted from the plasma of sows that were treated with the original organochlorine mixture in the study by Bilrha and colleagues (Bilrha et al., 2004). The metabolized mixture did not affect cumulus expansion, oocyte maturation, penetration of the egg, development to blastocyst, or the number of cells per blastocyst. These results suggest that metabolites of the parent compounds do not markedly increase the toxicity of the original exposure mixture on gametes. High concentrations of the metabolized mixture could not be tested because of the limited quantities which could be extracted from the plasma of the sows.

Toxicologists at Health Canada tested the capacity of another organochlorine mixture to interfere with development in the rat model (Chu et al., 2008). Their mixture (see Table 8.4) was designed to generate, in the plasma of treated dams, a mixture similar in composition to that found in plasma samples from Inuit mothers. Female Sprague-Dawley rats were bred and assigned to one of three doses of the chemical mixture (0.05, 0.5, 5.0 mg/kg/d) and dosed from gestation day one until PND 21. Offspring were exposed to the mixture *in utero* and through lactation.

Exposure to the chemical mixture had no effect on the reproductive parameters of dams (litter size, gestational weight gain and number of live offspring). However, treatment with the highest dose caused decreases in maternal weight gain during lactation and in offspring weight gain that persisted into adulthood. This dose also increased mortality rates in pups prior to weaning, but overall mortality rates for the offspring in this study were considerably lower than those reported by others using lower doses of only methylmercury (MeHg) (Beyrouty and Chan, 2006). In addition, the 5 mg/kg bw dose produced changes in organ weight, and biochemical and histopathological changes in liver, thyroid, and spleen.

Neurobehavioral disturbances were also noted in offspring at the 5 mg/kg bw dose including a decrease of pre-weaning neuromuscular development (grip strength) and hyperactivity at PND 16. These alterations in motor activity patterns were no longer present by PND 48. Evaluations in the Morris Water Maze revealed that the high dose affected learning and memory in adults. In the hole-board apparatus, there were indications of either altered motor performance or decreased reactivity to a novel environment in all dose groups. Dose-dependent changes in brain dopamine and serotonin levels were noted at PND 35 in high-dose group pups (Bowers, pers. comm., 2008). This study also demonstrated that the blood level in rats given the 5 mg/kg dose, where most of the effects were observed, is 100-fold higher than the blood level in the 0.05 mg/kg group, which is comparable to that found in humans living in the Canadian Arctic (Chu et al., 2008).

A preliminary report of the assessment of bone structure and morphology indicates that the highest mixture dose decreased femur length in both male and female offspring at PND 35 (Stern et al., 2004). Treatment with high doses also diminished bone cortical area and bone mineral content in male and female pups. Furthermore, bone strength was also decreased. The lowest mixture dose did not affect bone strength; however it appears to have increased femur length and bone cortical thickness in PND-35 pups. Thus even the lowest dose of the mixture, which generates plasma concentrations of key POPs in treated dams similar to those measured in plasma samples of Inuit mothers, appears to induce some measured changes in offspring bone development. Whether these modifications persist into adulthood is currently under evaluation. Interestingly, there was some indication of a negative association between PCB plasma levels and quantitative ultrasound bone parameters in a group of peri- and post-menopausal Inuit women from Greenland (see Côté et al., 2006 and section 8.4.7.8).

Table 8-4. Composition of the food chain contaminant mixture [a] in Health Canada studies. Source: Chu et al. (2008).

PCB Congener	mg/mL corn oil	Other compounds	mg/mL corn oil
28	0.0072	Aldrin	0.0049
52	0.0154	β-HCH	0.0746
99	0.0973	Cis-nonachlor	0.0525
101	0.0145	*p,p'*-DDE	0.9187
105	0.0165	*p,p'*-DDT	0.0569
118	0.0727	Dieldrin	0.0223
128	0.0071	Hexachlorobenzene	0.2961
138	0.2146	Heptachlor epoxide	0.0232
153	0.3177	Mirex	0.0291
156	0.029	Oxychlordane	0.1359
170	0.0562	Toxaphene	0.0699
180	0.1522	*trans*-Nonachlor	0.2203
183	0.0193	Methylmercury Cl	1.9965
187	0.0795		
Sum PCB	1.0992	Sum Non-PCB	3.9009
Total for all chemicals			5.0001

[a] Composition of the corn oil solution used to treat dams in the highest dose group (5mg/kg body weight).

A second series of mixture studies conducted by Health Canada researchers examined the potential impact of individual components of the chemical mixture described above (PCBs, organochlorine pesticides, Hg). Comparisons of the toxicity of the full mixture against specific components of the mixture indicated that the increase in pup mortality induced by the full mixture could be attributed to the MeHg component (Pelletier et al., 2009).

Padhi et al. (2008) examined modifications in the expression of genes involved in nerve cell differentiation, migration, myelination and synaptic transmission in the cerebellum of PND 14 pups of the full mixture and separate mixture groups. It was found that the full mixture produced minimal changes in gene expression, whereas PCB, MeHg and the organochlorine pesticide components all altered the expression of a number of genes.

Eriksson et al. (2006) published results indicating that PBDEs and PCBs can interact and enhance developmental neurobehavioral defects when the exposure occurs during a critical stage of neonatal brain development. Hence future studies should include PBDEs in the POPs mixture to be evaluated in animal models for adverse neurodevelopmental effects.

8.3.2.3. **Summary and concluding comments**

Investigating the toxicological properties of environmentally-relevant mixtures of POPs is essential to determine the biological plausibility of associations noted between exposure to these compounds and adverse health effects in epidemiological studies. For example, results indicating immunosuppression, expressed primarily as a reduction in antibody response, in piglets exposed prenatally to such a mixture have increased the credibility of the relation between transplacental POPs exposure and increased susceptibility to infections noted in Inuit and Faroese infants (see section 8.4.6.1).

In utero and lactational exposures to environmentally relevant organochlorine mixtures adversely affect the reproductive system of test animals, suggesting a possible reproductive health hazard for humans and other species. Studies with pigs, which have a similar reproductive system to humans, indicate that exposure of oocytes and sperm to environmentally pertinent organochlorine mixtures *in vitro* adversely affects oocyte development, polyspermy, sperm fertility and embryonic development.

Treatment of female rats with the highest dose levels of environmentally-relevant mixtures led to decreases in maternal weight gain during lactation, persistent weight gain in offspring and increased mortality rates in pups prior to weaning. The interactions between MeHg and POPs in the mixtures warrants further study as lower levels of MeHg administered alone have been found to lead to more pup mortality than found in mixture studies containing higher levels of MeHg.

Studies with rats have also confirmed that mixtures of environmental chemicals can adversely affect learning, memory, motor performance, reactivity, and brain dopamine and serotonin levels in adult animals. The effects on learning and memory appear to be elicited primarily by MeHg and PCB and to be additive based on studies using the compounds individually. These findings with animals support observations reported in some epidemiological studies of infants and children (see section 8.4.5).

Environmentally-relevant mixtures may also affect bone density (diminished bone cortical area and bone mineral content) in male and female rat pups. These findings may be significant for humans as indications of a negative association between PCB plasma levels and quantitative ultrasound bone parameters have been reported in a group of peri- and post-menopausal Inuit women from Greenland.

It is unclear if and how environmental mixtures affect gene expression. Exposure to the full mixture produced minimal changes in gene expression, whereas exposure to PCB, MeHg and the organochlorine pesticide components of the mixture each altered the expression of a number of genes. More research is needed to understand these findings.

In general, studies of chemical mixtures indicate that data from single-chemical experiments cannot be used to predict the risk resulting from exposure to complex mixtures of POPs. Interactions between components of the mixture not only modify the disposition of individual components but also their dose-response relationship for various developmental endpoints. Based on this conclusion, it is tempting to speculate that some of the discrepancies observed between epidemiological studies examining the neurobehavioral effects of perinatal MeHg exposure (see section 8.4.5) could be related to differences between populations in exposure to other POPs that may alter the developmental toxicity of MeHg.

There is also a need to monitor the occurrence of 'emerging' contaminants in the food chain such as brominated flame retardants and perfluoroalkyl compounds. Although existing data on exposure in the North do not currently indicate a risk from exposure to emerging compounds, the toxicology and epidemiology data base for these chemicals is weak and should be strengthened.

8.4. Epidemiology

8.4.1. **Introduction**

Over the past few decades most research efforts in the Arctic were focused on characterizing the exposure of Northerners to contaminants. In the early 1990s, epidemiological studies began to evaluate the possible health impacts of this exposure.

This section provides a brief overview and update of epidemiological findings since the previous AMAP assessment of human health in the Arctic (AMAP, 2003). Most of this section concerns prenatal exposure and adverse developmental effects resulting in altered immune and nervous system function early in life. However, cardiovascular outcomes related to Hg

exposure are now under investigation in children and adults. Some new data suggest that exposure to POPs might result in effects on the hormonal system. Steroid hormone disruption might be associated, for example, with osteoporosis and male fertility abnormalities. Thyroid hormone modulation might also be investigated considering preliminary experimental data on the toxicity of some relatively recently detected POPs.

Conducting epidemiological studies in the Arctic is difficult and should take into account the following specific considerations: mixtures of contaminants found in the Arctic, population size, toxicant–nutrient interactions, genetic factors, and non-dietary confounding factors.

8.4.1.1. **Mixtures of contaminants found in the Arctic**

Interactions between chemicals within ecologically-relevant mixtures (at relevant concentrations) can result in an effect different from the sum of the effects of each individual component of the mixture (see section 8.3.2). Some 'emerging' contaminants such as PFOS or PBDEs are now found in Arctic biota and humans due to both increasing concentrations within the Arctic environment and increases in analytical capabilities. These emerging contaminants have different pathways of exposure, and different half lives. Some are highly correlated with legacy POPs such as PCBs, others are not. Body burdens for emerging POPs are sometimes higher in Arctic populations compared to body burdens in populations at lower latitudes, but also sometimes lower. Using new complex matrices of exposure raises methodological challenges for ongoing and future epidemiological studies. Effects of mixtures need to be better understood to better classify individuals under study.

8.4.1.2. **Population size**

The small size of populations living in the Arctic limits the use of epidemiology. The number of disease cases is small and case control studies are extremely difficult to conduct. Usually, only cross-sectional and cohort designs are possible. Health outcomes most amenable to epidemiological research in the Arctic are those with a range of stages from normal to abnormal, which can be measured in all individuals (e.g., neurodevelopment, immune parameters, bone density, fertility parameters) and are not based on a stochastic distribution (having the disease or not; for example, cancer). One of the ways to avoid this limitation is to implement circumpolar studies such as the International Inuit Cohort Study which aims to recruit 10 000 Inuit or to merge ongoing cohorts as exist for children.

8.4.1.3. **Toxicant–nutrient interactions**

The possibility that nutrients present in seafood could modify or counteract the toxicity of contaminants is highly probable and specific to fish-eating populations. These interactions need to be better understood. Epidemiological studies looking at health outcomes associated with Hg or POPs exposure are at particularly high risk of being biased by confounding association.

The main source of most contaminants for human populations in the Arctic is fish and marine mammal consumption. This is also the main source of major nutrients such as polyunsaturated fatty acids (PUFAs) and Se in these populations; PUFAs are widely agreed to play an important role in brain development as well as cardiovascular protection. Thyroid abnormalities could be associated with POPs as well as with iodine intake; both of which are obtained from seafood. Controlling for these confounding factors is a major challenge when autocorrelations in the data are strong.

8.4.1.4. **Genetic factors**

It is important to recognize that genetic variability may affect the susceptibility of individuals or populations to the effects of pollutants. Gene/environment interactions could also explain why some populations or individuals are more susceptible than others. Because few genetic studies have been conducted in the Arctic, and because the various indigenous peoples have their own specific genetic background, it is important that the impact of genetic polymorphisms involved in the metabolism and toxicity of xenobiotic compounds in the Arctic are evaluated. New data suggest that the Inuit have specific gene polymorphism that could potentially modify their susceptibility to contaminants or nutrients. This is also discussed in Chapter 6.

8.4.1.5. **Non-dietary confounding factors**

Many health endpoints such as child neurodevelopment or cardiovascular diseases have multifactorial causes and environmental stressors can contribute in varying degrees to the etiology of these diseases. Compared to the role played by lifestyle factors (such as alcohol use, tobacco use, drug abuse, exercise and diet) and genetic factors in the etiology of most diseases, contaminants are likely to play only a modest role. Furthermore, these environmental stressors are highly preventable (e.g., through global restrictions on dangerous substances) and to a degree avoidable (e.g., through diet modification).

8.4.2. **Biomarkers of exposure and effects in human populations**

Biomonitoring studies are useful for identifying adverse responses induced by exposure to environmental contaminants in small populations, such as those living within the Arctic, in which epidemiological studies would not have the power to detect associations of public health relevance. Biomarkers of internal dose, biologically-effective dose, early biological effect and alteration of structure/function can be measured along the pathophysiological sequence from exposure to disease (Figure 8.8).

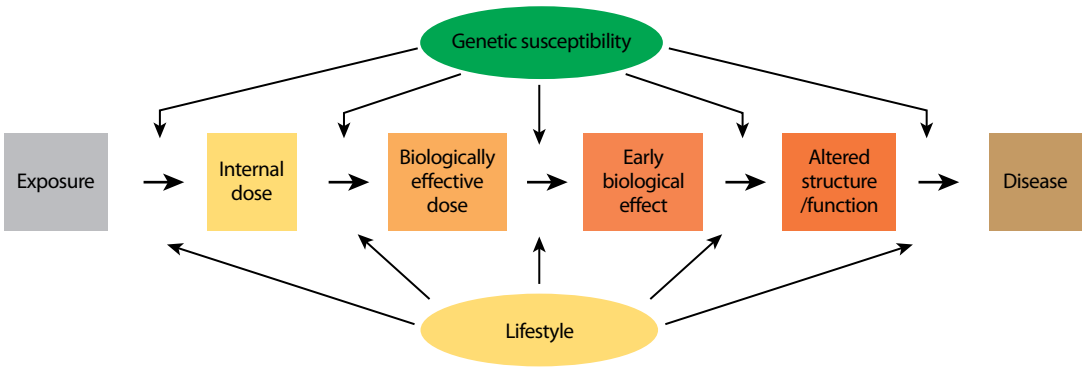


Figure 8·8. Different types of biomarker in the pathogenic sequence between exposure and disease.

8.4.2.1. **Cytochrome P450 activity**

A classic example of a biomarker of early biological effect is the activity/expression of cytochrome P450 enzymes (CYPs) which are involved in the biotransformation of a variety of exogenous and endogenous chemicals. Compounds such as PCBs and 1,1-dichloro-2,2-bis (*p*-chlorophenyl)ethene (*p,p'*-DDE) are well known CYP inducers. Through activation of the aryl hydrocarbon receptor (AhR) and pregnane X receptor, PCBs can induce various isoforms of CYPs including CYP1A1 and CYP3A4 (Safe, 1994; Easterbrook et al., 2001).

Petersen et al. (2007) determined the variability of CYP3A4 activity in relation to serum concentrations of PCBs and other organochlorines in 310 randomly selected healthy Faroese residents aged 18 to 60 years. CYP3A4 activity was determined based on the urinary 6ß-hydroxycortisol : cortisol ratio. While there were significant associations between this ratio and serum concentrations of ΣPCBs, *p,p'*-DDE, *o,p'*-DDT and hexachlorobenzene (HCB), the associations were statistically significant in men only. Men exhibited nearly two-fold higher concentrations of PCBs and other organochlorines than women, which may explain why the relation between CYP3A4 activity and serum concentrations of these contaminants was only observed in men. Female hormones may also mask the effect of organochlorines on CYP3A4 activity in women. According to Petersen and co-workers, attention should be paid to the possible disruption of endocrine homeostasis, because CYP3A4 catalyzes the 6β-hydroxylation of several steroids. Another cause for concern is the possible altered efficacy of drugs metabolized by CYP3A4 in this population highly exposed to PCBs.

Some PCB congeners are CYP1A1 inducers and induction of this enzyme in the placenta of smoking mothers has been linked to adverse effects on fetal development (Pelkonen et al., 1979). Genetic variants of CYP1A1 have also been linked to reduced birth weight in neonates born to smoking mothers (Wang et al., 2002). Pereg et al. (2002) examined the relation between plasma PCB concentrations and placental CYP1A1 activity measured as ethoxyresofurin-*O*-deethylase (EROD) activity in 35 Inuit women from Nunavik. Thirty women from a southern Québec community exposed to background levels of organochlorines constituted the reference group. Results showed that concentrations of PCBs in cord plasma were strongly correlated to levels in placenta and were on average 4-fold higher in Inuit women than in women from southern Québec. However, despite this difference in PCB body burden, both groups had similar EROD activities when the data were stratified according to tobacco smoking (non smokers, moderate smokers, heavy smokers). Multivariate analysis did not indicate that PCBs made a significant contribution to EROD activity when tobacco smoking was included in the model. This means that PCB exposure in these Inuit women did not significantly modulate CYP1A1 activity in the placenta; in this population only tobacco smoking was related to EROD activity.

8.4.2.2. **Activation of the aryl hydrocarbon receptor**

Polyhalogenated aromatic hydrocarbons that share structural similarities with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) are referred to as 'dioxin-like compounds'. These dioxin-like compounds bind to the AhR and can elicit a wide range of toxic effects (see Box 8.2). Analysis of plasma samples obtained from Inuit adults recruited during a Santé Québec study in Nunavik in 1992 revealed that concentrations of dioxin-like compounds were on average 7-fold higher than in samples from individuals living in southern Québec (Ayotte et al., 1997). In the latter study, analyses by HRGC/HRMS (high-resolution gas chromatography/high resolution mass spectrometry) were performed on pooled samples, because analysis of all 492 samples would have incurred prohibitive costs.

In the course of a prospective epidemiological study initiated in Nunavik, Medehouenou et al. (2007) analyzed plasma samples obtained from 874 Inuit adults using a dioxin-responsive reporter gene (see Box 8.3). The mean plasma concentration of dioxin-like compounds measured in dioxin 'toxic equivalents' (TEQs) was 89 pg TEQ/L (median: 65 pg TEQ/L), with values ranging from <30 to 533 pg TEQ/L. Age, body mass index and marine mammal blubber consumption were positively correlated to plasma concentrations ($p < 0.001$) of

Box 8·2. AhR-mediated dioxin-like serum activities

Exposure to dioxins (e.g., 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; TCDD) and dioxin-like compounds such as *non-ortho* and *mono-ortho* polychlorinated biphenyls (PCBs) may cause a series of negative effects both in laboratory animals and in humans, including dermal toxicity (Meulenbelt and de Vries, 2005), carcinogenicity (Steenland et al., 2004), immunotoxicity and adverse effects on reproductive, neurobehavioral, and endocrine functions (Lindstrom et al., 1995; Weisglas-Kuperus, 1998). The toxicity of dioxin and dioxin-like compounds is mediated mainly through binding to the aryl hydrocarbon receptor or AhR (Rowlands and Gustafsson, 1997). This receptor may also be involved in the reported interference of POPs or their metabolites with hormone receptors (Bonefeld-Jorgensen et al., 1997, 2001; Kato et al., 2005; Mortensen et al., 2007, Novák et al., 2009; Braathen et al., 2009). Studies have demonstrated the presence of a two-way cross talk between the intracellular signaling pathways involving the three receptors, ER (Kharat and Saatcioglu, 1996; Safe and Krishnan, 1995), AR (Kizu et al., 2003) and AhR. However, human epidemiological data are limited and major gaps in knowledge continue to preclude evidence-based risk assessment. Thus, there is a need for an integrated risk assessment of dioxins and dioxin-like compounds in humans (Box 8.3). In addition to 2,3,7,8-chloro-substituted dibenzo-*p*-dioxins and dibenzofurans, an array of xenobiotic dioxin-like compounds, including PCBs, plastic components (Bonefeld-Jorgensen et al., 2007; Krüger et al., 2008c) and pesticides such as iprodione, chlorpyrifos and prochloraz can activate the AhR pathway (Long et al., 2003). Because these compounds are often are found in low concentrations, large serum samples are needed for the expensive concentration determination by analytical chemistry methods. Therefore, a cheaper cell culture based bioassay (AhR-CALUX) requiring extraction of a smaller sample volume than the conventional analytical chemistry method has been developed for the determination of the activity of the summed dioxin-like compounds in serum collected during epidemiological studies (see Box 8.3).

Box 8·3. TEQs and the CALUX assay

Since dioxins and dioxin-like compounds exist as complex mixtures of various congeners throughout the environment, the concept of TEQ (TCDD toxic equivalent) has been introduced to simplify risk assessment and regulatory control (Van den Berg et al., 1998). The classical WHO-TEQs are calculated by multiplying the concentration of individual PCDDs/PCDFs/PCBs by their respective Toxic Equivalency Factors (TEFs), which correspond to the relative potency of each PCDD/PCDF/PCB congener to generate AhR-mediated effects in relation to that of TCDD, the most potent AhR ligand. Previous studies emphasize that assessment of the toxicological potential of a chemical mixture is much more complex than can be deduced by a given calculated TEQ value (Bonefeld-Jorgensen et al., 2001; Van Overmeire et al., 2001; Bonefeld-Jørgensen and Ayotte, 2003). There are several drawbacks to using the TEF concept for risk assessment of mixtures of POPs such as expensive and time consuming gas chromatography mass spectrometry (GC-MS) determinations, small concentrations of individual congeners, presence of compounds not routinely measured or unknown substances with AhR affinity, the lack of TEF values for several POPs, and possible antagonistic or synergistic interactions between POPs (Safe, 1994; Aarts et al., 1995; Long et al., 2003).

The *in vitro* AhR-mediated CALUX bioassay has proven to be a quick and sensitive assay to detect the AhR-mediated potential of pure chemicals (Safe, 1994; Aarts et al., 1995; Garrison et al., 1996; Long et al., 2003), extracts of environmental and biological matrices and thus the total AhR-TEQ value (CALUX-TEQ) of complex mixtures as found in sediment, groundwater, bovine and human milk, human serum and follicular fluid (Denison et al., 1996; Murk et al., 1996; Bovee et al., 1998; Pauwels et al., 2000; Behnisch et al., 2002; Laier et al., 2003). The AhR-TEQ (CALUX-TEQ) is obtained by interpolation of the AhR-CALUX values onto a parallel TCDD concentration-response sigmoid Hill curve (Long et al., 2006). Compared to the calculated chemical-derived TEQ (WHO-TEQ), the CALUX based AhR-TEQ might be more biologically relevant for the risk assessment of dioxins and dioxin-like compounds and is certainly far less expensive than high resolution mass spectrometry analysis.

dioxin-like compounds. Plasma concentrations of PCB congeners 105, 118, 153 and 156 were determined by HRGC/MS and were found to be positively correlated to concentrations of dioxin-like compounds (Pearson's r = 0.61–0.63, $p < 0.001$). These kinds of cohort studies and analyses enable scientists to establish associations between exposure to dioxin-like compounds and the risk of chronic diseases in the Inuit population. Activation of the AhR-signaling pathway by plasma extracts is further discussed in section 8.4.4.2.

8.4.2.3. **Genotoxicity**

In the course of the 2004 Nunavik Health Survey (see Box 8.4), biomarkers of genotoxicity were measured in subgroups of Inuit adults. The rationale for this work was that exposure to food-chain contaminants such as MeHg and PCBs can induce oxidative stress and DNA damage, which is a primary event in carcinogenicity. This hypothesis is supported by the work of Wulf et al. (1986), who reported that the frequency of sister chromatid exchanges (SCE/cell) in Greenlandic Inuit increased with the consumption of food items from seal. Further analyses revealed that blood Hg concentration explained 16.3% of the total variation in SCE/cell.

Laidaoui and Ayotte (2006) used the alkaline version of the Comet assay to evaluate DNA strand breaks in peripheral blood mononuclear cells (PBMCs) of 298 Inuit adults (131 men and 167 women) who participated in the Nunavik Health Study. Relations between DNA damage and lifestyle, nutritional and environmental factors were also examined. Examples of comets obtained in this study are shown in Figure 8.9.

Box 8·4. 2004 Nunavik Health Survey

In 2003, the Nunavik Regional Board of Health and Social Services decided to organize an extensive health survey in Nunavik in order to verify the evolution of health status and risk factors of the population. The Institut National de Santé Publique du Québec (INSPQ) planned, administrated and coordinated the survey. The general aim of the 2004 Nunavik Inuit Health Survey was to gather social and health information on a set of themes including various health indicators, physical measurements, social, environmental, and living conditions, thus updating the health and well-being profile of the Inuit population of Nunavik (approximately 10 000 population in 14 coastal communities). Over 500 households agreed to be interviewed and over 1000 individuals participated in more detailed surveys or biological tests. The survey was able to compare 2004 trends to those observed in an earlier survey in 1992. Data collected in 2004 also allowed researchers to compare the Inuit to other Quebecers. The findings of the survey are reported in a large number of journal publications and 20 sub-component reports. More details at: www.inspq.qc.ca/pdf/publications/nunavik.asp.

The percentage of DNA located in the tail of the comet (%DNA) reflects the number of DNA strand breaks. Mean %DNA was 4.0 (SD 1.9), with values ranging from 0.3 to 9.5. The %DNA values were similar in men and women. A negative correlation was observed between age and %DNA. Simple correlation analyses did not reveal any statistically significant association between DNA damage and concentrations of Hg, Pb or Cd in blood. DNA damage was also not related to dietary intake of traditional foods (as calculated from the food frequency questionnaire data) or to smoking. However, results did indicate a link between alcohol consumption and DNA damage in this population (drinkers, mean %DNA = 4.2 [SD 1.9] vs abstainers, mean %DNA = 3.4 [SD 1.7]; $p = 0.002$).

In order to assess whether genotoxic effects could result from exposure of environmental contaminants at the chromosomal level, the same research group performed the cytokinesis-blocked micronuclei (CBMN) assay in cultivated peripheral blood lymphocytes of 68 Inuit women recruited in the course of the Nunavik Health Study (Ayotte et al., 2006). Blood concentrations of Cd, cobalt, copper, Pb, Hg, molybdenum, nickel, Se, and zinc were determined by inductively-coupled plasma mass spectrometry. Socio-demographic characteristics and lifestyle habits were documented using questionnaires. The mean age of the Inuit women was 36 years, ranging from 18 to 74 years. The median frequency of micronucleated cells (MNCs) was 5 per 1000 binucleated cells (interquantile range, 2–8), a value 1.8-fold lower than that obtained from a group of 110 women from the Quebec City region who were tested in the same laboratory during the same time period by the same observer (9.0 MNCs per 1000 binucleated cells, SD 7.6). Results showed that age was positively correlated to the frequency of MNCs in both groups and that blood concentrations of the metals and metalloids studied were not. These results indicate that Inuit women do not exhibit an elevated level of genotoxic damage, despite their relatively high exposure to metals and metalloids (Ayotte et al., 2006).

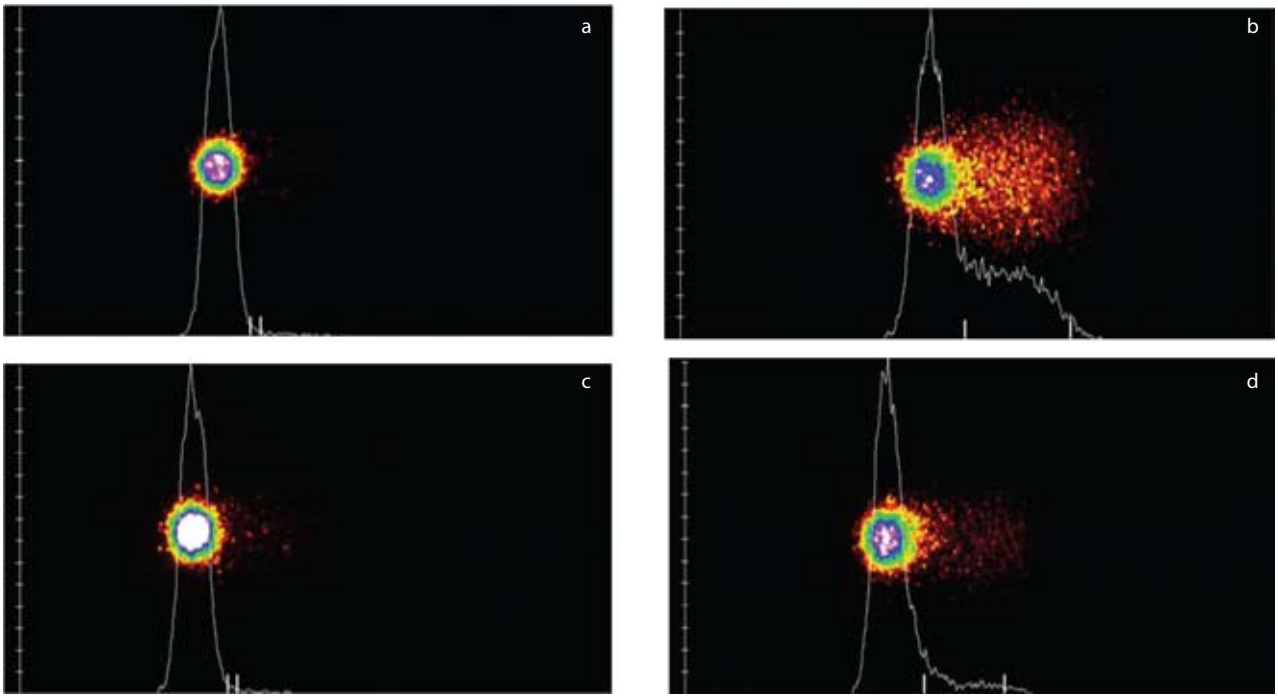


Figure 8·9. Representative comet images for (a) a healthy donor (%DNA in tail = 0.67); (b) benzo[*a*]pyrene diol epoxide treated cells from a healthy donor (%DNA in tail = 32.9); (c) a participant with low DNA damage (%DNA in tail = 0.28); (d) a participant with some DNA damage (%DNA in tail = 9.50). Source: Laidaoui and Ayotte (2006).

8.4.2.4. **Epigenetic modifications**

Xenobiotic agents, such as POPs may operate at the epigenetic level, meaning that they can influence chromosomal stability and gene expression, instead of directly changing DNA sequences. An epigenetic mechanism, DNA methylation, has been associated with cancer initiation and progression. Greenlandic Inuit have some of the highest reported levels of POPs worldwide. Rusiecki et al. (2008) analyzed the relationship between plasma POPs concentrations and global DNA methylation levels (% methylated cytosine) in DNA extracted from blood samples of 70 Greenlandic Inuit (61 men, 9 women). The authors used pyrosequencing to estimate global DNA methylation via *Alu* and long interspersed nucleotide element (LINE-1) assays of bisulfite-treated DNA. Linear regressions, adjusted for age and tobacco smoking, showed significant inverse linear relationships mainly for the Alu assay for the following POPs: *p,p'*-DDT ($\beta = -0.26$, $p = 0.01$), *p,p'*-DDE ($\beta = -0.38$, $p = 0.01$), β-BHC ($\beta = -0.48$, $p < 0.01$), oxychlordane ($\beta = -0.32$, $p < 0.01$), α-chlordane ($\beta = -0.75$, $p = 0.05$), mirex ($\beta = -0.27$, $p = 0.01$), ΣPCBs ($\beta = -0.56$, $p < 0.01$), and ΣPOPs ($\beta = -0.48$, $p < 0.01$). Results for linear regressions using the LINE-1 assay generally showed beta estimates of a similar magnitude to those using the Alu assay; however, none was statistically significant. This is the first study to investigate environmental exposure to POPs and DNA methylation levels in a human population. Global methylation levels were inversely associated with blood plasma levels for several POPs and merit further investigation to assess the possible association with cancer risk.

8.4.2.5. **Paraoxonase activity**

In a recent review of the literature examining the evidence of cardiovascular effects induced by exposure to MeHg, Stern (2005) concluded that realistic exposure to MeHg from fish consumption could be associated with heart diseases, in particular myocardial infarction. The main evidence supporting this conclusion was provided by Finnish studies conducted among consumers of non-fatty fish (Salonen et al., 1995). As different populations consume different species of fish and in some cases marine mammals, the risk of cardiovascular effects may not be related simply to MeHg exposure, but also to nutrients such as n-3 polyunsaturated fatty acids (n-3 PUFAs) and Se that are known to be abundant in some marine foods. Paraoxonase 1 (PON1), an enzyme located in the high density lipoprotein (HDL) fraction of blood lipids, may play a role in cardiovascular disease by metabolizing toxic oxidized lipids associated with low density liproprotein (LDL) and HDL (Mackness et al., 1998; Aviram, 2000). MeHg has been shown to inhibit PON1 activity *in vitro* (Gonzalvo et al., 1997; Debord et al., 2003) and therefore it was hypothesized that blood Hg levels may be linked to decreased serum PON1 activity in Inuit people who are exposed to MeHg through their marine-based diet. Carrier et al. (2007) measured serum PON1 activity and blood concentrations of Hg and other metals in 900 Inuit adults who participated in the Nunavik Health Study (see Box 8.4). Univariate analyses indicated that PON1 activities were positively correlated to blood Se (Pearson's $r = 0.12$; $p < 0.001$) and blood Hg levels ($r = 0.10$, $p = 0.004$). However, in a multiple regression model adjusted for age of participants, alcohol consumption, blood HDL levels and eicosapentaenoic content of erythrocyte membranes, blood Se concentrations remained positively associated with PON1 activities (standardized beta = 0.13, $p = 0.007$), whereas blood Hg concentrations were negatively associated with PON1 activities (standardized beta = -0.14, $p = 0.013$). These results suggest that MeHg exposure may have a slight inhibitory effect on PON1 activity which seems to be offset by Se intake. The research group will also examine the relation between PON1 activity, the concentration of oxidized LDL and the thickness of the carotid artery *intima media*, the latter being a biomarker of atherosclerosis (see also Chapter 7).

8.4.2.6. **Summary and concluding comments**

Several epidemiological biomonitoring studies have been conducted in circumpolar populations aimed at investigating relationships between exposure to POPs and biomarkers of enzyme induction, alterations of activity of the AhR (that might increase the risk of endocrine disruption), genetic alterations and cardiovascular effects.

Relationships have been observed between exposure to PCBs and other POPs and CYP3A4 activity in Faroese men, which could have consequences for metabolism of steroid hormones, hormone homoestasis and drug metabolism.

In the Inuit population of Nunavik, a negative association was found between MeHg exposure and paraoxonase activity, suggesting a possible adverse effect of the organometallic compound on the cardiovascular system. It will be interesting to see if paraoxonase activity is in turn linked with markers of atherosclerosis in this population.

Finally, global hypomethylation of the genome has been linked to genomic instability and the risk of cancer. The possibility that organochlorines can decrease global genomic methylation is intriguing and should be examined in other circumpolar populations.

8.4.3. **Maternal and child health and contaminants**

In general, the biggest 'health problem' in the circumpolar areas is the large inequality in health care and socio-economic conditions compared to those in the south (see section 8.2). A number of studies are underway that explore the long-term effects of contaminants on maternal and child health. Comprehensive information about circumpolar maternal and child health conditions has been reported by Health Canada (2005).

The growing fetus and newborn children are especially sensitive to the toxic effects of many POPs and heavy metals found in the environment. Several

of these substances move from mother to fetus via the umbilical cord and to the developing child via breast milk. Levels of these contaminants in maternal blood during pregnancy give an indication of the potential risk to the developing fetus. Of particular concern are long-term, subtle effects, for example, adverse reproductive and pregnancy outcomes, reduced childhood defense against diseases (immune system impacts), and impairment of children's mental development.

There is a lack of recent literature on pregnancy outcomes and contaminants in the Arctic. The literature cited in this section is based on new Norwegian-Russian projects on reproductive health and contaminants, partly on indigenous population studies, and partly on studies of populations living in the vicinity of big refineries, such as the Pechenganikel metallurgical complex on the Kola Peninsula in northwest Russia. Outcomes of concern include maternal health during pregnancy, placenta function and impact from contaminants, incidence of spontaneous abortions, gestational age at birth, premature deliveries, low birth weight or dysmature babies, birth weight, child's body mass index, perinatal mortality and morbidity, child mortality and morbidity in the first year of life. A comprehensive overview of occupational exposure to metals was given by Nieboer et al. (2005, 2007).

8.4.3.1. **POPs and maternal and child health**

The Russian Persistent Toxic Substances (PTS) study of 2001–2004 explored the reproductive situation for indigenous groups in the Russian Arctic (AMAP, 2004b). POPs concentrations in blood were highly dependent on age and parity. Significant associations were found between maternal blood concentrations of total PCBs and Pb and a number of non-specific reproductive and developmental health effects, such as prevalence of low birth weight, premature births, stillbirths and malformations (non-specific).

Reproductive health effect analyses described in the first report on the results of the Russian PTS study (AMAP, 2004b) were based on 220 mother–child pairs. Additional blood samples (also collected in 2001–2003 and stored) were analyzed during 2004–2006 and new results have been added to the data base. The current Russian database contains 346 mother–child pairs (1.5 times larger than the original PTS study) and increases the statistical power of the overall study considerably.

Dudarev and colleagues (Dudarev, 2006, 2007a; Dudarev and Chashchin, 2006; Dudarev et al., 2006) reported statistically significant higher levels of total PCBs in serum of women who had had premature births, stillborn cases and newborn children with birth defects compared to the control group (women with normal pregnancies and healthy newborn children). Concentrations of HCB and chlordanes in serum of women who had had stillborn cases and newborn children with malformations were about 2-fold higher than in women of the control group. The findings for HCB were statistically significant. The relative risk of spontaneous abortion increased with rising total Hg in maternal blood and at lower concentrations than those reported to date from other studies. It is unknown whether this sensitivity is related to poorer general health status of the Russian mothers cohort, genetic factors, confounding dietary factors, or other factors.

The Russian PTS study also found a statistically significant correlation between early age of first menstruation and higher levels of total PCBs. In addition, concentrations of total PCBs were lower in blood of women who reported menstruating for less than four days.

A close correlation between levels of persistent toxic substances in blood and breast milk was documented for indigenous women of the Chukchi area, demonstrating the rationale for using blood as a relevant and important medium for contaminant studies (Anda et al., 2007a).

8.4.3.2. **Metals and maternal and child health**

Based on a comprehensive study of nickel workers on the Kola Peninsula, Vaktskjold and colleagues examined pregnancy outcome in relation to environmental and occupational exposure for nickel and other toxic metals (Vaktskjold et al., 2004a,b, 2006, 2007, 2008a,b; Talykova et al., 2007). The overall study did not confirm any significant negative effects of occupational metal exposure on reproductive outcome. This has significance for local, non-occupationally exposed populations who may live within the contamination zone of the smelter. There were three key findings:

- While the incidence of musculo-skeletal defects was high, especially for feet, no correlation with maternal exposure to water-soluble nickel was demonstrated. However, the incidence of musculo-skeletal defects in the maternal group working in the copper refinery was higher than in the other groups.
- No adverse effects of water-soluble nickel exposure in the first part of pregnancy could be associated with small-for-gestational-age newborns, but exposure to nickel throughout the pregnancy has not been explored.
- There was no association between nickel exposure and genital malformations such as hypospadias or undescended testicles; however, there were very few cases in the high exposure group so the results should be assessed with caution.

Toft et al. (2008) found no consistent effects of PCB and DDE exposure on menstrual cycle characteristics observed across populations in the INUENDO study populations. However, in the Greenland study population it seemed that high levels of PCB or DDE were possibly protective against long menstrual cycles.

Preliminary analyses of blood data from the expanded PTS study (Dudarev, pers. comm., 2008) indicated that there may be associations between reproductive outcome for Russian indigenous women and low levels of Cd, Hg and Pb. While there were no

increased relative risks of adverse pregnancy outcome for mothers with blood levels of Cd greater than 1 μg/L and Pb greater than 30 μg/L, there was a significantly increased risk of spontaneous abortion in women with blood levels of Hg greater than 2 μg/L. No association between Cd, Hg or Pb levels in maternal blood and changes in menstrual status have been observed, nor has any association been found between Cd, Hg or Pb levels in maternal blood and offspring sex ratio.

8.4.3.3. **Summary and concluding comments**

The growing fetus and newborn children are especially sensitive to the toxic effects of many POPs and heavy metals found in the environment. In the Russian Arctic, some associations were found between high *in utero* exposure to POPs and non-specific newborn health outcomes. Some new findings related to spontaneous abortions and Hg suggest that further study of population sensitivity to Hg in Russia is warranted. No significant associations were found between exposure to nickel and health outcomes on the Kola Peninsula, northwest Russia.

8.4.4. **Reproduction, sexual maturation, sex ratios**

Over recent years there have been concerns expressed over a possible time-related deterioration of human sperm production and a concomitant increase in the incidence of testicular germ cell cancer as well as congenital abnormalities of male reproductive organs such as hypospadias and cryptorchidism (Toppari et al., 1996; Manson and Carr, 2003; Huyghe et al., 2003; Skakkebaek et al., 2003; Vidaeff and Sever, 2005). It has been suggested that abnormalities of male genital organs, poor sperm counts, testicular cancer, hypospadias and cryptorchidism are all part of the so-called Testicular Dysgenesis Syndrome (TDS), which is believed to be the result of genetic predisposition combined with certain environmental and lifestyle-related exposures, including exposure to exogenous endocrine-disrupting substances (Virtanen et al., 2005a).

The development and maintenance of reproductive tissues are to a large extent controlled by steroid hormones. Several POPs have been shown to possess hormone-disrupting activity in experimental studies (see Box 8.5). Some environmental chemicals mimic natural hormone activity, while others antagonize natural hormone activity when tested with *in vitro* assays or in whole animal models. Prenatal animal exposures to several pesticides, PCBs and *p,p'*-DDE have clearly demonstrated reproductive-disrupting effects (Kelce et al., 1997; Gray et al., 2000, 2005; Kitamura et al., 2003; Shono et al., 2004).

Certain male reproductive tract disorders (cryptorchidism, hypospadias and testicular cancer) have been reported to be increasing in parallel with the introduction of xenoestrogens such as DDT into the environment. Reduced semen quality was also reported in certain regions of the world during the latter half of the 20th century. Although these alterations are thought to be mediated by the estrogen receptor, they are also consistent with inhibition of androgen receptor-mediated events. Kelce et al. (1995) identified *p,p'*-DDE, as a potent anti-androgenic agent in male rats. Treatment of some test animals 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 has been shown to alter sexual development in test animals (decreased epididymis and caudal epididymis weights, daily sperm production and caudal epididymal sperm number). More discussion of laboratory animal responses to mixtures can be found in section 8.3.2.2.

Typical organochlorine mixtures found in Arctic populations contain a wide range of different compounds, including substances with estrogenic (such as some PCBs), anti-estrogenic (some PCBs), or anti-androgenic (such as DDE) capacities. It may therefore be anticipated that complex real life mixtures, comprising compounds that can interact with different receptors involved in cell differentiation and growth, could affect reproduction and development, and be involved in the pathogenesis of hormonally-responsive cancers.

Box 8.5. Contaminants as endocrine disruptors

The combined effects of the large number of environmental contaminants present in humans are relatively poorly explored. Studies performed *in vitro* and *in vivo* as well as the combined effects of some estrogenic and anti-androgenic chemicals in rats (Gray et al., 2001, 2004; Payne et al., 2001; Nellemann et al., 2003; Birkhoj et al., 2004; Hotchkiss et al., 2004) have shown that the combined effects of single compounds of low potency cannot be ignored. Rajapakse et al. (2002) showed using *in vitro* methodology that xeno-estrogen mixtures below their no-observed-effect concentration (NOECs) were able to cause a dramatic additive enhancement of hormone-related activity. Thus the epidemiological evaluation of POPs as endocrine disruptors is complicated by the extent to which the chemicals measured in a study population may also interact with other chemicals present in the study population but not identified. Other factors such as dietary, lifestyle and genetic differences must also be taken into consideration when assessing overall effects of mixtures of POPs.

New and promising techniques which can evaluate the combined overall xenohormone activity in human blood have been developed (Rasmussen et al., 2003; Fermamdez et al., 2004; Ibarluzea et al., 2004; Hjelmborg et al., 2006) and can identify blood samples from population studies which warrant more expensive chemical analysis. Serum extraction and fractionation, combined with cell culture based analyses provide useful screening tools to determine the overall POP related xenohormone activities in serum fractions free of endogenous sex hormones.

8.4.4.1. **Xenohormone serum activity in Inuit and Europeans**

Several contaminants found in human blood can act as xenoestrogens (see Box 8.6). A recent study of healthy men from Greenland (Inuit), Sweden (fishermen), Poland (Warsaw), and the Ukraine (Kharkiv) referred to as the 'INUENDO' study (see Box 8.7) aimed to compare the level of xenoestrogenic activity in serum of groups with varying POPs exposure (Rylander and Hagmar, 1995; Svensson et al., 1995; Van Oostdam and Tremblay, 2003; Deutch, 2003a; Jonsson et al., 2005) to POPs proxy markers CB153 and *p,p'*-DDE (Bonefeld-Jorgensen et al., 2006). It was found that the xenoestrogenic serum activity of Greenlandic Inuit differed significantly from the three European study groups between which there were no differences. In the Inuit serum samples, the antiestrogenic action was predominant; in the European study groups there was a higher frequency of agonistic xenoestrogenic activity and higher estimated estradiol equivalence (EEQ) levels (Figure 8.10a). The xenoestrogenic activity of the Inuit samples was negatively associated with levels of CB153 and *p,p'*-DDE. For the Polish samples the xenoestrogenic data were positively associated with *p,p'*-DDE level, and the EEQ level decreased with increasing CB153 concentration (Bonefeld-Jorgensen et al., 2006). Overall, the results could be explained by the high level of PCBs in Greenland with predominant anti-estrogenic actions (Connor et al., 1997; Bonefeld-Jorgensen et al., 2001; Gregoraszczuk et al., 2003; Rasmussen et al., 2003; Pliskova et al., 2005) and the relatively high level of *p,p'*-DDE in the Polish group having weak estrogenic action (Chen et al., 1997; Andersen et al., 1999a; Payne et al., 2001; Rasmussen et al., 2003). However, it is problematic that no correlations were observed for the Swedish and Ukrainian groups because they had CB153 and *p,p'*-DDE marker profiles similar to the Greenlandic and Polish cohorts, respectively. This finding might indicate that there is a limitation in use of the two POP proxy biomarkers chosen as representatives of the entire exposure mixture.

Other contaminants found in human blood can also act as xenoandrogens (see Box 8.8). It is well documented,

Box 8·6. The estrogen receptor

The estrogen receptor (ER) is found in almost all human tissues of both genders and plays an important role in neonatal and post neonatal development, puberty and reproductive development of both sexes (Pedram et al., 2002; Dickerson and Gore, 2007). There are extensive data to support mechanistic models of the effects of endocrine-related POPs on sex hormone systems (Andersen et al., 2002a; Long et al., 2003; Hofmeister and Bonefeld-Jorgensen, 2004; Grunfeld and Bonefeld-Jorgensen, 2004). The PCB congeners CB138, CB153 and CB180, comprising up to 50% of the total bioaccumulated PCBs, elicit an ER-mediated antiestrogenic and/or antiandrogenic *in vitro* activity (Bonefeld-Jorgensen et al., 2001). Similarly, some hydroxylated PCBs exert low potency estrogenic and/or antiestrogenic effects (Brouwer et al., 1999; Rasmussen et al., 2003). Generally, PCBs do not bind to the sex hormone binding globulin or only bind with very low affinity (Jury et al., 2000), which may cause a higher bioavailability of the compounds. Several POPs, including TCDD, CB126, CB28, CB105 and pesticides such as DDT, prochloraz, and endosulfan, were reported to affect aromatase which converts testosterone to estrogens. Effects on aromatase influence the ratio between the two sex steroid hormones (Gerstenberger et al., 2000; Andersen et al., 2002a; Lai et al., 2005).

Box 8·7. INUENDO study

An international study of reproductive outcomes was undertaken in the early 2000s under the acronym INUENDO. The objectives of the INUENDO study were to establish the impact of environmental exposure to xenobiotic compounds with hormone-like actions on human fertility. The multi-national research team, led by Denmark, developed a series of interrelated studies of Inuit and European populations with a high contrast of exposure to persistent and biologically active chemical pollutants. Focus was on time to pregnancy as a measure of a couple's joint reproductive performance, semen quantity and quality to substantiate whether possible effects on couples fertility was attributable to reduced male fecundity, reproductive hormones in adults and male offspring to indicate whether a possible adverse effect on time to pregnancy or semen quality is attributable to disruption of sex hormone regulation, and total estrogenic and androgenic activities in blood as a direct measure of the potential hormone-like action of a wide range of environmental pollutants. The research combined identical interview studies of couple fertility, biological studies of semen quality and neonatal studies of reproductive hormone profiles in Greenland, Sweden, Poland and the Ukraine. In some studies, sample sizes of populations investigated were as high as 4000. To date the website for the INUENDO study lists 26 publications from 2004 to 2007. For more details see http://www.inuendo.dk.

Box 8·8. The androgen receptor

The androgen receptor (AR) is the key regulatory element of the androgen cell signaling system and is essential for male reproductive functions and development, including spermatogenesis (Sharpe, 2006). Antagonistic effects on the AR activity *in vitro* have been reported for several pesticides including *p,p'*-DDE (Kelce et al., 1995), dieldrin (Andersen et al., 2002a; Roy et al., 2004), fenarimol (Andersen et al., 2002a), methiocarb (Andersen et al., 2002a; Birkhoj et al., 2004), and prochloraz (Andersen et al., 2002a; Vinggaard et al., 2002; Birkhoj et al., 2004). Furthermore, several PCB congeners (CBs 49, 66, 74, 77, 105, 118, 126, 138, 153 and 156) have been reported to act as AR-antagonists (Bonefeld-Jorgensen et al., 2001; Endo et al., 2003; Schrader and Cooke, 2003). In animal studies, prenatal exposure to POPs such as PCBs, PCDDs and *p,p'*-DDE has been associated with reduced male fertility (Sager et al., 1987; Peterson et al., 1993; Kelce et al., 1995; Fielden et al., 2001; Anbalagan et al., 2003; Steinhardt, 2004); however, the effect of POPs on human fertility is still controversial (Yu et al., 2000; Axmon et al., 2001, 2004; Dallinga et al., 2002; Younglai et al., 2002; Toft et al., 2005). There is a need for an integrated risk assessment of endocrine disruptors in humans (Bridges and Bridges, 2004).

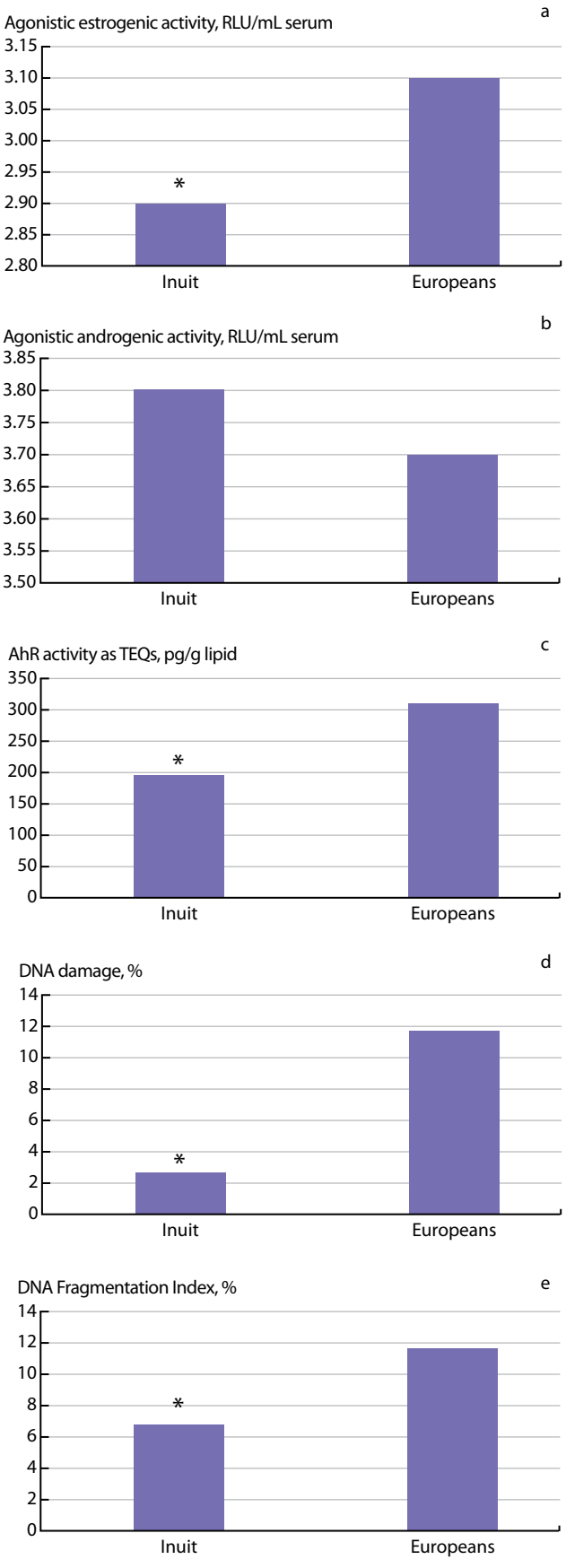


Figure 8·10. POPs related xenobiotic serum activities in Inuit and combined European study groups (a) agonistic serum xenoestrogenic activity; (b) agonistic serum xenoandrogenic activity; (c) serum AhR activity; (d) sperm DNA damage; (e) sperm DNA fragmentation index. * indicates significant difference vs Europeans at $p < 0.05$.

both *in vitro* and *in vivo,* that *p,p'*-DDE is an androgen receptor (AR) antagonist (Gray et al., 1999; Vinggaard et al., 1999; Roy et al., 2004; Araki et al., 2005), which is consistent with the observed decreasing effect of the xenoandrogenic serum activity in the European groups (Figure 8.10b) in which *p,p'*-DDE levels are lower. The agonistic AR activity of serum extracts from the Inuit and the three European study groups were not significantly different, however, a higher mean value was observed in Inuit compared to Europeans (Krüger et al., 2007).

Although high *p,p'*-DDE serum levels were also found in the Inuit, this study group showed the highest percent of serum samples (22%) with augmented AR function. The results for the different ethnic groups (Inuit and European men) could be caused by a different composition of serum POPs. Based on these data, it appears that the concentrations of two selected POPs proxy markers cannot adequately predict the integrated xenohormone serum activity and that the variation in serum xenobioactivity across the four study groups reflected differences in the mixture profile of the POPs exposure, genetic factors and/or lifestyle factors.

The antiestrogenic and increased xenoandrogenic effect of serum found for Inuit men suggests that a net androgenic effect might result from POPs exposure in the Arctic. The POPs-related hormone-like activities are expected to contribute to the assessment of potential reproductive health risks of POPs.

A recent study in Greenland indicated, in support of the INUENDO serum xenobioactivity data, that serum xenobioactivity cannot be predicted from single POP proxy markers alone. The Greenlandic study was designed to determine the integrated xenoestrogenic and xenoandrogenic serum activity as an exposure marker of POPs, comparing the effect on ER and AR transaction levels between Inuit from different Greenlandic districts. The study was also intended to evaluate whether the activity was associated with POPs serum concentrations (14 PCBs and 10 organochlorine pesticides were determined) and/or lifestyle factors. Overall, although the two xenohormone activities differed between the Nuuk, Sisimiut (southwest) and Qaanaaq (north) districts as well as between genders, across the districts the xenoestrogenic and xenoandrogenic serum transactivities correlated negatively to the POPs for the combined female and male data, respectively. Age and/or n-3 : n-6 fatty acid ratio were correlated with xenohormone activity for both genders in Nuuk and Sisimiut. Smoking was positively related to xenohormone activity for all men (combined data) and for men and women (combined data) (Krüger et al., 2008b). In summary, the non-steroidal xenohormone transactivities can be used as an integrated biomarker of POPs exposure and lifestyle characteristics. The actual serum POP mixtures antagonized the age-adjusted sex hormone receptor functions. In addition to age, comparison of different study populations requires the inclusion of diet and lifestyle factors. In conclusion, the data suggest that geographic and sex differences might be caused by the variation in POPs profiles in the diet in concert with lifestyle and genetic factors.

Moreover, as found for the Inuit in the INUENDO study, a predominant antiestrogenic effect of the serum POPs fraction was found. The xenoestrogenic data were negatively associated with POPs for the combined genders in Nuuk and Sisimiut, as well as for men from Sisimiut and Qaanaaq. In contrast, Qaanaaq women had positive associations between xenoestrogenic activity and POPs levels. As for the Inuit male data in the INUENDO study, the serum extract of Nuuk and Sisimiut males further increased an already ligand-activated AR, whereas for Qaanaaq males and women, a higher percentage of samples decreased the AR activity (Krüger et al., 2008b). The xenoandrogenic activities were positively associated with the POPs for the combined genders in Nuuk but negatively associated for the combined male data across all four districts. Again, the serum xenohormone activity cannot be predicted from single POPs proxy markers alone. Age, food intake and lifestyle factors all affect the mixture profile and levels of POPs in each district, making the integrated xenohormone activity a suitable exposure effect biomarker of the sum of POPs.

8.4.4.2. **AhR-mediated dioxin-like serum activity in Inuit and Europeans**

The INUENDO study (see Box 8.7) found that the European groups had higher median levels of AhR-TEQ (TCDD toxic equivalents) (see Box 8.3) than the Inuit group (Figure 8.10c) (Long et al., 2006). AhR-TEQ was not correlated with CB153 or *p,p'*-DDE for any of the study groups alone; whereas, for serum + TCDD coactivated AhR, negative associations with CB153 were found for the Polish study group. It was concluded that: (1) the difference between serum dioxin-like activity in European and Inuit men could not be explained by CB153 or *p,p'*-DDE levels alone; (2) the variation of serum AhR-induced activity reflects different patterns of POP exposures, genetics and/or life style factors, and (3) the serum AhR activity measurements can be used as a biomarker of effect and contribute to risk assessments.

The higher AhR-TEQ level found for the Europeans (Figure 8.10c) suggests a higher exposure to dioxins and dioxin-like compounds, probably because of closer proximity to the pollutant sources than the populations living in remote areas such as the Greenlandic Arctic region (Dewailly et al., 1994). In addition, dietary habits/lifestyle factors and the genetic difference between Inuit and Caucasians (de Maat et al., 1999) may also need to be taken into account. Furthermore, the higher median AhR-TEQ of the serum extract of samples from Poland and Sweden might be explained by: (1) the relatively higher level of dioxins and dioxin-like compounds reported to be produced and emitted to the Polish environment (Grochowalski, 1998; Lassen et al., 2003); and (2) a relatively higher exposure to dioxins and/or dioxin-like PCBs in the Swedish study group (Svensson et al., 1995).

The AhR-TEQ of the combined European study groups was significantly associated with the CB153 level. However, because CB153 and *p,p'*-DDE showed no correlation with the AhR-mediated agonistic response in the single study groups, these two POPs markers alone cannot, in all populations, predict the contribution of POPs and polycyclic aromatic hydrocarbons (PAHs) and other lipophilic xenobiotic compounds to serum dioxin-like activity. Other more sensitive and specific tentative markers such as dioxin-like PCBs (e.g., CB118) should be included in future epidemiology studies. However, it should be remembered that the AhR-CALUX bioassay is not a substitute for actual chemical analysis by GC-MS techniques; it is a measure of biologically-relevant response (see Box 8.3). The CALUX bioassay is normally used as a first tier screening tool followed by chemical analysis to identify specific response compounds (Windal et al., 2005).

In a recent study of AhR transcriptional activity in serum of Inuit across Greenlandic districts, 85% of all Inuit samples elicited agonistic AhR transactivity in a district-dependent pattern. The median level of the AhR-TCDD equivalent (AhR-TEQ) of the separate genders was similar in the different districts. For the combined data the order of the median AhR-TEQ was Tasiilaq > Nuuk ≥ Sisimiut > Qaanaaq, possibly being related to the different composition of POPs. Overall, the AhR transactivity was inversely correlated to the levels of the sum of POPs, age and/or intake of marine food. Moreover, the proportion of dioxin-like (DL) compounds in the POP mixture was observed to be the dominating factor affecting the level of serum AhR-TEQ even at very high levels of non DL-PCBs. It was suggested that the inverse association between the integrated serum AhR transactivity and sum of POPs might be explained by the higher level of compounds antagonizing the AhR function probably due to selective POP bioaccumulation in the food chain (Long et al., 2007a).

8.4.4.3. **Male fertility**

8.4.4.3.1. *Sperm quality*

In a parallel INUENDO sub-study, lower sperm DNA damage (TUNEL assay) and sperm chromatin integrity, assessed as DNA Fragmentation Index (DFI%), were reported in the Inuit study group compared to the European study groups (Figures 8.10d and Figure 8.10e). No correlations between the two proxy POPs markers (CB153, *p,p'*-DDE) and the sperm DNA damage or the sperm apoptotic markers Fas and Bcl-xL were observed for the single study groups, whereas, for the combined European study groups, DNA damage and Bcl-xL were found to be positively related to CB153 (Stronati et al., 2006). In addition, a strong correlation was found between DFI% and the serum level of CB153 for the European study group, but not for Inuit men displaying the lowest level of DFI% (Spano et al., 2005). Thus, in comparison to European men, the Inuit showed a significantly lower xenoestrogenic response (Figure 8.10a) (Bonefeld-Jorgensen et al., 2006) and AhR-TEQ (Figure 8.10c) (Long et al., 2006), significantly less semen DNA damage (Figure 8.10d) (Stronati et al., 2006) and significantly lower semen DFI% levels (Figure

8.10e) (Spano et al., 2005), but had a tendency to higher xenoandrogenic serum activity (Figure 8.10b) (Krüger et al., 2007). Evaluation of possible associations between xenohormone action and impact on male fertility factors such as traditional semen quality markers and specific markers of DNA damage, seminal apoptosis and DFI% gave the following results: negative correlations between xenoestrogenic and AhR-mediated dioxin-like serum activity and sperm DFI% and DNA damage for Inuit and positive correlations between xenoandrogenic and dioxin-like serum activity and sperm chromatin integrity and DNA damage for the pooled European data (Long et al., 2007b; Kruger et al., 2008a).

The inverse correlation of xenobiotic-induced receptor activities to sperm DNA damage in Inuit suggests that the AhR activity might be involved in the protection of sperm DNA in concerted action with genetic and/or diet and lifestyle factors. Furthermore, the positive association between serum xenobiotic-induced receptor activities and sperm DNA damage for the combined European groups suggests that proximity to the source and the potential of the bioaccumulated compounds to exert possible adverse effects on human sperm cells play an important role.

However, the direct biological consequences of these associations are difficult to identify because a large number of other factors, probably related to intrinsic population differences, also influence the outcome. Because this study explored for the very first time the correlation of serum xenobiotic-induced receptor activity and sperm DNA damage/DFI% and apoptosis in humans, interpretation of the data is difficult.

There is scientific evidence to show that high detoxifying activity (generally involving cytochrome P450 enzymes, some of which are induced by AhR activation) causes an important increase in reactive-oxygen-species-mediated oxidative stress, which can cause DNA damage in spermatozoa (Lewis and Aitken, 2005). However, it is known that the Ah gene battery has the capacity not only to promote oxidative stress but also to prevent it by increasing levels of oxidative stress-detoxifying enzymes. Thus the total action of AhR and the Ah gene battery represents a pivotal upstream event in the apoptosis cascade (Nebert et al., 2000). Previous studies showed that oxidative stress can inhibit apoptosis (Lee and Shacter, 1999), but to date no such evidence for sperm cells has been reported.

The reason and mechanism are not clear at this stage. Because human spermatozoa contain high levels of PUFAs, they are particularly susceptible to oxidative stress. Antioxidants such as vitamin E, vitamin C and carotenoids can restore a proper prooxidant-antioxidant balance and maintain the integrity of sperm cells. Previous studies showed that Se and vitamin E supplementation seemed to improve sperm motility and morphology (Wong et al., 2000). Selenium-deficient animals have consistently lower sperm production and sperm quality. In humans, both low and high sperm Se were reported to have negative influences. However, Se supplementation was reported to result in improved sperm quality and fertility for the population with low Se intake (30–40 μg/d) (Hansen and Deguchi, 1996; Beckett and Arthur, 2005). It must be emphasized that the intake of Se and n-3 fatty acids, including docosahexaenoic acid (DHA), was much higher (up to 10 times) for Inuit than Caucasians (Deutch, 2003a; Hansen et al., 2004). Whether the higher intake of Se and n-3 fatty acids can contribute to an explanation of the relatively better sperm quality in Inuit merits further research.

These statistically significant but relatively weak associations between xenobiotic serum activity and sperm DNA damage need to be confirmed in future studies before strong conclusions can be drawn. Future studies might more accurately determine possible adverse endocrine-disrupting effects of the combined xenohormone activity in serum of adult men in support of the traditional analysis of single or a few chemical compounds.

Finally, it must be considered that interactions between AhR, ER and AR (Pocar et al., 2005) may result in other responses on the receptors *in vivo*, compared to the *ex vivo* tests used in the present study, where the response on the single receptor was tested. Such interactions may further complicate interpretation of the associations of the xenobiotic activities and sperm apoptotic markers. However, it would be valuable to evaluate the integrated effects *in vivo* of the combined responses on the different receptors.

8.4.4.3.2. *Sex organ development*

Normal development of male genitalia in mammals depends on androgen action. Longnecker et al. (2002) used stored serum samples to examine the relationship between maternal DDE levels during pregnancy and adjusted odds of cryptorchidism (n = 219), hypospadias (n = 199), and polythelia (extra nipples) (n = 167) among male offspring, using a nested case-control design with one control group (n = 552). Subjects were selected from twelve urban centers of a U.S. birth cohort study beginning in 1959–1966, when DDE levels were much higher than at present. Compared with boys whose mother's recovery-adjusted serum DDE level was less than 21.4 μg/L, boys with maternal levels greater than or equal to 85.6 μg/L had adjusted odds ratios of 1.3 (95% CI: 0.7–2.4) for cryptorchidism, 1.2 (95% CI: 0.6–2.4) for hypospadias, and 1.9 (95% CI: 0.9–4.0) for polythelia. For cryptorchidism and polythelia, the results were consistent with a modest-to-moderate association, but in no instance was the estimate very precise. In this cohort, DDE concentrations in umbilical cord serum were much higher than in contemporary Arctic blood concentrations.

A study by Vaktskjold et al. (2006) investigated whether pregnant women employed in nickel-exposed work areas are at elevated risk of delivering a newborn with a genital malformation. In this register-based cohort study, data about pregnancy outcome and occupation were obtained using the Kola Birth Registry. The odds ratio for nickel-exposed women delivering a newborn with a genital malformation was 0.81 (95% CI: 0.52–1.26), and that for an undescended testicle was 0.76 (95% CI: 0.40–1.47).

In this study no negative effect of maternal exposure to water-soluble nickel was found on the risk of delivering a newborn with malformations of the genital organs.

8.4.4.3.3. *Sex ratio*

Results from the INUENDO study (see Box 8.7) showed that when sperm Y:X chromosome distribution was assessed, Swedish and Greenlandic men had on average significantly higher proportions of Y sperm (in both cohorts, 51.2%) and correspondingly higher lipid-adjusted concentrations of CB153 (260 ng/g and 350 ng/g, respectively) compared with men from Poland (50.3% and 22 ng/g) and the Ukraine (50.7% and 54 ng/g) (Tiido et al., 2006). This study indicates that POP exposure might be involved in changing the proportion of ejaculated Y-bearing spermatozoa in human populations. Inter-country differences, with different exposure situations and doses, may contribute to varying Y:X chromosome ratios. However, the higher proportion of Y sperm did not support the observed increase in the female:male ratio reported previously.

Analyses of the new Russian Arctic mother–child database of 346 pairs showed some associations between total PCBs in maternal blood and newborn sex ratios (Dudarev, 2006). The average blood levels of grouped PCB congeners were higher among mothers of girls, compared to mothers of boys, but these differences were not statistically significant. Analysis of dose-effect relationships suggests some increase of boy:girl ratios (1.37 to 1.87) with increasing PCB levels in three initial dose ranges for total PCBs, CB28 and CB101; the group of dioxin-like congeners and CB170 and CB187. In the fourth dose range, the ratio decreased. The dependence follows a parabolic pattern; initially, the numbers of newborn boys exceed the numbers of girls and then (in the highest range of PCB levels in maternal blood) the numbers of newborn girls became close to the numbers of newborn boys (ratios descend to 1). There were no associations between maternal blood levels of DDTs, other organochlorines and metals and boy:girl ratios of newborns or menstrual status of mothers. New studies point to some similar associations (Hertz-Picciotto et al., 2008), but conclusive evidence of a cause-effect relationship is still lacking.

The male hypothalmo-pituitary-gonadal axis was also assessed in Greenland through the INUENDO study and a positive association between CB153 exposure and leutinizing hormone was reported. Gonadotropin levels and sex hormone binding globulin (SHBG) seemed to be affected by POPs exposure, but the pattern of endocrine response shows considerable geographic variation (Giwercman et al., 2006).

Epididymal and accessory sex gland function was also measured within the INUENDO study (Elzanaty et al., 2006). Negative associations with the activity of neutral-alpha glucosidase (NAG), a marker of epidydimal function, were found among Greenlandic men. The negative effects of POPs on sperm motility, observed in the same study population might partly be caused by post-testicular mechanisms, involving a decreased epididymal function as has been reported in other studies. Also, a sperm chromatin structure assay (SCSA) was used to assess sperm DNA/chromatin integrity. A strong and monotonically increasing DNA fragmentation index with increasing serum levels of CB153 was found among European but not Inuit men, reaching a 60% higher average level in the highest exposure group. No significant associations were found with DDE serum concentrations. The results of this study raise the question of the importance of genetic background and dietary habits in the modulation of such effects. Sperm DNA fragmentation was also evaluated in these study groups using a TUNEL assay. Again, Inuit showed significantly lower levels of sperm DNA damage than European men. However, no correlations between either sperm DNA fragmentation or apoptotic sperm parameters and variations in POPs exposure were observed across the study groups or for the separate study groups (Spano et al., 2005; Stronati et al., 2006) (see also section 8.4.4.3.1).

Time-to-pregnancy (TTP) and fecundity were also studied in the INUENDO population groups in relation to POPs. Greenlandic Inuit with high levels of both of the two POPs proxy markers, CB153 and DDE were included in this study. Swedish fishermen and their wives had high blood levels of CB153 but low levels of blood DDE. Couples from Kharkiv in the Ukraine were high in DDE and low in CB153 while participants from Warsaw (Poland) were low in CB153 and had intermediate DDE levels. Among the pregnant women and their partners (1505 women and 778 men) there seemed to be an association between serum concentrations of the POPs proxy markers and prolonged TTP among couples from Greenland only (Axmon et al. 2006). Based upon TTP interviews obtained from 2269 women and semen samples from 798 men, fecundity was lower among couples from the Ukraine (adjusted fecundability ratio [FR] 0.64 [95% CI: 0.5–0.8]) and elevated in Swedish fishermen families (FR 1.26 [95% CI: 1.0–1.6]) compared to the Polish couples. Adjusted geometric means of sperm counts and morphology did not differ between regions while sperm motility was higher in Polish men, although a tendency to a positive correlation between sperm motility and serum CB153 concentration was observed (Toft et al. 2005).

Although the data suggest that dietary POPs exposure might affect couple fertility it has not been established whether the risk is associated with CB153 or *p, p′*-DDE or whether there is an interaction between the two compounds because of the high intercorrelation between the two biomarkers. Moreover, regional differences in TTP and sperm motility may be related to regional differences in the profile of POPs mixtures in blood, differences in diet and lifestyle factors, and genetic background as well as to differences in the prevalence of contraceptive failures which can bias comparisons of TTP. Further study is needed to establish fertility rates for couples in relation to POPs body burden.

8.4.4.4. **Summary and concluding comments**

Many POPs, including PCBs, polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and pesticides can mimic hormone activities. As potential endocrine disrupters, they are suspected to be capable of increasing the risk of cancer, birth defects and reproductive and neuro-immune disorders (Carpenter et al., 1998; Bonefeld-Jørgensen and Ayotte, 2003; Bonefeld-Jorgensen, 2004). To date, no clear evidence for adverse endocrine-related human health effects of POPs has been obtained at the individual or population level. However, data from studies on wildlife species, laboratory animals and biomarker effects *in vitro* have strengthened the need for further research to address the potential impacts on human populations.

Results from the INUENDO study did to some degree support the potential of POPs to act as endocrine disruptors. However, serum concentrations of CB153 and *p,p´*-DDE, the two POP proxy markers used in the study, were not consistently related to either endogenous or exogenous hormone activity. Nevertheless, several links between POP exposure and biomarkers of male reproductive function were identified. First, an association between high CB153 serum levels and low sperm counts was detected within a subgroup of men with short androgen receptor nucleic acid CAG repeat length. Second, a relationship between increased CB153 serum concentrations and decreased sperm motility was seen in populations from all four study regions and indications of reduced NAG activity in seminal plasma indicate a post-testicular effect. Third, damage of sperm chromatin integrity was considerably less frequent in Greenlandic Inuit compared to European groups and only in the latter was impairment of sperm chromatin integrity related to POPs. In spite of these effects the fertility in terms of time taken to conceive was not related to POPs except in Inuit. A likely explanation for the latter was not identified. POPs may interfere with male reproductive function without major impact on fertility. The data do not provide direct evidence for endocrine disruption, and other mechanisms should also be considered (Bonde et al., 2008). In general, no definitive conclusion can be drawn from these studies. This is in part because the two POP proxy markers alone cannot be used for assessing adverse effects of POPs mixtures. There are also open questions related to the role of genetic background, lifestyle and/or diet nutrition factors such as trace elements/antioxidants that may interfere with the possible adverse health effects of POPs.

However, new and promising techniques which can evaluate overall xenohormone activity in human blood are useful screening tools and can identify blood samples from population studies which warrant more expensive chemical analysis. The results from xenobiotics studies clearly indicate that single or a few POPs proxy markers cannot be used by themselves for assessment of either bioactivity or possible adverse effects of POP mixtures. Recent studies in Greenland showed that the actual serum POP mixtures antagonized the age-adjusted sex hormone receptor functions, and that the non-steroidal xenohormone serum transactivities can be used as an integrated biomarker of POP exposure and lifestyle characteristics. Moreover, the data suggested that geographic and sex differences might be caused by the variation in POPs profiles in the diet in concert with lifestyle and genetic factors. Further research is needed to elucidate the relationships between effect biomarkers such as higher sperm DNA damage, higher xenoestrogenic and higher AhR-TEQ and lower xenoandrogenic serum levels as found in European men compared to Greenlandic Inuit. Moreover, further research is needed regarding the role of genetic background, lifestyle and/or diet nutrition factors, including trace elements and antioxidants such as Se as factors modifying the possible adverse health effects of POPs.

For POPs, results from the INUENDO study showed that when sperm Y:X chromosome distribution was assessed, Swedish and Greenlandic men having the highest level of the POP proxy markers also had on average significantly higher proportions of Y sperm (see section 8.4.4.3.3). However, the higher proportion of Y sperm did not support the observed increase in the female:male ratio reported previously in Seveso, Italy after a major dioxin contamination event. In general, no definitive conclusion could be drawn from these studies. Emerging data from a larger cohort in the Russian Arctic indicate that increasing maternal PCB concentrations may be associated with an initial effect of increasing the ratio of male:female newborns. The Russian results appear to confirm the trend reported in the previous AMAP Human Health assessment (AMAP, 2003); however, causality has not been determined and the increase in the ratio appears to disappear in the highest concentration group. This finding has also been reported in other recent research in the continental United States; however, the detection limit might play a role. The possible effects of other contaminants have not been determined. Systematic epidemiological studies, including all possible confounding factors and other relevant contaminants, must be performed before any conclusive statements can be made. Paternal exposure might be important to consider in further studies.

Preliminary findings from a large Russian Arctic cohort add evidence to the findings identified earlier (AMAP, 2004b) that higher levels of maternal blood serum PCBs might be associated with more frequent occurrences of low birth weight, premature births, stillbirths, and menstrual irregularities. These possible adverse reproductive health effects of POPs and metals require more detailed evaluation. Detailed analyses of all available data and systematic epidemiological studies, which take into account relevant confounding factors and other contaminants, must be undertaken before conclusive statements can be made. Other studies undertaken in Russia identified no negative effect of maternal exposure to nickel and the risk of delivering a newborn with malformations of the genital organs.

8.4.5. **Neurodevelopment**

There is widespread concern about potentially adverse health effects of environmental chemicals on children. Infants exposed *in utero* and during the early neonatal period are particularly vulnerable because of their rapid growth, cell differentiation, immaturity of metabolic pathways, and development of vital organ systems, including the central nervous system.

8.4.5.1. **Polychlorinated biphenyls**

Several prospective longitudinal studies have been conducted since the 1980s to study the effects of prenatal exposure to background levels of PCBs and other organochlorine compounds from environmental sources. The first generation of studies included the North Carolina (Rogan et al., 1986), the Michigan (Jacobson and Jacobson, 1993), the Germany (Winneke et al., 1998) and the Oswego (Stewart et al., 1999) cohorts of fish consumers, and the Netherlands cohort where exposure was related to consumption of dairy products (Koopman-Esseboom et al., 1994a). Comparisons of PCB exposure between these cohorts have been provided by Longnecker et al. (2003).

Other more contemporary cohort studies of fish consumers have been conducted in the Faroe Islands (Grandjean et al., 2001a), Nunavik (Muckle et al., 2001a,b), West Greenland (Bjerregaard and Hansen, 2000), Germany (Walkowiak et al., 2001; Winneke et al., 1998) and Hokkaido (Nakajima et al., 2006). Several other POPs-related studies have been conducted with general populations from the United States: the National Collaborative Perinatal Project (NCPP) (Daniels et al., 2003), The New York City Children's Environmental Health Study (Wolff et al., 2007), and the Child Health and Development Study conducted in the San Francisco Bay Area (Hertz-Picciotto et al., 2005). Overall, the Hokkaido, Oswego and North Carolina studies are the least PCB-exposed cohorts, while the Faroe Islands is the highest, followed by the German, the NCPP, the Michigan, the Nunavik and the Netherlands cohorts.

Gestational growth was evaluated in several cohorts. In Michigan, higher cord plasma PCB concentrations were associated at birth with lower weight, smaller head circumference and shorter gestation (Fein et al., 1984; Jacobson et al., 1990a). In the Netherlands, *in utero* PCB exposure was associated with lower birth weight and growth until three months of age (Patandin et al., 1998). However, in the two most highly PCB-exposed cohort studies conducted in the Faroe Islands and West Greenland, fetal growth and duration of gestation were not related to prenatal exposure to PCBs (Grandjean et al., 2001a). However, in the Nunavik cohort where PCB exposure was similar to that in Michigan and the Netherlands and two to three times lower than that in Greenland and the Faroe Islands, cord plasma PCB concentrations were associated with reduced physical growth at birth and shorter duration of pregnancy (Muckle et al., 2004).

In most of the general population studies conducted in the United States, prenatal PCB exposure was not associated with fetal growth and duration of gestation (for North Carolina, Gladen et al., 2000, 2003; Rogan et al., 1986; for Oswego, Stewart et al., 2000; for the New York Children's Environmental Health Study, Wolff et al., 2007). This result was expected due to their low exposure levels. In the NCPP cohort, which involved infants born in the United States between 1959 and 1965 (before PCBs were banned) and which reported PCB exposure in a similar range to that observed in the Michigan cohort, PCB exposure was not related to preterm birth, birth weight and length of gestation (Longnecker et al., 2005). However, in a recent re-analysis of a subsample of the NCPP cohort, maternal levels of *ortho*-substituted PCBs were associated with reduced body weight through 17 years of age among girls but not among boys (Lamb et al., 2006). Another re-analysis of the Child Health and Development Study conducted in the San Francisco Bay Area with children born in the years 1964 to 1967 found that prenatal PCB exposure is related to reduced birth weight and weight-for-gestational age in boys only (Hertz-Picciotto et al., 2005). Furthermore, although no PCB effects were noticed in the New York Children's Environmental Health Study, prenatal DDE exposure was related to lower birth weight and head circumference and interestingly, maternal susceptibility factors including PON1 contributed to the observed effects (Wolff et al., 2007).

Nine prospective PCB cohort studies have provided empirical data on neurobehavioral function during infancy and childhood. Three studies out of six, those from North Carolina (Gladen et al., 1988; Rogan and Gladen, 1991), the Netherlands (Koopman-Esseboom et al., 1996) and Germany (Walkowiak et al., 2001; Winneke et al., 1998), suggested effects of prenatal PCB exposure on general development (mental or psychomotor) during infancy. Negative effects of PCBs on fine and gross motor development were not observed in children from three highly exposed fish-eating cohorts (in Michigan, Jacobson et al., 1990a; in Nunavik, Despres et al., 2005; in the Faroe Islands, Grandjean et al., 2001b) but were reported in the Netherlands where exposure is related to consumption of dairy products and meat (Vreugdenhil et al., 2002a).

Six studies used IQ-type tests, and four (the Oswego, Netherlands, Michigan and German cohorts) reported a lower IQ score as a function of *in utero* exposure to PCBs (Jacobson and Jacobson, 1996; Patandin et al., 1999; Walkowiak et al., 2001; Vreugdenhil et al., 2002a; Stewart et al., 2003b). PCB effects on IQ were seen in specific sub-groups in the Netherlands (those children not breastfed and born to younger mothers) and German cohorts (parents with lower verbal IQ scores) suggesting that perinatal environmental exposure may impact fetal programming changes which occurred as a result of prenatal exposures. Poorer vocabulary and verbal comprehension have been consistently associated with prenatal PCB exposure in all cohorts that included these tests in their study protocols (i.e., in Oswego, Stewart et al., 2003b; the Netherlands, Patandin et al., 1999; in Michigan, Jacobson and Jacobson, 1996; and in the Faroe Islands, Grandjean et al., 2001b). Associations between prenatal PCB exposure and visuo-spatial functions were

tested in the Michigan, Netherlands, Faroe Islands and Oswego cohorts but were only found to be significant in the lowest exposed Oswego cohort (Stewart et al., 2003b) at three years of age and were not replicated when children were tested a year and a half later.

Several components of human memory have been assessed at multiple ages and with different tests in these PCB cohort studies, which makes comparisons of study results very difficult. However, it appears that consistent effects were found on visual recognition memory tasks during infancy in the Oswego (Darvill et al., 2000), Nunavik (Jacobson et al., 2008) and Michigan (Jacobson et al., 1985) cohorts, but not in the highly exposed German cohort (Winneke et al., 1998). Visual recognition memory has also been assessed at four years of age in the Michigan study and negative effects of prenatal PCB exposure were found, suggesting long-lasting effects on this component of cognition (Jacobson et al., 1992). Episodic long-term memory was not related to prenatal PCB exposure in the two cohort studies in the Netherlands and the Faroe Islands that documented this domain of effects (Grandjean et al., 2001b; Vreugdenhil et al., 2004). Short-term memory has been assessed in four different PCB cohorts: North Carolina, Michigan, Netherlands and Faroe Islands. Results from the Michigan and the Netherlands cohorts supported a negative effect of prenatal PCB exposure on short-term verbal memory but the effects could rather be due to decreased attention allocation or poorer executive control, which are also involved during the completion of these tasks. In fact, consistent negative effects were observed between studies on attentional function, especially on speed of information processing. These effects have been observed in three out of four studies (in Michigan, Jacobson et al., 1992; Jacobson and Jacobson, 2003; in the Netherlands, Vreugdenhil et al., 2004; and in the Faroe Islands, Grandjean et al., 2001b). Furthermore, effects on executive functions are reported for 'planning' on both cohorts that documented this (in the Netherlands, Vreugdenhil et al., 2004; and in Michigan, Jacobson and Jacobson, 1996). Another executive function referred to as poorer 'response inhibition' has been consistently related to prenatal PCB exposure in both the Michigan (Jacobson and Jacobson, 2003) and Oswego (Stewart et al., 2003a, 2005, 2006) cohorts.

Because behavioral impairment may occur independently from cognitive dysfunction, the effects of PCBs on behavior were specifically examined in four studies conducted in different locations by different authors. In the Michigan study, perinatal exposure to PCBs was related to decreased 'activity' in children at four years of age (Jacobson et al., 1990a) and to higher 'impulsivity' but not to 'activity' in 11 year-old children (Jacobson and Jacobsen, 2003). The association with lower activity at birth was corroborated in the North Carolina cohort (Rogan et al., 1986). The Netherlands study was the only one to assess 'play behavior' at school age; less masculinized play behavior in boys and more masculinized play behavior in girls were associated with elevated exposure to PCBs, dioxins, and other related organochlorine compounds (Vreugdenhil et al., 2002b). Finally, in the Oswego study, prenatal PCB exposure was related to 'emotional reactivity' which was assessed by physiological reaction to stress at birth (Stewart et al., 2000), to 'response inhibition' at four and a half years of age which is crucial to the ongoing regulation of behavior (Stewart et al., 2003a), and to 'impulsivity' at eight years of age (Stewart et al., 2005).

A consensual hypothesis to understand the neurobehavioral effects associated with *in utero* exposure to POPs is that these effects are mediated through the disruption of the thyroid system during brain development. First, in the Netherlands study involving 418 mother–infant pairs, thyroid hormone levels were in the normal range, but higher dioxin and PCB-TEQ levels in human milk were significantly correlated with lower triiodothyronine (T3) and thyroxine (T4) levels and with higher levels of thyroid-stimulating hormone (TSH) in the infants' plasma at the age of two weeks and three months. Thyroid hormone level alterations detected in this study, however, were not directly associated with neurological dysfunction (Koopman-Esseboom et al., 1994b). Sandau et al. (2002) examined chlorinated phenolic compounds in umbilical cord plasma of newborns in three populations with different PCB exposures, including an Inuit population. Retinol and thyroid hormone status (T3, T4, TSH and thyroxin-binding globulin) were determined in most samples. The authors found an inverse association ($r = -0.47$; $p = 0.01$) between log-normalized free thyroxine and log-normalized total phenolic compounds (ΣPCB and hydroxy-PCBs). Total chlorinated phenolic compounds were also negatively associated with T3 ($r = -0.48$, $p = 0.03$). In 182 singleton term births from Faroe Islands, 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. Thyroid function was normal and not associated with PCB exposure in this cohort (Steuerwald et al., 2000).

In conclusion, study results on human growth and PCB exposure are contradictory in general population studies where the exposure does not come from fish or marine mammal consumption. When data from more highly exposed cohorts with PCB exposure due to fish and marine mammal consumption are compared, study results are also inconsistent but cannot rule out the hypothesis of growth effects associated with *in utero* PCB exposure. Recent results by Wolff et al. (2007) underlined that individual susceptibility due to the presence/absence of specific genetic polymorphisms in studied populations may explain discrepancies between study results and emphasized that genetic specificity of studied populations should be taken into account in future studies.

Results from the PCB studies conducted to date suggest that prenatal exposure to PCBs is related to a relatively specific profile of cognitive impairments in children. Among the cognitive functions assessed, effects have been most clearly demonstrated on 'executive functions' and speed of 'information processing'; these effects could

be responsible for the small decreases in IQ observed in most studies. Verbal abilities and visual recognition memory are also likely to be impaired. However, no conclusive effects have been found on visuo-spatial abilities, episodic memory and sustained attention. Moreover, PCB effects appear to be independent of sensory and motor functions. Child behaviors were not documented in most of the PCB studies cited above because these effects have been associated with other toxicants such as alcohol and Pb. Future studies should evaluate this outcome.

To date, it is not clear whether the mechanism of action of PCBs on neurobehavioral function is through the disruption of the endocrine system during prenatal development. Further empirical work is needed with thyroid hormone homeostasis being measured at different prenatal periods and especially at the first trimester of pregnancy when thyroid hormones regulate neuronal proliferation, cell migration and differentiation.

8.4.5.2. **Perfluorinated compounds**

Epidemiological studies have not revealed a consistent association between serum perfluorochemical levels and adverse health effects in humans. Although thyroid hormone imbalance has been reported in laboratory animal studies, corresponding findings have not been consistently reported in humans. Recently, Apelberg et al. (2007) examined relationships between cord serum concentrations of PFOS and PFOA and gestational age, birth weight and measures of birth size, including head circumference, length and ponderal index (a measure of body mass at birth) in a population of newborns in the United States. Although negative associations were noted between both PFOS and PFOA concentrations and birth weight, ponderal index and head circumference after adjusting for potential confounders, it is possible that other unmeasured factors in this study, such as diet, may be influencing the observed relationships. A significantly elevated risk of bladder cancer has been observed for one group of workers exposed to PFOS, however, the available epidemiological studies of workers occupationally exposed to PFOS are considered inadequate to assess the potential of this substance to induce cancer in humans.

8.4.5.3. **Methylmercury**

Growth and developmental effects of prenatal MeHg exposure have been studied since the 1970s in nine large birth-cohort and retrospective studies. Neurobehavioral effects during childhood have been documented. Three well-designed, prospective, longitudinal studies have examined the neurodevelopmental effects of prenatal exposure to MeHg. Sources of exposure were from fish and pilot whale consumption in the Faroe Islands (Grandjean et al., 1992), deep-sea and reef fish consumption in the Seychelles (Myers et al., 1995b) and from fish consumption in New Zealand (Kjellstrom et al., 1982). Other cohort studies were conducted in Michigan, Madeira, Brazil, French Guyana, the Philippines, Greenland, and also in Cree Indians and Inuit from northern Quebec. MeHg-contaminated fish was also the main source of exposure in these cohorts.

In the Seychelles study, maternal hair Hg was related to increased birth weight but this association was only significant for males (Myers et al., 2000a). In the Faroe Islands cord blood Hg was not associated with birth weight (Grandjean et al., 2001a); a doubling of the cord blood Hg concentration was however associated with lower bodyweight at 18 months and at 42 months of age (Grandjean et al., 2003). In the Philippines, where MeHg exposures were 2-fold higher than those in the Faroe Islands, prenatal Hg exposure was not associated with birth weight but was related to smaller head circumference at birth (Ramirez et al., 2000). Finally, in Michigan, where maternal hair Hg levels were half those reported for the Seychelles cohorts, exposure to Hg was related to an increased incidence of preterm delivery (<35 weeks) (Xue et al., 2007). In Greenlanders, a negative association has previously been shown between blood Hg concentrations and birth weight (Foldspang and Hansen, 1990), but in a reanalysis with a completed dataset, this result was disproved (Bjerregaard and Hansen, 1996). In Nunavik, birth weight was not associated with cord Hg concentrations in the first study conducted between 1993 and 1996 (Lucas et al., 2004) and was confirmed in a more recent study conducted with the same population (Muckle et al., 2004).

In the Faroe Islands, several associations have been observed between hair Hg or cord blood Hg concentrations and neurobehavioral outcomes such as decreased neurologic optimality score in newborns, decreased performance in domains of language, attention and memory, auditory and visual brain processing in seven year-olds (Grandjean et al., 1997, 1998; Murata et al., 1999a,b) which persisted at 14 years of age (Debes et al., 2006; Murata et al., 2004). Similar neurobehavioral effects were observed in the New Zealand study at six to seven years of age (Crump et al., 1998). In contrast, prenatal Hg exposure in the Seychelles studies was not related to development during infancy and childhood although a broad range of neurobehavioral endpoints including language, memory, motor, perceptual-motor and behavior were documented from 6 to 108 months of age (Davidson et al., 1995, 1998, 2000; Axtell et al., 2000; Myers et al., 1995a,b, 1997, 2000b). The authors of the Faroe Islands cohort study pointed out the possibility that MeHg neurotoxicity might be potentiated by simultaneous PCB exposure in their population, which had about 3- to 4-fold higher PCB levels than for most other cohorts (Grandjean et al., 2001b). When the study results were examined by neurobehavioral domains, the domains of effect observed in two or three cohorts were:

- verbal function (in the Seychelles-pilot study, Myers et al., 1995a; in New Zealand, Crump et al., 1998 and Kjellstrom et al., 1982; in the Faroe Islands, Debes et al., 2006 and Grandjean et al., 1997);

- visuo-motor integration (in the Faroe Islands, Grandjean et al., 1997; in Brazil, Grandjean et al., 1999a; in French Guyana, Cordier et al., 2002); and
- verbal memory and attention (in the Faroe Islands, Debes et al., 2006 and Grandjean et al., 1997; in Brazil, Grandjean et al., 1999a).

Brainstem auditory evoked potentials have shown much consistency in finding detrimental effects of prenatal MeHg exposure (Murata et al., 2007). This neurophysiological measure of auditory processing was used in Madeira (Murata et al., 1999b), in the Faroe Islands at 7 and 14 years (Grandjean et al., 1997; Murata et al., 2004) and in Greenland (Weihe et al., 2002). Both the Faroese and the Madeiran studies found a positive association between MeHg exposure and latencies of brainstem auditory evoked potentials. Results from the Greenland cohort somewhat corroborate these findings despite its lack of statistical power due to the small sample size. These results are also in accordance with those obtained in Ecuador with school-age children of gold miners exposed to elemental Hg vapor and MeHg in food (Counter, 2003).

Although it appears that the most consistent marker of prenatal MeHg exposure is delayed auditory processing assessed from brainstem auditory event potentials, there are many inconsistencies between studies, and there is a need for other well-conducted prospective studies to elucidate the specific growth and neurobehavioral effects of MeHg. The conflicting results suggest that differences in maternal diet during pregnancy may impact on fetal susceptibility to MeHg exposure and that potential neurobehavioral effects of MeHg exposure could be found in domains of verbal function, visuo-motor integration and attention.

8.4.5.4. **Lead**

Although 10 to 15 μg/dL has long been considered the lower bound threshold for Pb neurotoxicity in children (CDC, 2003), recent improvements in study design have provided empirical evidence that there may be no safe level of Pb exposure (Finkelstein et al., 1998; Wigg, 2001; Chiodo et al., 2004). Results from prospective cohort studies have provided evidence that low-level *in utero* Pb exposure can impair infant growth and development. Cord blood Pb levels below 10 μg/dL have been associated with decreased birth weight (Dietrich et al., 1989), weight gain (Sanin et al., 2001) and decreased body mass index (Odland et al., 1999). A wide range of developmental effects were observed in several birth cohorts with prenatal Pb exposure below 10–16 μg/dL either in cord or maternal blood. Abnormal reflexes, occurrence of some neurological signs and changes in muscle tonicity were observed in neonates (Ernhart et al., 1986), delayed brainstem auditory evoked responses were observed at birth, during infancy and during childhood (Rothenberg et al., 1994, 2000), and most recently, deficits in visual function were observed in children seven to ten years of age (Rothenberg et al., 2002). Furthermore, the effects on mental development originally observed in the Boston and Cincinnati cohorts during the 1980s were recently corroborated in a Mexican cohort (Hu et al., 2006).

Fewer studies have examined infant and child behavior in relation to prenatal exposure to Pb. Only one study (Tang et al., 1999) has focused on the association between low-level prenatal Pb and behavioral development during infancy; adverse effects were observed on sociability at nine months of age. Studies with preschool and school-aged children did not report any behavioral effects associated with prenatal exposure (Padich et al., 1985; Wasserman et al., 1998). In contrast, effects of postnatal Pb exposure were documented on various aspects of child behavior, including activity, attention, anxiety, sleep disturbances, and conduct disorders (Padich et al., 1985; Hansen et al., 1989; Sciarillo et al., 1992; Wasserman et al., 1998, 2001; Chiodo et al., 2004; Davis et al., 2004). However, most of these studies did not control for prenatal exposure and for exposure during early infancy.

Recently, results from one cohort study conducted with preschool aged Inuit children from Nunavik Arctic Quebec (Canada) indicated that blood lead levels at five years of age were associated with changes in neuromotor performance (reaction time, sway oscillations, alternating arm movements and action tremor) (Despres et al., 2005). Behavioral effects were also observed with increased impulsivity and activity during neuropsychological testing, as rated by child testers (Fraser et al., 2006). These effects were correlated with venous blood Pb levels collected at the time of test, not with newborn cord blood Pb concentrations. However, a recent analysis of another Nunavik cohort study, this one with infants being followed-up at 11 months of age, has shown that cord blood Pb concentrations were related to observational measures of inattention (Plusquellec et al., 2007). This association remained significant even after removing children whose cord blood Pb concentrations were over 10 μg/dL. These results emphasize that behavioral effects of low prenatal Pb exposure are likely to be observed when testing protocols include sensitive measures of behavior.

8.4.5.5. **Nutrient effects on the neurotoxicity of environmental contaminants**

8.4.5.5.1. Selenium

It has been suggested during the last decade that the neurotoxicity of environmental contaminants found in marine mammals consumed by some indigenous people might be partially or totally attenuated by some nutrients and antioxidants found in this same seafood but this hypothesis has not been adequately tested empirically in humans.

In order to address this hypothesis in a Nunavik preschool cohort, Saint-Amour et al. (2006) included the interaction factor 'child blood mercury/child blood selenium' in the multivariate analysis. This interaction variable was not associated with latencies and amplitudes of visual evoked potentials. In contrast, high intake of Se

during childhood had a negative impact on the visual system instead of being beneficial or protective against Hg neurotoxicity. Although such associations with Se were unexpected, it is known that very high intake of essential elements for brain development may turn out to have adverse effects, as was recently demonstrated for vitamin E (Miller et al., 2005). Se toxicity has been documented in adults (Yang and Xia, 1995; Hansen et al., 2004), but there is a lack of reliable scientific information regarding toxicity thresholds for infants and children. The Food and Nutrition Board of the National Research Council (USA) recommends a 'Tolerable Upper Intake Level' of Se of 150 µg/d for children four to eight years old, which corresponds to an average blood concentration of 2.76 µmol/L (National Academy of Sciences, 2000). The average blood Se concentration observed in Nunavik was on average twice that limit, i.e., 5.6 µmol/L. Moreover, almost 20% of children tested had blood Se concentrations exceeding the maximum safe level recommended for adults (i.e., between 8 and 10 µmol/L). It is therefore likely that the visual evoked potentials protocol was sensitive enough in the Nunavik cohort to reveal sub-clinical effects of high Se intake, but more research is needed to address the issue of the threshold for Se toxicity in pediatric populations. The results also provide some support that nutritional factors may account for differences between the two major Hg studies; the Seychelles Child Development study and the Faroe Island study.

8.4.5.5.2. Polyunsaturated fatty acids

There is a growing body of research data indicating that imbalances or deficiencies of certain PUFAs of the n-3 and n-6 series may contribute to shorter duration of pregnancy and a wide range of childhood difficulties including 'attention deficit/hyperactivity disorder' (ADHD) or related symptoms, disruptive behaviors, and learning difficulties (Richardson, 2003, 2006; Hibbeln et al., 2006). Two PUFAs, arachidonic acid (AA) and docosahexaenoic acid (DHA), play a major structural role in the brain and the visual system, making up 20% of the dry weight of the brain and more than 30% of the retina (Helland et al., 2001; Innis, 2004). Two other PUFAs, dihomogamma-linolenic acid (DGLA) and eicosapentaenoic acid (EPA) play a more minor structural role but are also crucial for normal brain function (Marszalek and Lodish, 2005). These PUFAs are synthesized from essential fatty acids (EFAs) via processes of desaturation and elongation (Richardson, 2003). EFAs from the n-6 and n-3 series are linoleic acid (LA) and alpha-linolenic acid (ALA), respectively. PUFA and its precursor EFAs cannot be synthesized *de novo* by mammals; they must be ingested from dietary sources and transported to the brain (Marszalek et al., 2005). Furthermore, DHA synthesis from dietary ALA is limited in humans (Gerster, 1998; Pawlosky et al., 2001; Burdge and Calder, 2005), therefore, preformed DHA and EPA should be obtained directly from the diet (Gerster, 1998; Burdge and Calder, 2005; McNamara and Carlson, 2006). In modern diets, vegetable oils, nuts, seeds and grains are the main sources of LA intake, while green leafy vegetables, seaweed, some nuts and seeds, such as flax and walnut, are the dietary sources of ALA. Consumption of meat and dairy products provides additional PUFAs (DGLA and AA) from the n-6 series, while fish and seafood are dietary sources of PUFAs (EPA and DHA) from the n-3 series (Richardson, 2003; McNamara and Carlson, 2006). Prenatal PUFAs are thus of interest in circumpolar populations because their source is, as for environmental contaminants, mainly through fish and seafood consumption and they may act as protective factors against the neurotoxicity of environmental contaminants.

In the Faroe Islands, despite MeHg exposure, increased weight and length at birth was related to higher frequency of seafood meals consumed during pregnancy (Olsen et al., 1992). In contrast, the ratio of plasma n-3 : n-6 as a marker of high dietary intake of local marine mammals was not related to birth weight in Greenlandic newborns (Deutch et al., 2006). In the cord blood monitoring program conducted in Nunavik from 1993 to 1996, n-3 PUFAs were associated with increased duration of gestation and birth weight (Lucas et al., 2004). A recent cohort of Seychelles children has been established to help document whether nutrients (e.g., DHA, iodine, iron) derived from fish can explain the absence of association between *in utero* exposure to MeHg and neurobehavioral development (Clarkson and Strain, 2003) but results are not yet available. In Nunavik, higher cord plasma DHA concentration was associated with longer gestation, better visual acuity and recognition memory at six months, and better Bayley Scale mental and psychomotor performance at 11 months (Jacobson et al., 2008). In contrast, DHA from breast-feeding was not related to any indicator of these parameters. In preschool-aged children from Nunavik, n-3 PUFA concentrations on the day of child testing were related to faster processing of information in the visual system (Saint-Amour et al., 2006). In contrast, in this study, no significant interactions between nutrients and contaminants were found, which did not support the hypothesis that these nutrients could afford protection against environmental neurotoxicants. The results with Se and PUFAs highlighted the importance of taking into account nutrients that may co-occur with environmental contaminants when attempting to study the complex associations between pollutants and human growth and development in fish-eating populations.

8.4.5.6. **Summary and concluding comments**

New findings from several cohort studies examining fish consumers have been reported recently; some have taken place in the Arctic (Greenland, Nunavik, Faroe Islands). Other cohort studies in the United States have looked at relationships between health and POPs.

Although there have been associations found in individual cohort studies between fish consumption or POPs exposure and head circumference, birth

weight, duration of pregnancy and infant growth, the relationships observed differ between studies. It is clear that different contaminant levels, different mixtures of chemicals, diet, maternal susceptibility factors and other confounding factors play a significant role in changing the associations found from one study to the next. It is also clear that exposure to POPs and Hg can adversely affect prenatal and postnatal development in human populations.

Results from the PCB studies conducted in the Faroe Islands and Nunavik to date suggest that prenatal exposure to PCBs is related to a relatively specific profile of cognitive impairments in children. Among the cognitive functions assessed, effects have been most clearly demonstrated on executive functions and speed of information processing and those effects can be responsible for the small decreases in IQ observed in most studies. Verbal abilities and visual recognition memory are also likely to be impaired.

Perfluorochemicals are known to be present in human tissues in the Arctic and have been increasing over the past 15 years in several areas where monitoring has taken place. They are expected to adversely affect human health, although epidemiology evidence is weak. Negative associations between both PFOS and PFOA concentrations and birth weight, ponderal index and head circumference could also be related to other co-contaminants and unmeasured factors. The risk posed by PFOS exposure for cancer is still uncertain. More careful animal and human studies are urgently needed to assess the full implications of this ubiquitous environmental pollutant for the health of Arctic populations.

For Hg exposure, potential neurobehavioral effects have been found in the Faroe Islands in the domains of verbal function, visuo-motor integration and attention. However, the most consistent marker of prenatal MeHg exposure is delayed auditory processing assessed from brainstem auditory event potentials. Because of the inconsistencies between studies, there is a need for additional well-conducted prospective studies to elucidate the specific growth and neurobehavioral effects of MeHg and to assess the impacts of differences in maternal diet during pregnancy on susceptibility to MeHg exposure.

Lead is well known to adversely affect neurodevelopment and behavior in children. Until recently, studies of behavioral effects of Pb in children have only confirmed effects from postnatal exposure, not from prenatal exposure. New studies with children from Nunavik have shown that cord blood Pb concentrations were related to observational measures of inattention (Plusquellec et al., 2007) even at cord blood Pb concentrations below 10 μg/dL. These new data indicate that behavioral effects of low prenatal Pb exposure are likely to be observed when testing protocols include sensitive measures of behavior.

Some nutrients and antioxidants found in seafood are thought to be capable of attenuating the effects of some environmental pollutants, especially Hg; however, the hypothesis has not been adequately tested in humans. Very high intakes of Se, a well-studied antioxidant, may actually have had a negative impact on the visual system in Nunavik children instead of being beneficial or protective against Hg neurotoxicity; very high level intakes of Se have also been shown to have adverse effects in adults. There remains a lack of reliable scientific information regarding toxicity thresholds for infants and children. Even though average levels of Se in children in a recent Nunavik study were twice the 'Tolerable Upper Intake Level' set for children in the United States, no adverse effects were seen in children in the visual system tested (Saint-Amour et al., 2006).

Imbalances or deficiencies of certain PUFAs of the n-3 and n-6 series are also thought to contribute to shorter duration of pregnancy and a wide range of childhood difficulties including ADHD or related symptoms, disruptive behaviors, and learning difficulties (Richardson, 2003, 2006; Hibbeln et al., 2006): however, study results between cohorts are not entirely consistent. Recently, Muckle et al. (2004) demonstrated significant beneficial effects of n-3 fatty acid on growth and duration of gestation in Nunavik newborns. A recent cohort of Seychelles children has been established to help document whether nutrients (e.g., DHA, iodine, iron) derived from fish can explain the absence of association between *in utero* exposure to MeHg and neurobehavioral development (Clarkson and Strain, 2003) but results are not yet available.

The results may provide some support that nutritional factors including antioxidants and PUFAs may alter responses to contaminant exposures and could account for differences in the results found in the Seychelles Child Development and the Faroe Islands cohort studies. They also underscore the importance of nutrient considerations in the design of cohort studies attempting to study the complex associations between pollutants and human growth and development in fish-eating populations.

8.4.6. **Immune system function**

In children and young adults accidentally exposed to large doses of PCBs and PCDFs in Taiwan ('Yu-Cheng disease'), serum immunoglobulin A (IgA) and immunoglobulin M (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. The 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 or pneumonia during their first six months of life than unexposed infants from the same neighborhoods. The authors speculated that the increased frequency of pulmonary diseases could result from a generalized immune disorder induced by transplacental or breast milk exposure to dioxin-like compounds, most likely 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.

In Dutch preschool children, the effects of perinatal background exposure to PCBs and dioxins persisted into childhood and were associated with a greater susceptibility to infectious diseases. Based on serum CB153 values, levels of PCB exposure of this cohort from two Dutch cities were comparable with those found among northern Québec Inuit. Common infections acquired early in life may prevent the development of allergy, so PCB exposure might be associated with the lower prevalence of allergic diseases found in this study. It should also be noted that Inuit from northern Québec have higher levels of CB153 than modern U.S. populations (1990s) studied, but similar levels to those reported historically in the United States (1960s and 1970s) and lower levels than seen in the Faroe Islands.

Organic or inorganic Hg has cytotoxic activities for cellular components of the immune system in several species of rodents. MeHg, a form of organic Hg, can alter non-specific defense mechanisms such as inhibition of natural killer (NK) cell's activity in rats and mice. It also decreases the expression of certain activation markers of T-cells (HLA-Dr, IL-2R). Moreover, it has been well demonstrated that MeHg can affect the function of B-cells and therefore reduce the humoral-mediated response (Daum et al., 1993).

8.4.6.1. **Clinical outcomes**

In Nunavik, an epidemiological study conducted during 1989 to 1991 investigated whether organochlorine exposure is associated with the incidence of infectious diseases and immune dysfunction in Inuit infants (Dewailly et al., 2000a). The study examined the number of infectious disease episodes during the first year of life of 98 breast-fed and 73 bottle-fed infants. Concentrations of organochlorines were measured in early breast milk samples and used as surrogates for prenatal exposure levels. Otitis media (middle ear infection) was the most frequent disease with 80% of breast-fed and 81% 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, HCB and dieldrin. The relative risk (RR) for 4- to 7-month old infants in the highest tertile of *p,p'*-DDE exposure compared to infants in the lowest was 1.87 (95% CI: 1.07–3.26). The lowest tertile had a breast milk concentration of *p,p'*-DDE of <730 µg/kg lipid versus >1320 µg/kg lipid in the third or highest tertile. 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 prenatal organochlorine exposure was not associated with these biomarkers. In this study, the potential confounders (n-3 fatty acids, vitamin A and smoking) were not fully controlled. For this reason, new studies were designed and initiated to address these issues.

Inuit children from Nunavik have high rates of both acute otitis media and lower respiratory tract infections. Such rates were higher than those of other non-indigenous North American populations previously published. Admission for lower respiratory tract infections is up to ten times more frequent in Nunavik Inuit compared to other Canadian populations (Dallaire et al., 2006b).

Two other epidemiology studies have since been conducted on the effect of POPs on immune function and infectious disease incidence. The first was a component of the Child Cohort Study, in which infectious diseases were monitored during the first year of life (Dallaire et al., 2004). Results showed that prenatal exposure to PCBs and DDE was associated with a higher incidence rate of acute infections during the first six months of life. Infants in the highest quartiles of PCBs and DDE exposure had statistically significantly more episodes of infections than their counterparts in the lowest quartile of exposure, although the associations at lower quartiles of exposure were not always statistically significant because of limited statistical power. Infant infections were mostly observed during the first six months of life; the association was much weaker when infections during the first 12 months of life were considered. This study supported 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 (Dallaire et al., 2004, 2006a,b).

The second follow-up study was a review of all the medical files for 350 preschool children who participated in the Nunavik umbilical cord blood monitoring program in 1993 to 1996 (Dallaire et al., 2006a). Results showed that during the first five years of life, children in the highest quartiles of PCB prenatal exposure had a significantly higher incidence rate of outpatient visits for otitis media and lower respiratory tract infections, but not for upper respiratory tract infections. The association between PCB exposure and otitis media adopted a clear dose-response pattern. The study confirms the associations previously observed in the same population. Furthermore, it shows that the relation between PCB (as a marker of organochlorine exposure) and respiratory infection seems to persist past the first months of life.

Other factors such as vitamin A and n-3 fatty acids can also modulate immune function and vitamin A has been found to be deficient in some Canadian Inuit populations (Blanchet et al., 2000). Neonatal vitamin A deficiency has also been found to have an impact on acute respiratory infections among preschool Inuit children from Nunavik (see section 8.4.6.3.2).

8.4.6.2. **Immunization**

Antibody response to vaccination is an intermediate marker of the competence of the adaptive immunity to infections. Vaccination programs include essentially

three types of products: (1) killed vaccine (influenza, whole-cell pertussis, inactivated polio); (2) protein-conjugated or protein-based vaccine (Haemophilus influenza type b, diphtheria, tetanus, acellular pertussis vaccine, hepatitis B); and (3) attenuated live virus (measles-mumps-rubella, varicella, BCG). Antibody response to conjugated Haemophilus influenza type b (Hib) is of great interest because, prior to immunization, Hib was the most frequent cause of bacterial meningitis in Inuit children, which was five to ten times more frequent than in Caucasian children.

In the Faroe Islands, a study was done to assess whether prenatal and postnatal exposure to PCBs impacted upon antibody response to childhood immunizations. Following routine childhood vaccinations against tetanus and diphtheria, 119 children were examined at 18 months and 129 children at age 7 years and their serum samples were analyzed for tetanus and diphtheria toxoid antibodies and for PCBs. The antibody response to diphtheria toxoid decreased at age 18 months by 24.4% for each doubling of the cumulative PCB exposure at the time of examination. The diphtheria response was lower at age 7 years and was not associated with PCB exposure. However, the tetanus toxoid antibody response was affected mainly at age 7 years, decreasing by 16.5% for each doubling of prenatal exposure. The results suggest that perinatal exposure to PCBs may adversely impact on immune responses to childhood vaccinations (Heilmann et al., 2006).

8.4.6.3. **Immune biological markers**

8.4.6.3.1. Lymphocyte subsets and immunoglobulins

In the course of the 1989–1991 Inuit cohort study conducted in Nunavik, biomarkers of immune system function (lymphocyte subsets, plasma immunoglobulins) were determined in venous blood samples collected from breast-fed and bottle-fed infants at 3, 7 and 12 months of age. Results showed that at age 3 months, concentrations of white blood cells (lymphocytes, more specifically those of the CD4 subtype), were lower ($p < 0.05$) in blood samples from breast-fed babies than in the bottle-fed group. At 7 and 12 months of age, IgA concentrations were lower ($p < 0.05$) in breast-fed infants than in bottle-fed infants. This also appeared to be the case for CD4:CD8 ratios, although differences were not statistically significant. None of the immunological parameters was associated with prenatal organochlorine exposure (Dewailly et al., 2000a).

8.4.6.3.2. 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. Results from different animal and human studies vary; however, almost all studies revealed that lymphopoiesis and/or maturation of lymphocytes are altered (generally reduced) with vitamin A deficiency. Vitamin A deficiency could increase the frequency, severity, and duration of infections. Lower respiratory tract disease has been associated with vitamin A deficiency in many cross-sectional clinical and population-based studies. Otitis media was among the first infections to be associated with vitamin A deficiency in humans.

Vitamin A clinical deficiency has never been documented in Canadian Arctic populations. However, many studies have documented inadequate intakes of vitamin A (Receveur et al., 1998). A more recent report suggested that the daily vitamin A intake in Nunavik falls below the recommended intake (Blanchet et al., 2000). Furthermore, POPs such as organochlorines have been shown to alter vitamin A homeostasis in many species, including primates. It is important, therefore, to gain a better understanding of the relationships between vitamin A, organochlorine levels, and infectious disease incidence in Arctic populations.

In a recent pilot study, plasma concentrations of retinol were measured in cord blood samples to assess the vitamin A status of 135 Inuit newborns from Arctic Québec and 22 newborns from the general population of southern Québec. Mean retinol concentrations were 14.8 μg/dL and 24.3 μg/dL, respectively. Vitamin A levels of over 20 μg/dL have been considered as normal vitamin A status, those between 10 and 20 μg/dL as low, and those below 10 μg/dL as deficient. The difficulty of using vitamin A as an effect biomarker of PCB exposure is related to the variability of vitamin A intake among individuals and non-systematic supplementation programs in pregnant women.

Vitamin A status was also associated with incidence of infectious events. Vitamin A concentration in umbilical cord blood was associated with incidence and severity of respiratory infections in preschool Inuit children from Nunavik, Québec. The medical charts of 305 children were reviewed from 0 to 5 years of age. The association between vitamin A concentration in umbilical cord plasma and the incidence rates of acute otitis media (AOM), lower respiratory tract infections (LRTIs) and hospitalization rates for LRTIs was evaluated. Compared to children with vitamin A concentrations of 20 μg/dL or over, adjusted rate ratios for children below 20 μg/dL were 1.06–1.62 for AOM, 1.12–1.34 for LRTIs, and 1.09–1.43 for hospitalization for LRTIs. Most adjusted rate ratios were statistically significant for AOM and LRTIs, but not for hospitalization for LRTIs. It was concluded that neonatal vitamin A deficiency appeared to be a significant risk factor for AOM and LRTIs in this population (Cameron et al., 2008).

8.4.6.4. **Summary and concluding comments**

Effects of POPs on the immune systems of laboratory animals and humans have been addressed in previous AMAP assessments (AMAP, 1998). Several recent studies in Arctic Canada confirm and support the relationship between contaminant exposure and depressed immunity. Both PCBs and DDE are associated with a higher incidence rate of acute infections in Inuit children during the first six months of life. These children also have high rates of acute otitis media and respiratory tract

infections. Dallaire et al. (2006b) reported that hospital admissions for 'lower respiratory tract' infections among Inuit from Nunavik are ten times higher than in other Canadian populations. Follow-up studies by the same authors confirmed that the relationship between PCB (as a marker of organochlorine exposure) and lower respiratory tract infections and otitis media seems to persist past the first months of life and follows a dose-response pattern.

Vitamin A and n-3 fatty acids are also known to be capable of modulating immune function. Several organochlorines have been shown to alter vitamin A homeostasis in a number of species and vitamin A levels among Arctic Inuit are known to be lower than among non-Arctic populations. New data for preschool Inuit children from Nunavik indicate that vitamin A deficiency is a 'significant risk factor' for acute respiratory infections and otitis media among Inuit children from Nunavik.

Vitamin A appears to be able to affect gene expression, which in turn affects cellular differentiation (including immune cell development). Concentrations of lymphocytes and immunoglobulin A have been found to be depressed in breast-fed babies when compared to bottle-fed babies, even though these depressed levels are not associated with prenatal exposure to contaminants. Studies of effectiveness of vaccination programs among Inuit children and children from the Faroe Islands indicate that perinatal exposure to PCBs (as a marker of POPs) may adversely affect immune responses to childhood vaccinations. A more complete understanding of the overall relationship between vitamin A, contaminants and infectious disease among Arctic populations needs to be developed.

Despite the effects of organochlorines on the immune system, breast-fed babies were healthier overall than bottle-fed babies. As a consequence, these findings are not a reason for mothers to curb breast feeding or for public health officials to withdraw from a policy that promotes breast feeding of newborns.

8.4.7. **Metabolic and cardiovascular effects**

The environment interacts with many functions of the body, including the cardiovascular system. These interactions are often complex, sometimes indirect and generally difficult to study. To date, most of the available information is from epidemiological studies.

8.4.7.1. **POPs and cardiovascular disease**

The dioxin 2,3,7,8-tetrachlorodibenzodioxin (TCDD) is a highly toxic POP that accumulates in animal fat; the local food web is the main source of exposure in the human population. The acute effects of TCDD exposure are well described in the literature but the long-term consequences have been underevaluated and may include atherosclerosis, hypertension and diabetes, all known risk factors for cardiovascular disease (Pelclova et al., 2006). A recent U.S. study (Huang et al., 2006) focused on the relationship between POPs and hypertension. After control for covariates, a statistically significant elevation in hypertension discharge rates was related to living close to a waste site. The same authors also studied the relationship between living close to waste sites and the occurrence of stroke. The results suggest that living near a source of POPs contamination constituted a risk of exposure and an increased risk of acquiring cerebrovascular disease (Sergeev and Carpenter, 2005). Another study from this group, found that living close to a waste site was associated with giving birth to a male infant of low birth weight (Shcherbatykh et al., 2005).

Trichloroethylene (TCE) is a common, persistent drinking water contaminant. Epidemiological studies have linked TCE exposure during pregnancy to health problems in offspring, including cardiac anomalies. However, a thorough literature analysis revealed that no single process was clearly affected by TCE, providing support for the hypothesis that gestational TCE exposure does not increase the prevalence of coronary heart disease (Watson et al., 2006).

In an animal study it was shown that CB126 exposure in female rats resulted in effects on cardiovascular risk factors, such as serum cholesterol, blood pressure and heart weight (Lind et al., 2004). No epidemiological studies have examined this potential association between cardiovascular disease and CB126 exposure.

8.4.7.2. **Toxic metals and cardiovascular disease**

Most studies of the relationship between toxic metals and the risk for clinical cardiovascular disease have focused on Hg exposure. The first studies reporting a relation between MeHg exposure and carotid intima-media thickness were from Finland (Salonen et al., 2000). Since then, other studies have been published, offering varying degrees of support. In a follow-up study the same group suggested that a high content of Hg in hair may be a risk factor for acute coronary events and cardiovascular disease and all-cause mortality in middle-aged eastern Finnish men. Hg may also attenuate the protective effects of fish on cardiovascular health (Virtanen et al., 2005b). The U.S. Health Professionals' Follow-up Study reported only a minimal overall cardiovascular risk associated with the Hg exposure levels among participants (Yoshizawa et al., 2002).

8.4.7.3. **Oxidative stress**

Studies on Nunavik Inuit suggest that consumption of marine products, a major source of n-3 PUFAs, is beneficial to cardiovascular health (Dewailly et al., 2001a). The authors concluded that the traditional Inuit diet was probably responsible for the low mortality rate from ischemic heart disease in this population. In Greenland, however, in spite of their high consumption of n-3 PUFAs, the Inuit have a similar prevalence and mortality of ischemic heart disease as European populations (Bjerregaard et al., 2003; Jørgensen et al.,

2008) while their mortality from other cardiovascular disease (stroke and other heart diseases) is significantly higher. This could be due to the presence of other active substances in the marine diet or to lifestyle factors such as smoking and decreased physical activity, which counteract the beneficial effect of n-3 PUFAs.

Fish and marine mammals consumed by the Inuit are highly contaminated by MeHg (Wagemann et al., 1996) and other potentially prooxidant contaminants such as PCBs (Dewailly et al., 1993; Muckle et al., 2001a). Both MeHg (LeBel et al., 1990; Sarafian and Verity, 1991; Lund et al., 1993; Yee and Choi, 1994) and PCB (Slim et al., 1999, 2000; Ryu et al., 2003) are documented sources of oxidative stress. For example, CB153, the main PCB congener found in Inuit, was reported to induce concentration-dependent formation of reactive oxygen species and death of cerebellar granule cells (Mariussen et al., 2002). The mean concentrations of PCB, MeHg and Se in Inuit of Salluit, Quebec were respectively 16- to 18-fold, 10- to 14-fold, and 8- to 15-fold higher than reported for reference Caucasian populations consuming little fish (Bélanger et al., 2006). The low risk of cardiovascular disease observed in an Inuit population highly exposed to MeHg contrasts strongly with the increased risk of cardiovascular disease and acute myocardial infarction found to be associated with Hg exposure in Finnish men (Salonen et al., 1995; Virtanen et al., 2005b). The potentially deleterious effects of MeHg on cardiovascular health have been the focus of vigorous debate (Salonen et al., 2000; Guallar et al., 2002; Yoshizawa et al., 2002; Seppanen et al., 2004; Virtanen et al., 2005b), and it would be of particular interest to find out which factors may account for the contrasting results obtained in different populations.

In Inuit from Nunavik, no evidence of alterations in plasma concentrations and redox states of α-tocopherol (α-TOH) and coenzyme Q10 (CoQ10) associated with MeHg exposure was found. Oxidative stress was assessed by measuring the plasma concentrations and redox states of α-TOH and CoQ10, two sensitive biomarkers of oxidative stress, in relation to exposure. Ubiquinol-10, ubiquinone-10 and the ubiquinone-10 : $CoQ10_{total}$ ratio were elevated compared to ratios calculated for Caucasian populations but showed no associations with PCBs, MeHg or n-3 PUFAs. Ubiquinol-10 (β = 0.23, p = 0.007) and $CoQ10_{total}$ (β = 0.27, p = 0.009) were predicted by blood Se, and α-TOH by PCB (β = 4.12, p = 0.0002), n-3 PUFAs (β = 9.16, p = 0.02) and OxLDL (β = 3.04, p = 0.05). Unexpectedly, the α-TOH quinine:α-TOH ratio, in the normal range, was negatively predicted by PCB (β = -0.41, p = 0.02). Using sensitive biomarkers of redox alterations, no evidence was found for MeHg- or PCB-associated oxidative stress in these Inuit. However, despite robust blood antioxidant defenses, the unusually elevated ubiquinone-10 : $CoQ10_{total}$ ratio (0.21 ± 0.11) suggests some form of oxidative stress of unknown origin (Bélanger et al., 2006).

Susceptibility to MeHg toxicity is likely to depend on many environmental factors including diet and possible genetic factors. The traditional Inuit diet is unusually rich in Se (Blanchet et al., 2000), CoQ10 (Bliznakov, 1976) and vitamin E (Blanchet et al., 2000), all of which might be beneficial for cardiovascular health. An inverse relationship between serum Se concentrations and risk of coronary heart disease or myocardial infarction was found in Finnish men (Salonen et al., 1982) even though the Se concentrations in this population were relatively low. Se is essential to human health (Rayman, 2000), being a key component of several antioxidant proteins including selenoprotein and glutathione peroxidase and thioredoxin reductase enzyme families, which harbor a critical seleno-cysteine at their active sites. Blood glutathione peroxidase activity was found to be elevated in Inuit of Nunavik (Bélanger et al., 2006) and within the range associated with lower risk of cardiovascular disease in Caucasians (Blankenberg et al., 2003). The Inuit also showed favorable lipid profiles and low levels of oxidized LDL (Bélanger et al., 2006), a factor implicated in the pathophysiology of atherogenesis (Stocker and Keaney, 2004).

LDL particle susceptibility to oxidation is likely to depend on blood and LDL antioxidant status. Circulating LDL contains two lipid-soluble antioxidants, α-TOH, the main component of vitamin E, and CoQ10. CoQ10 is found in two redox forms: the reduced form ubiquinol-10 ($CoQ10H_2$) and the oxidized form ubiquinone-10. In addition to its classic role as an electron carrier in the mitochondrial respiratory chain, CoQ10 has gained much interest as a potential antioxidant in plasma and lipoproteins (Murthy, 2001). The antioxidant function of ubiquinol-10 has been related to a chain-breaking radical quencher in the oxidative cycle and as a regenerator of α-TOH from its oxidized derivative α-tocopheryl quinone (α-TQ) (Sunesen et al., 2001). Most attention has focused on vitamin E because it is the major lipid-soluble antioxidant in LDL. Lipoproteins isolated from carotid plaques are apparently not grossly deficient in α-TOH (Niu et al., 1999), and the relative extent of α-TOH oxidation in human atherosclerotic lesions was found to be maximal early in the disease where it exceeded lipid oxidation (Terentis et al., 2002). The major LDL oxidation product was α-TQ, which only reached ~10% of LDL - α-TOH, suggesting that vitamin E did not contribute much to prevent LDL lipid oxidation in the artery wall (Terentis et al., 2002). The respective roles of vitamin E and CoQ10 as potential antioxidants inhibiting LDL particle oxidation and as antiatherogenic agents remain controversial (Stocker and Keaney, 2004). The results of vitamin E supplementation studies in animal models of atherosclerosis (Suarna et al., 2006) and the outcome of clinical interventions with α-TOH supplements have generally been disappointing (Stocker, 1999; Stocker and Keaney, 2004). In contrast, ubiquinol-10 was reported to be much more efficient than α-TOH in inhibiting LDL oxidation (Stocker et al., 1991), suggesting that CoQ10 would be the first line antioxidant defense in LDL particles. In support, CoQ10 proved to be a much more efficient antiatherogenic agent than α-TOH in ApoE-deficient mice (Witting et al., 2000; Suarna et al., 2006).

In order to investigate the relationships between Hg,

Se and oxidative stress, Bélanger et al. (2008) measured glutathione peroxidase and glutathione reductase activities in blood samples from 142 residents of Salluit and Nunavik. Hg was found to be negatively correlated with glutathione reductase activity, an NADPH-dependent enzyme that regenerates glutathione from glutathione disulfide. In contrast, plasma Se concentration was positively correlated with glutathione peroxidase activity, a selenoenzyme that catalyzes the conversion of hydrogen peroxide to water. Hg exposure may, therefore, diminish defense mechanisms against oxidative stress by limiting the availability of glutathione, while Se may afford protection by favoring the destruction of hydrogen peroxide.

A biochemical assessment of the oxidative stress in adult residents of Nunavik is ongoing. The level of plasmatic LDL oxidation has been measured during the Qanuippitaa survey as a potential marker of oxidative stress. Preliminary results indicate that oxidized LDL was 1.6 times lower ($p < 0.0001$) in Inuit subjects than in individuals from a Caucasian population, supporting the previous observation that n-3 fatty acids and Se could be strong protective factors for cardiovascular diseases among Inuit (Bélanger et al., 2003).

8.4.7.4. **Mercury exposure and changes in blood pressure**

Intake of Hg with food items from marine mammals and fish has been suggested to be involved in cardiovascular disease. In Greenland, Hg was measured in blood together with 24-h blood pressure (BP) in four groups of healthy subjects: Group 1, Danes living in Denmark consuming European food; Group 2, Greenlanders living in Denmark consuming European food; Group 3, Greenlanders living in Greenland consuming European food; and Group 4, Greenlanders living in Greenland consuming mainly traditional Greenlandic food. Hg in blood was highest in Greenlanders and increased when they lived in Greenland and consumed traditional Greenlandic food (Group 1, 2.2 μg/L (median); Group 2, 4.8 μg/L; Group 3, 10.8 μg/L; and Group 4, 24.9 μg/L). The 24-h BP was the same in all three groups of Greenlanders. However, 24-h diastolic BP was lower among Greenlanders than Danes (71 v 76 mm Hg, $p < 0.001$) and 24-h pulse pressure was higher (54 v 50 mm Hg, $p < 0.001$). Hg in blood was significantly and positively correlated to pulse pressure (rho = 0.272, $p < 0.01$). Pulse pressure was higher and diastolic BP was lower in Greenlanders than Danes. Pulse pressure increased with higher Hg content in blood. Although genetic factors may be responsible to some extent for the difference in pulse pressure between Greenlanders and Danes, the present results seem to support the hypothesis that Hg intake from marine food is involved in cardiovascular disease (Pedersen et al., 2005).

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 at age 7 years blood pressure, heart rate and heart rate variability were determined (Sorensen et al., 1999). After adjustment for body weight, diastolic and systolic blood pressure increased by 13.9 mm Hg (95% CL: 7.4, 20.4) and 14.6 mm Hg (95% CL: 8.3, 20.8), respectively, when compared to newborn cord blood Hg concentrations of 10 μg/L compared to a base value of 1 μg/L. Above 10 μg/L, which corresponds to a current exposure limit, no further increase in blood pressure 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 exposures, particularly from 1 to 10 μg/L cord blood, at which the variability was reduced by 47% (95% CL: 14%, 68%). These findings suggested that prenatal exposure to MeHg might affect the development of cardiovascular homeostasis.

In Nunavik, the impact of Hg levels on blood pressure was recently studied among Inuit adults, taking into account potential confounding factors. Systolic blood pressure and diastolic blood pressure were measured during a clinical visit and pulse pressure was calculated. Pearson correlation was used to study simple relations between Hg and blood pressure parameters while multiple regressions were carried out to control for confounders. It was found that Hg was correlated with systolic blood pressure ($r = 0.15$; $p < 0.0001$) and pulse pressure ($r = 0.17$; $p < 0.0001$) while the correlation with diastolic blood pressure did not reach statistical significance. After adjusting for confounders, the association with systolic blood pressure ($\beta = 2.41$; $p = 0.0004$) and pulse pressure ($\beta = 1.18$; $p = 0.02$) remained statistically significant while the association with diastolic blood pressure became significant ($\beta = 1.01$; $p = 0.04$). The results of this study suggest a negative impact of Hg on blood pressure after controlling for confounding factors (Valera et al., 2008).

Cardiovascular effects associated with low level Hg exposure may be of greater public health significance than some other end points such as neurotoxicity. The low incidence of coronary heart disease in Inuit proposed to be due to the fatty acid composition of their diet could be attenuated by high Hg exposure because recent studies indicate that Hg can have a negative effect on the cardiovascular system. Although the mechanism is still uncertain, it is possible that Hg may inhibit important antioxidative mechanisms in humans and could promote the peroxidation of unsaturated fatty acids such as docosahexaenoic acid (DHA) and decosapentaenoic acid (DPA). Regarding cardiovascular toxicity at low-level MeHg exposures, the first Faroe Island cohort showed that blood pressure tended to increase and heart rate variability tended to decrease when prenatal Hg exposures increased in the low-dose range (Sorensen et al., 1999). Alkyl-mercury poisoning is associated with increased blood pressure and children with Hg poisoning often have increased heart rate and blood pressure. Experimental evidence shows that MeHg toxicity results in hypertension that

remains many months after cessation of exposure. Although insufficient for risk assessment purposes, this evidence suggests that the cardiovascular system should be considered a potential target for MeHg. When considering Hg exposure, a slight negative impact on the cardiovascular system could be of greater public health relevance than a slight impact on the central nervous system.

8.4.7.5. **Mercury and heart rate variability**

Methylmercury is well known for its toxic activity on the central nervous system but recently, some authors have suggested that it can also interfere with the normal functioning of the cardiovascular system (Sorensen et al., 1999; Guallar et al., 2002; Oka et al., 2002; Grandjean et al., 2004; Pedersen et al., 2005). Some studies have reported an association between Hg and myocardial infarction (Guallar et al., 2002), elevated blood pressure (Sorensen et al., 1999; Pedersen et al., 2005), and reduced heart rate variability (HRV) (Sorensen et al., 1999; Oka et al., 2002; Grandjean et al., 2004). HRV reflects the balance between the cardiac parasympathetic and sympathetic activities of the autonomic nervous system but information concerning the influence of MeHg on HRV is sparse. Reduced HRV can be a marker for an increased arrhythmia risk, causing ventricular fibrillation (and other outcomes) which can lead to sudden cardiac death (Galinier et al., 2000; Makikallio et al., 2001; Kruger et al., 2002; La Rovere et al., 2003; Kataoka et al., 2004). The diminution of HRV has been also associated with increased cardiac mortality and all cause mortality (Tsuji et al., 1994, 1996; Seccareccia et al., 2001).

The effect of MeHg on HRV was first studied in subjects exposed to MeHg *in utero* (Sorensen et al., 1999; Oka et al., 2002; Grandjean et al., 2004). In a cohort study of 7-year-old children from the Faroe Islands, the coefficient of variance of the heart rate in boys decreased by 47% in a range of cord blood concentrations from 1 to 10 μg/L (5–50 nmol/L). This was depicted as an indication of parasympathetic nervous dysfunction in children exposed to low doses of MeHg during the prenatal period (Sorensen et al., 1999). This cohort was re-examined at 14 years old and a diminution of the coefficient of variation of heart rate of 2.7% was detected as well as a diminution in parasympathetic and sympathetic activity of 6.7% (Grandjean et al., 2004).

In contrast, Oka et al. (2002) conducted a case-control study to assess the chronic effect of exposure to high doses of MeHg on HRV in subjects suffering from the fetal Minamata disease. Some HRV indices were lower in fetal Minamata disease patients.

A component of the Nunavik Inuit study (see Box 8.7) recently assessed the impact of MeHg levels on HRV in an adult population of Nunavik taking into account the influence of possible confounding factors such as n-3 fatty acids, age, gender, cholesterol, diabetes, obesity, smoking and alcohol consumption. Several indices of HRV from the time and the frequency domains were derived from a 2-hour Holter monitoring assessment. MeHg was weakly associated with low frequency in simple correlation but these associations became non-significant after adjusting for confounders. No impact of Hg levels on HRV was observed in this population although HRV was mainly associated with obesity measured as waist circumference (Valera et al., 2008).

8.4.7.6. **POPs exposure and metabolic effects in Inuit**

Legacy POPs found in the Inuit traditional diet include organochlorines, such as PCDDs, PCDFs, PCBs and various chlorinated pesticides or industrial products. More recently, new POPs have emerged as potential environmental health threats to Arctic people. Brominated flame retardants such as PBDEs (de Boer and Denneman, 1998; Meironyte et al., 1999; Noren and Meironyte, 2000; Ikonomou et al., 2002) show similar physico-chemical and toxicological properties to PCBs, PCDDs and PCDFs (Darnerud et al., 2001; McDonald, 2002; Zhou et al., 2002; Birnbaum and Staskal, 2004; Gill et al., 2004) and have been measured in human milk (Pereg et al., 2003) and plasma (Dewailly et al., 2005) of Nunavik Inuit. Perfluorinated compounds such as PFOS and PFOA are found in several Arctic wildlife species (Giesy and Kannan, 2001; Kannan et al., 2001, 2002; Tomy et al., 2004; Bossi et al., 2005b; Smithwick et al., 2005, 2006) including some that are part of the Inuit traditional diet (Tittlemier et al., 2006). They are also found in human blood from several populations (Kannan et al., 2004), including Nunavik Inuit (Dewailly et al., 2005; Dallaire et al., 2009). Unlike brominated flame retardants, perfluorinated compounds are not structurally similar to organochlorines, but tend to resemble the structure of essential PUFAs that are abundant in the Inuit traditional diet, and have been shown to exert similar hypolipidemic effects in Nunavik Inuit (Pereg et al., submitted). However, despite their structural similarity to PUFAs, the inability of perfluorinated compounds to be converted to Acyl-CoA esters and to enter into intermediary metabolism of lipids suggests different mechanisms of action that could possibly lead to toxic effects (Vanden Heuvel et al., 2006). While POPs have been shown to interact with steroid (De Rosa et al., 1998; Sonnenschein and Soto, 1998; Soto et al., 1998; Davis et al., 2005; Turyk et al., 2006) and thyroid hormones (Koopman-Esseboom et al., 1994b; Langer, 2005), to affect neurodevelopment and behavior (Jacobson and Jacobson, 1996, 1997; Jacobson et al., 1985, 1992; Gladen et al., 1988; Rogan and Gladen, 1991; Huisman et al., 1995a,b; Koopman-Esseboom et al., 1996; Winneke et al., 1998; Despres et al., 2005; Saint-Amour et al., 2006) and to disrupt immune functions (Dewailly et al., 2000a; Weisglas-Kuperus et al., 2000; Dallaire et al., 2004, 2006a) in many populations including Nunavik Inuit, the higher risk of developing diabetes has recently received more attention from the scientific community and is now emerging as a potential additional adverse effect related to POPs exposure. Although the

association between POPs exposure and type II diabetes has been reported in several populations exposed through different routes, including the dietary route (Henriksen et al., 1997; Pesatori et al., 1998; Calvert et al., 1999; Cranmer et al., 2000; Longnecker et al., 2001, Longnecker and Daniels, 2001; Steenland et al., 2001; Remillard and Bunce, 2002; Fierens et al., 2003; Glynn et al., 2003; Rylander et al., 2005; Vasiliu et al., 2006), it has not yet been investigated in Arctic populations.

8.4.7.7. **POPs and diabetes**

'Metabolic Syndrome' is a condition associated with several genetic and environmental determinants (Zimmet et al., 2001) that represents a growing health concern because it precedes the onset of type II diabetes as well as the development and progression of atherosclerosis and other cardiovascular diseases. It is mainly characterized by a general resistance of glucose and lipid metabolism to the action of insulin (termed insulin resistance), abdominal obesity, dislipidaemia and hypertension (Zimmet et al., 2005). It is possible that POPs exposure may be involved in the development of metabolic syndrome through endocrine disruption affecting glucose and lipid metabolism (Heindel, 2003; Grun and Blumberg, 2006; Tabb and Blumberg, 2006) even if they are not the main determinant of this condition (genetic background and lifestyle habits may be important determinants of metabolic syndrome). There is a growing body of recent literature reporting that exposure to POPs, especially dioxins, is related to a greater risk of developing diabetes. Earlier studies first reported higher incidences of glucose intolerance and/or type II diabetes associated with dioxin exposure in the Italian population exposed in the Seveso accident (Pesatori et al., 1998, 2003; Bertazzi et al., 2001), veterans exposed during Operation Ranch Hand in Viet Nam (Henriksen et al., 1997; Cranmer et al., 2000; Longnecker et al., 2000) and chemical workers exposed in the United States (Calvert et al., 1999; Steenland et al., 1999).

More recently, similar associations have been reported in populations environmentally exposed to dioxins and other POPs elsewhere in the world and even in populations showing relatively low levels of exposure (Fierens et al., 2003; Glynn et al., 2003; Lee et al., 2006; Porta, 2006). Background PCB exposure was also related to a higher incidence of diabetes in a random sample of the American population (Lee et al., 2006) and in a cohort of pregnant women (Longnecker et al., 2001). A similar association was reported in populations exposed to PCBs through dietary sources (fish consumers) in Sweden (Rylander et al., 2005) and in Michigan (Vasiliu et al., 2006). Further evidence of a causal relationship between POPs and diabetes comes from the Michigan study because the diabetes status was related to exposure levels prevailing before the onset of the disease, so rendering unlikely the possibility of reverse causation, i.e., diabetic status affecting circulating levels of POPs (Vasiliu et al., 2006). This issue needs to be investigated in POPs-exposed Inuit populations.

8.4.7.7.1. Diabetes in Inuit

Early studies conducted during the 1960s and 1970s suggested that Inuit had been spared the diabetes epidemic experienced by many sub-Arctic North American Indian groups (Scott and Griffith, 1957; Sagild et al., 1966; Mouratoff et al., 1967; Mouratoff and Scott, 1973; Bjerregaard et al., 1998). However, recent data from the Alaskan Native Diabetes Registry indicate that the prevalence among Inuit is rising, although it is still lower than the rate in the United States. The lower prevalence of diabetes among Inuit has been attributed to their higher consumption of PUFA-rich traditional foods (Adler et al., 1994; Murphy et al., 1995; Cervenakova et al., 2002). In Inuit from Nunavik the situation is similar. However, despite the low prevalence of diabetes, the main conclusions from the 1992 health survey indicate a relatively high prevalence of major risk factors for diabetes such as obesity and smoking (Blanchet et al., 2002). These increased rates coupled with changes in dietary habit (notably the reduction of highly nutritional traditional food intake and the rising consumption of store-bought foods high in refined carbohydrates, saturated and trans fatty acids) enjoined researchers to suggest a closer surveillance of diabetes in individuals aged 45 years and over (Blanchet et al., 2002). Twelve years later, preliminary results from the Qanuippitaa survey still show a low prevalence of diabetes (5%) comparable to the rest of Canada (4.8%) in people aged 20 and over (Centre de prévention et de contrôle des maladies chroniques, 2002) but also reveal a considerable increase in diabetes risk factors, especially in women (Dewailly et al., 2007c). The prevalence of diabetes (adjusted for age) is significantly higher in women (6.6% vs 3.3% in men, $p < 0.0001$) and 3.4% of participants exhibited a pre-diabetic state, showing impaired fasting glucose (glycemia level between 6.1 and 6.9 mmol/L). Hyperinsulinemia under fasting conditions was detected in 12.7% of participants and its prevalence was significantly higher in women (15.2%) than men (10.2%) ($p = 0.03$). Moreover, most diabetics in this study were obese (65%) and an additional 23% of diabetics were overweight. In the Inuit population, the prevalence of obesity defined by the body mass index is 19.4% and abdominal obesity is 38.9%. There is a clear link between type II diabetes and obesity (Zimmet et al., 2001; Pincock, 2006) and in this study, 70.8% of women showed abdominal obesity. The high prevalence of diabetes risk factors now raises health concerns for this population, especially for women.

Diabetes was believed to be rare in Greenland until the results from a population survey in 1999–2001 proved the prevalence to be about 25% higher than in Denmark; 70% of the cases had not been diagnosed prior to the study (Jørgensen et al., 2002).

Alaska Natives, in common with Canadian and Greenlandic indigenous peoples, have experienced profound changes in diet, activity, and lifestyle over the past 50 years. One of the most striking changes is the increase in overweight and obesity and the

accompanying change in prevalence of type II diabetes mellitus. Among Alaska Natives in 2005, 37% of adults were overweight (BMI 25–29.9) and 27% were obese (BMI 30 or more); a total of 64% of adults beyond the normal weight range (State of Alaska, 2004). The prevalence of diabetes among 16 000 Yupik residents receiving care at Alaska Native health care facilities in 1965 was 0.8–1.6/1000, depending on the diagnostic criteria (Mouratoff et al., 1967). The prevalence of diabetes in Alaska Natives rose to 38/1000 age-adjusted population in 2005 (ANTHC, 2005). Among the different tribal groups and regions of Alaska, the prevalence varies considerably with the Yupik population in southwest Alaska having a prevalence of 22/1000 and the Tsimpshian population in southeast Alaska having a prevalence of 96/1000 in 2005 (ANTHC, 2005). The rate of increase in diabetes prevalence among Alaska Native groups also varies, with the greatest rate of increase occurring in the Athabascan Indians of interior Alaska, at 157% for the period 1990 to 2005 (ANTHC, 2005).

8.4.7.8. **Environmental risk factors for osteoporosis**

POPs have recently been associated with an increased risk of osteoporosis in animals (see section 8.3.2.2) and humans. The relationship between DDE and bone mineral density was recently examined in 68 sedentary Australian women who reported adequate dietary intake of calcium (Beard et al., 2000). Reduced bone mineral density was correlated significantly with age ($r = -0.36$, $p = 0.004$), as well as with increases in the log of DDE levels in serum ($r = -0.27$, $p = 0.03$). Beard and co-workers also used multiple-regression analysis to examine the influence of other predictor variables on the relationship between log DDE and bone mineral density. The strongest model ($p = 0.002$) included log DDE ($p = 0.018$), age ($p = 0.002$) and years on hormone replacement therapy ($p = 0.10$) as predictor variables; this model afforded a prediction of 21% of bone mineral density variation. 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 cause an inappropriate turnover of osteoclasts or inadequate production of osteoblasts within bone marrow leading to reduced bone density. These are interesting results, but must not be overinterpreted as this was a small study and the menopausal status and time since menopause, two important determinants of osteoporosis, were not included in the analyses.

A study was conducted in Nuuk, Greenland in 2000 to evaluate the prevalence of risk factors for osteoporosis fracture and more particularly environmental factors and their association with bone mass in menopausal women (Côté et al., 2006). The risk of osteoporosis fracture was assessed using an ultrasound bone densitometer. All three ultrasound parameters adjusted for age were lower in this Inuit population compared with women from southern Québec. The study found that 19% of the Inuit women had a high risk of osteoporosis fracture compared to 7.2% for the women of southern Québec. To identify which risk factors were associated with ultrasound parameters, a multiple linear regression model involving the stepwise removal of non-significant independent variables was used. The independent predictors of bone density were age ($p = 0.018$), BMI ($p = 0.018$), former users of oral contraceptives ($p = 0.003$), current hormone replacement therapy users ($p = 0.005$) and the sum of log of *mono-ortho* PCB TEQs ($p = 0.004$). These variables accounted for 36% of the variance of the bone density ($R^2 = 0.359$) (Côté et al., 2006). *Mono-ortho* substituted congeners (CBs 105, 118, 156) share some structural similarities with TCDD and can bind to the AhR. The consequences of activation of the AhR pathway on osteoporosis, however, are not clear. One possible explanation is that dioxin-like compounds elicit a broad spectrum of anti-estrogenic activities and may reduce bone density through this mechanism. In summary, concentrations of CB153, a surrogate of exposure to most organochlorines present in plasma samples, were inversely correlated to quantitative ultrasound parameters in univariate analyses ($p < 0.001$). However, CB153 concentrations were not associated with quantitative ultrasound values in multivariate analyses that comprised potential confounding factors such as age, body weight, former oral contraceptive use and current hormone replacement therapy use, which were all significant predictors of bone stiffness (total $R^2 = 0.39$; $p < 0.001$). Overall, little evidence was found that organochlorines exposure is related to osteoporosis in Greenlandic Inuit women, but the hypothesis that exposure to dioxin-like compounds might be linked to decreased bone quality and osteoporosis deserves further attention (Côté et al., 2006). Work is ongoing to assess the role of dioxin-like compounds in this association.

The 2004 Nunavik Inuit survey included bone density measurements of 207 peri-menopausal women. Regression analyses are ongoing to see whether exposure to dioxin-like compounds (as measured by the CALUX assay) is a risk factor for osteoporosis as found among Greenlandic women (Côté et al., 2006).

8.4.7.9. **Summary and concluding comments**

Contaminants, diet and genetics are likely to be significant co-factors implicated in cardiovascular diseases and metabolic disturbances. How they interact is an emerging area of research.

Recent studies in the Faroe Islands, Greenland and Nunavik (Canada) all indicate that Hg can affect circulatory parameters such as pulse pressure, heart rate and heart rate variability, blood pressure and hypertension. Prenatal exposures to MeHg may also affect the development of cardiovascular homeostasis. If these preliminary findings are confirmed, the estimated attributable burden of diseases due to contaminant exposure might increase. Even small relative risks have a large impact on diseases having high incidence and

mortality and could affect policy development on safe levels of exposure.

Both Hg and Se can modulate coronary heart disease risk and this has been confirmed in several studies of fish-eating coastal populations such as Inuit living in Arctic regions. Inuit consume large amounts of fish and marine mammals and consequently receive large doses of Hg. Contrary to the situation in eastern Finland reported by Salonen et al. (2000), the mortality rate from coronary heart disease in Canadian Inuit is low. Although, it was reported that n-3 fatty acids are strong protective factors for cardiovascular diseases among Inuit (Dewailly et al., 2001a), the protection could also result from a high intake of Se (Bélanger et al., 2003) through the consumption of traditional/country food such as *muktuk* (beluga and narwhal skin) and marine mammal liver which are both rich in Se.

MeHg and PCBs are prooxidant contaminants found in traditional diets. This diet is also an abundant source of n-3 PUFAs, Se and antioxidants, which might reduce cardiovascular risk. Although Inuit from Nunavik, Quebec have low concentrations of plasma oxidized LDL and elevated glutathione-related antioxidant defenses, the variance in OxLDL was predicted by PCB and blood glutathione, leaving the issue of contaminant-associated oxidative stress unresolved.

It is highly likely that oxidative stress is a significant underlying biochemical mechanism in MeHg neurotoxicity (Sarafian and Verity, 1991). Hg increases production of reactive oxygen species via deregulation of mitochondrial electron transport, as well as through glutathione depletion (Lund et al., 1993). The oxidative stress hypothesis is clearly supported by the finding that MeHg neurotoxicity can be inhibited by various antioxidants, including Se (Park et al., 1996) and N-acetyl-L-cysteine, a precursor of GSH (growth stimulating hormone). New studies in Arctic Canada indicate that 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. It will be important to continue to assess oxidative stress in adult residents of Nunavik and to further understand these and other mechanisms of Hg toxicity.

Exposure to POPs may contribute to the development of metabolic syndrome and diabetes type II among Inuit and other Arctic indigenous groups. The endocrine-disrupting properties of several contaminants, especially dioxin-like compounds, can affect glucose and lipid metabolism which in turn affect onset of metabolic syndrome. Genetic factors and lifestyle are also important determinants of metabolic syndrome. The dramatic increase in the rate of diabetes among Inuit and Alaskan Natives may be affected by multiple factors; however, the role played by contaminant exposure warrants further research.

Contaminant exposure may affect bone density. One study has reported that past exposure to DDT reduced bone mineral density in women through an effect on bone forming and reshaping cells. Inuit women in Greenland were found to have lower bone density than a southern Quebec population of non-Inuit. While there is no strong evidence from human studies that contaminants cause osteoporosis, the hypothesis that exposure to dioxin-like compounds might be linked to decreased bone quality and osteoporosis deserves further attention. Other studies are underway to explore this outcome in Arctic populations.

8.4.8. **Future studies with human population cohorts**

There are a number of population cohorts in the Arctic region which have been developed and are under active study. Others are being planned or are in the recruitment stage. These cohorts will be used to try to address emerging questions related to contaminants and health.

8.4.8.1. **Alaska, USA**

There are three cohorts in place or planned in Alaska: cohort 1 contains 150 Yupik infants recruited in 1999–2001; cohort 2 has 200 children recruited in 2004–2006; cohort 3 is being developed in 2008–2009 and will include 200 Yupik infants.

8.4.8.2. **Canada**

The Nunavik Study of the Université de Laval, Quebec is a cohort of approximately 300 children up to 10 years of age from the 14 Nunavik communities. It comprises three subgroups: 133 children assessed from the INFANT study in early childhood; 85 children from the PRESCHOOL study assessed at 5 years of age; and a group of 89 children from the Cord Blood Monitoring Program not previously assessed. A comprehensive protocol has been developed for the Nunavik study.

8.4.8.3. **Greenland**

The Greenland Child Cohort recruited 403 mothers and newborn children during 1999–2005. The exposure data are available while a follow-up is being planned.

The Greenland Adult Cohort is part of the international Inuit Cohort Study. Recruitment and basic cross sectional data collection from 2226 Inuit aged 18 years or older from West Greenland was completed during 2005–2007. Further recruitment from East Greenland will take place in 2008.

A new Greenlandic cohort is planned for 2008–2009 under the auspices of Centre for Arctic Environmental Medicine, Aarhus, Denmark.

8.4.8.4. **Faroe Islands**

In the Faroe Islands several cohort studies are ongoing. Cohort 1, established in 1986/87, is planned to be re-examined in 2008 and 2009. The clinical examination of cohort 2, established in 1999/00, was concluded in 2007.

A new birth cohort of 500 is now being recruited. All persons between 70 and 75 years of age have been

invited to undergo examination of their central nervous system and cardiovascular system.

In the field of reproductive health, 500 men in the second decade of life have been invited to give a semen and blood sample. All pregnant women and the biological fathers of the fetus are included in this TTP study. The maternal parents of the mothers and fathers in the study will be invited to be interviewed and lifestyle choices such as tobacco use, alcohol intake, and diet during pregnancy will be registered.

8.4.8.5. **Norway**

The University of Tromsø, Institute of Community Medicine, in cooperation with all delivery departments in northern Norway is developing a new North-Norwegian birth cohort, fully financed by the Norwegian Research Council. Populations are rural, coastal, urban, and a specific indigenous Sami population in Finnmark. Approximately 600 children are now included in the main study and a systematic clinical follow-up is planned for January 2009.

8.4.8.6. **Finland**

There is an ongoing cohort study in northern Finland, started in 1980, giving access to retrospective clinical information and stored blood samples for contaminant trends in human materials. A new child cohort of Arctic Indigenous Peoples of Lapland is at the planning stage, organized by The University of Oulu.

8.4.8.7. **Russia**

The North West Public Health Research Center, St. Petersburg established two cohorts in 2001–2003. Blood samples were collected and frozen. The samples will supplement those collected in 2001–2002. Follow-ups are planned for both cohorts (346 mother–child pairs; and 360 individuals from the general population, both genders and different ages) similar to the original PTS study of the Indigenous Populations of the Russian Arctic (AMAP, 2004b). Study areas include the three main regions of the Russian Arctic (Kola, Taymir and Chukotka Peninsulas). The follow-up study in Chukotka began in 2007 and continued in 2008. Eighty individuals from the general population of inland Kanchalan were invited to give blood samples and to be interviewed.

8.4.8.8. **Summary and concluding comments**

Cohort development and evaluation is extensive in the northern regions of several Arctic countries. Many new data on child development will come from the cohort started in Russia, Norway, and Finland, as well as those ongoing in the Faroe Islands and Nunavik. For adults, the Finnish cohort and the International Inuit Cohort Study (Canada–Greenland) will contribute extensively to knowledge of the impact of contaminants on chronic diseases.

8.5. Conclusions

8.5.1. General health of Arctic populations

- The health status of indigenous people of the Arctic regions of the United States, Canada, Greenland, and the Russian Federation is characterized by lower life expectancy, higher infant mortality, higher rates of infectious diseases (particularly among children) and much higher incidences of injuries and suicide when compared to the non-indigenous populations of these countries.
- It is very likely that the higher prevalence of tobacco use, less active lifestyles and consumption of more calorie-rich and nutrient-poor store-bought foods among some indigenous populations in the Arctic have contributed to an increasing burden of chronic diseases.
- Health intervention strategies and population health in the Arctic will only improve with better information and better cooperation between all players. A full understanding of ethnic-specific health status can only arise if common health status indicators are selected and then monitored, reported and analyzed consistently. This will require that indigenous peoples' organizations, tribal governments and other levels of government in each country work together and support the establishment and/or active utilization of indigenous status identifiers for ethnic-specific public health surveillance.
- While contaminants certainly play a role in the current health status of indigenous populations in many areas of the Arctic, it is also certain that other determinants of health are involved, including: education, economic wellbeing, cultural strength, community engagement in shaping its present and future, lifestyle choices, genetic susceptibility, and availability of public health services.
- Conducting epidemiological studies in the Arctic is difficult due to a variety of limiting factors: exposure to complex contaminant mixtures, small population size, contaminant-nutrient interactions, genetic factors, confounding factors, and health priorities. For this reason, epidemiological studies conducted in other parts of the world on POPs and metals-induced toxicity should be used as much as possible for risk assessment. However, different factors may limit the applicability of findings from these studies for Arctic populations.
- Indigenous populations in the Arctic are exposed to mixtures of contaminants and primarily through food. Investigating the toxicological properties of environmentally-relevant mixtures of POPs in laboratory species is essential for determining the biological plausibility of associations identified in epidemiology studies between exposure to these compounds and adverse health effects. It is clear from studies of chemical mixtures that data derived

from single chemical experiments cannot be used to predict the risk resulting from exposure to complex mixtures of POPs. Interactions between components of the mixture not only modify the disposition of individual components but also their dose-response relationship for various developmental endpoints. These interactions, coupled with differences in nutrient levels could explain some of the differences between the findings of the Faroe Islands and Seychelle Islands cohort studies.

- New and promising techniques which evaluate overall xenohormone activity in human blood are useful screening tools and can identify blood samples from population studies which warrant more expensive chemical analysis. The results from xenobiotics studies clearly indicate that single or a few POPs proxy markers cannot be used by themselves for assessment of either bioactivity or possible adverse effects of POP mixtures on human populations.

8.5.2. **Environmental POPs and health**

- Many POPs, including PCBs, PCDDs, PCDFs and pesticides can mimic hormone activities. As potential endocrine disrupters, they are suspected to be capable of increasing the risk of cancer, birth defects and reproductive and neuro-immune disorders. To date, no clear evidence for adverse endocrine-related human health effects of POPs has been obtained at the individual or population level. However, data from studies on wildlife species, laboratory animals and biomarker effects *in vitro* have strengthened the need for further research to address the potential impacts of endocrine disruptors on human populations.
- Although there have been associations found in individual cohort studies between fish consumption or POPs exposure and head circumference, birth weight, duration of pregnancy and infant growth, the relationships observed differ between studies. It is clear that different contaminant levels, different mixtures of chemicals, diet, maternal susceptibility factors and other confounding factors play a significant role in changing the associations found from one study to the next. It is also clear that exposure to POPs can adversely affect prenatal and postnatal development in human populations.
- Results from the PCB studies conducted in the Faroe Islands and Nunavik to date suggest that prenatal exposure to PCBs is related to a relatively specific profile of cognitive impairments in children. Among the cognitive functions assessed, effects have been most clearly demonstrated on executive functions and speed of information processing and those effects can be responsible for the small decreases in IQ observed in most studies. Verbal abilities and visual recognition memory are also likely to be impaired.
- Several recent studies in Arctic Canada confirm and support the relationship between contaminant exposure and depressed immunity. Both PCBs and DDE are associated with a higher incidence rate of acute otitis media and respiratory tract infections in Inuit children during the first six months of life. Concentrations of lymphocytes and immunoglobulin A have been found depressed in comparative studies of breast-fed babies and bottle-fed babies. The effectiveness of vaccination programs among Inuit children and children from the Faroe Islands appears to be compromised by perinatal exposure to PCBs (as a marker of POPs). New research with piglets supports these findings and indicates that transplacental POPs exposure leads to a reduction in antibody response.
- Preliminary findings from a large Russian Arctic cohort adds evidence to the findings identified earlier that higher levels of maternal blood serum PCBs might be associated with more frequent occurrences of low birth weight, premature births, stillbirths, and menstrual irregularities. These possible adverse reproductive health effects of POPs and metals will require more in-depth evaluation. Detailed analyses of all available data and systematic epidemiological studies, which take into account relevant confounders and other contaminants, must be undertaken before conclusive statements can be made.
- POPs exposures have been suggested as the reason for observed alterations in birth sex ratios in animal populations and occasionally in human studies. New research results with pigs, which have a similar reproductive system to humans, indicate that exposure of sperm to environmentally pertinent organochlorine mixtures *in vitro* adversely affects oocyte development, polyspermy, sperm fertility and embryonic development. However, a comparison of existing population studies, one including Arctic countries, did not reveal any definitive or consistent relationship between POPs, sperm X:Y ratios or male:female birth ratios. Emerging data from a larger cohort in the Russian Arctic indicate that increasing maternal PCB concentrations may be associated with an initial effect of increasing the male:female newborn ratio; however, causality has not been determined and the increase in the ratio appears to disappear in the highest concentration group. The possible effects of other contaminants have not been determined. Systematic epidemiological studies, including all possible confounders and other relevant contaminants, must be performed before any conclusive statements can be made about contaminants and sex ratios in Arctic populations.
- A large international study indicated some links between POP exposure and biomarkers of male reproductive function. Associations were found between high CB153 serum levels and low sperm counts, decreased sperm motility, and damage to sperm chromatin integrity in some of the sub-

populations studied. In spite of these effects, fertility was not related to POPs except in Inuit. Definitive conclusions cannot be derived from these studies, in part because the two POPs proxy markers measured did not represent the biological activity of the entire POPs mixtures. There are also open questions related to the role of genetic background, lifestyle and/or diet nutrition factors such as trace elements/antioxidants (e.g., Se) that may interfere with the possible adverse health effects of POPs.

- Exposure to POPs may contribute to the development of metabolic syndrome. The endocrine-disrupting properties of several contaminants, especially dioxin-like compounds, can affect glucose and lipid metabolism which in turn affect the onset of metabolic syndrome. Genetic factors and lifestyle are also important determinants of metabolic syndrome. The dramatic increase in the rate of diabetes among Inuit and Alaskan Natives may be affected by multiple factors; however the role played by contaminants in obesity, metabolism and diabetes warrants urgent study.
- Environmental mixtures may also be able to affect bone density (diminished bone cortical area and bone mineral content) in male and female rat pups. These findings may be significant for humans as indications of a negative association between PCB plasma levels and quantitative ultrasound bone parameters have been reported in a group of peri- and postmenopausal Inuit women from Greenland.

8.5.3. **Environmental metals and health**

- The growing fetus and newborn children are especially sensitive to the toxic effects of environmental Hg and Pb.
- Animal studies indicate that exposure to environmentally-relevant mixtures of POPs and metals have significant effects on reproduction. Exposures led to decreases in maternal weight gain, weight gain in offspring and increased mortality rates in pups prior to weaning. Interactions between MeHg and POPs in mixtures warrants further study as lower levels of MeHg administered alone have been found to lead to more pup mortality than found in mixture studies containing higher levels of MeHg.
- Potential neurobehavioral effects associated with MeHg exposure have been found in the Faroe Islands in the domains of verbal function, visuo-motor integration and attention. However, the most consistent marker of prenatal MeHg exposure is delayed auditory processing assessed from brainstem auditory event potentials. Because of the inconsistencies between studies, there is a need for additional well-conducted prospective studies to elucidate the specific growth and neurobehavioral effects of MeHg and to assess the impacts of differences in maternal diet during pregnancy on susceptibility to MeHg exposure.
- Recent studies in the Faroe Islands, Greenland and Nunavik all indicate that Hg can affect circulatory parameters such as pulse pressure, heart rate and heart rate variability, blood pressure, hypertension and atherosclerosis. Prenatal exposures to MeHg may also affect the development of cardiovascular homeostasis. If these preliminary findings are confirmed, the estimated attributable burden of diseases due to contaminant exposure might increase. Even small relative risks have a large impact on diseases having high incidence and mortality and could affect policy development on safe levels of exposure. Confirmation of these findings in other studies is needed as the current findings have potentially significant implications for Hg intervention policies. In addition, more research is needed to determine the relationship between changes in risk of cardiovascular disease and changes in diet among Arctic indigenous populations.
- It is highly likely that oxidative stress is a significant underlying biochemical mechanism in MeHg neurotoxicity. MeHg neurotoxicity can be inhibited by various antioxidants, including Se. New studies in Arctic Canada indicate that 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. It will be important to continue to assess oxidative stress in adult residents of Nunavik and to further understand interactions which affect the mechanisms of Hg toxicity.
- Lead is well known to adversely affect neurodevelopment and behavior in children. Until recently, studies of behavioral effects of Pb in children have only confirmed effects from postnatal exposure, not from prenatal exposure. New studies with children from Nunavik have shown that cord blood Pb concentrations were related to observational measures of inattention even at cord blood Pb concentrations below 10 μg/dL. The new data indicate that behavioral effects of low prenatal Pb exposure are likely to be observed when testing protocols include sensitive measures of behavior.
- Some new associations have been reported in Arctic Russia between spontaneous abortions and Hg levels in blood. No negative associations were found between maternal exposure to nickel and the risk of delivering a newborn with malformations of the genital organs. Further study to confirm the associations between Hg exposure and abortion rates is warranted.

8.5.4. **Nutrients, contaminants and health**

- Some nutrients and antioxidants found in seafood are thought to be capable of attenuating the effects of some environmental pollutants, especially Hg; however, the hypothesis has not been adequately tested in humans. Very high intakes of Se, a well-studied antioxidant, may actually have had a negative impact on the visual system in Nunavik children instead of being beneficial or protective against Hg neurotoxicity; very high level intakes of Se have also been shown to have adverse effects in adults. There remains a lack of reliable scientific information regarding toxicity thresholds for infants and children. Further research on the relationships between nutrients, especially Se, and contaminants is needed.
- Vitamin A and n-3 fatty acids are known to be capable of modulating immune function. Several organochlorine contaminants have been shown to alter vitamin A homeostasis in a number of species. Vitamin A levels among Arctic Inuit are known to be lower than among non-Arctic populations. New data for preschool Inuit children from Nunavik indicate that vitamin A deficiency is a 'significant risk factor' for acute respiratory infections and otitis media among Inuit children from Nunavik.
- Imbalances or deficiencies of certain PUFAs of the n-3 and n-6 series are also thought to contribute to shorter duration of pregnancy and a wide range of childhood difficulties including ADHD or related symptoms, disruptive behaviors, and learning difficulties; however, study results between cohorts are not entirely consistent. A recent study has demonstrated significant beneficial effects of n-3 fatty acids on growth and duration of gestation in Nunavik newborns.
- Nutritional factors including antioxidants and PUFAs can alter responses to contaminant exposures and could account for differences in the results found in the Seychelles Child Development and the Faroe Islands cohort studies. A recent cohort of Seychelles children has been established to help document whether nutrients (e.g., DHA, iodine, iron) derived from fish can explain the absence of association between *in utero* exposure to MeHg and neurobehavioral development but results are not yet available. Nutrient-contaminant interactions also underscore the importance of nutrient considerations in the design of cohort studies attempting to study the complex associations between pollutants and human growth and development in fish-eating populations.
- MeHg and PCBs are prooxidant contaminants found in traditional diets. This diet is also an abundant source of n-3 PUFAs, Se and antioxidants, that might reduce cardiovascular risk which has been found to be low in Canadian Inuit. Low cardiovascular risk among Canadian Inuit could also result from a high intake of Se through the consumption of traditional/country food such as *muktuk* and marine mammal liver which are both rich in Se.

8.5.5. **Genetics and health**

- Some contaminants (PCB and MeHg) and some nutrients (vitamin A) are able to directly affect gene expression. These findings have consequences for health outcomes and may indicate modes of action of some of these entities and how they interact. More research is needed to understand these findings.
- Global hypomethylation of the genome has been linked to genomic instability and cancer. The possibility that organochlorines adversely affect the genome by decreasing global genomic methylation is intriguing and should be examined in other circumpolar populations.

8.5.6. **Monitoring of contaminants**

- There is an urgent need to monitor the occurrence of emerging contaminants in the food chain such as brominated flame retardants and perfluoroalkyl compounds. Although existing data on exposure in the North do not currently indicate a risk from exposure to these compounds, the toxicology and epidemiology data base for these chemicals is weak and should be strengthened. Focus should be placed on monitoring levels and evaluating whether these chemicals can affect growth, developmental and behavioral outcomes.

Chapter 9

Risk Communication

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Summary

This chapter addresses how research results and the subsequent public health advice can be effectively communicated back to communities. It also describes the types of methodologies used, how advice impacts on communities and possible changes that could be made to improve the circumpolar communication strategy. Human health risk assessment topics are defined, and risk perception is discussed in general terms. Several national strategies on risk communication and risk management are described. There are significant differences in the national strategies, depending on the severity of contamination and its influence on food security, especially for indigenous peoples. It is concluded that the communication of risk needs to embrace the right-to-know and other fundamental human rights, as well as the precautionary principle.

Regular monitoring of food consumption behavior, food safety perspectives, and concerns and determinants of food choice should continue to support the development and provision of information that aids 'informed decision making' by northern residents. Communication of AMAP results should be undertaken in a more professional manner with the help of professional communicators. There is a need for more comprehensive tools and strategies for the communication of AMAP results; for the general population groups, public health purposes and decision makers, and specifically for the most vulnerable indigenous population groups. It is important that governmental authorities give more focus to professional communication strategies and that AMAP should use national authorities to develop communication strategies for this issue. The benefits of traditional food consumption should be communicated along with the results of technical risk assessments to support the provision of information to residents in these regions; to help residents make informed decisions about food and health has become critical to successful risk communication processes. Risk communication must be undertaken with great care and respect toward the receiver culture. Recommendations should always be based on a combination of evidence, experience, and common sense. Pre-testing of messages and an evaluation of risk perception by the public might be beneficial. It is crucial to involve the populations affected as well as external stakeholders (e.g., indigenous organizations) in the communication and evaluation processes in order to build trust and credibility. Good cooperation with the media is also very important.

Communication effort should be evaluated systematically and incorporated into AMAP's future monitoring program. Both northern residents and public health professionals require or request more information and support to interpret the implications of such technical risk assessment guidelines, viable risk optimization strategies, and risk communication processes and emerging issues in environmental health and toxicological research.

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. Human contaminant levels are too high, especially in the Arctic, and there is a need for strongly restricting the use and emissions of chemicals that are persistent, toxic, and able to accumulate in food chains. A forum for initiatives on this topic should be the Stockholm Convention.

9.1. Introduction

This chapter describes and assesses how research results and the subsequent public health advice can be communicated back to communities. The methodologies used, how advice affects communities, and changes that could be made to improve the circumpolar communication strategy are also discussed.

Chapter 7 concluded that 'It is essential that a better understanding of the health consequences of the nutritional transition and the nutrient/contaminant interaction in Arctic populations is achieved, and that this information is communicated to the Arctic populations in a correct and understandable way.' The primary issue for risk communication with Arctic peoples is their diet, which provides both essential nutrients and potentially harmful contaminants ('The Arctic Dilemma') (see Chapters 3 and 7). Figure 9.1 depicts the relationships

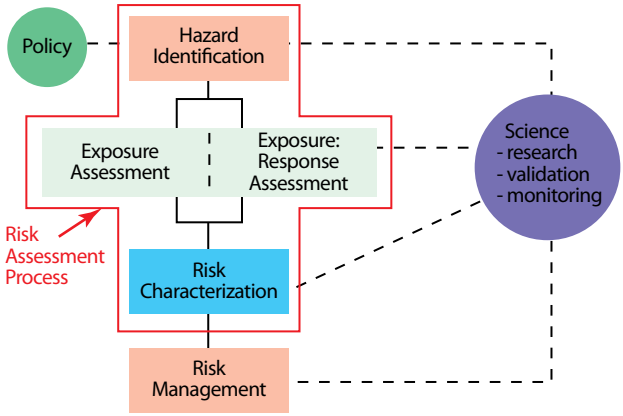

Figure 9.1. The various elements of the risk assessment process. Source: US EPA (2007a).

between risk assessment, toxicology, risk management, science, public policy, and risk communication (US EPA, 2007b). The basic human health risk assessment topics are defined in Box 9.1.

Box 9·1. Definition of the main human health risk assessment topics

Based on the US Environmental Protection Agency Waste and Cleanup Risk Assessment Glossary (US EPA, 2007b).

Hazard. The likelihood that a substance will cause an injury or adverse effect under specified conditions.

Toxicity (Hazard Identification and Dose-Response). *Dose-Response Assessment* is the process of quantitatively evaluating the toxicity of a given chemical agent as a function of human exposure to that chemical agent. The relationship between the dose of the contaminant administered or received and the incidence of adverse health effects in the exposed population forms the basis for the quantitative dose-response relationship. From these relationships, toxicity values (e.g., reference doses and slope factors) are derived that can be used to estimate the incidence or potential for adverse effects in an exposed population. *Hazard Identification* is the process of determining whether exposure to a chemical agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defects) and whether the adverse health effect is likely to occur in humans. The process examines the available scientific data for a given chemical (or group of chemicals) and develops a weight of evidence to characterize the link between the negative effects and the chemical agent.

Risk characterization. A phase of risk assessment that integrates the results of the exposure and effects analyses to evaluate the likelihood of adverse effects associated with exposure to the stressor. The ecological significance of the adverse effects is discussed, including consideration of the types and magnitudes of the effects, their spatial and temporal patterns, and the likelihood of recovery.

Risk assessment. Qualitative or quantitative evaluation of the risk posed to human health and/or the environment by the actual or potential presence or release of hazardous substances, pollutants or contaminants.

Risk management. Risk management is a distinctly different process from risk assessment. Risk assessment establishes whether a risk is present and, if so, the range or magnitude of that risk. In the risk management process, the results of the risk assessment are integrated with other considerations, such as economic or legal concerns, to reach decisions regarding the need for and practicability of implementing various risk reduction activities. Risk managers also use risk assessment results as a basis for communicating risks to interested parties and the general public.

Risk communication. Risk communication, the exchange of information about health or environmental risks among risk assessors, risk managers, the local community, news media and interest groups, is the process of informing members of the local community about environmental risks associated with a site and the steps that are being taken to manage those risks.

This chapter focuses on the human side of risk communication in the different Arctic countries. It is a human right to know about risks associated with living conditions and food availability in a community (WHO, 2003). Risk communication should therefore include the right-to-know and other fundamental rights, including the precautionary principle. As stated in the Rio Declaration, nations shall use the precautionary principle to protect the environment: 'Where there are threats of serious or irreversible damage, scientific uncertainty shall not be used to postpone cost-effective measures to prevent environmental degradation' (UNEP, 1992). When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. Essential features are: 1) taking preventive action in the case of uncertainty; 2) shifting the burden of proof to the proponents of an activity; 3) exploring a wide range of alternatives to possible harmful actions; and 4) increasing public participation in decision-making (right-to-know) (Kriebel et al., 2001).

9.2. Communication of risks and benefits associated with traditional food

Specific criteria for evidence standards employed to evaluate dietary risks or benefits, examining toxicological risk, interpreting risk assessment, and guiding risk communication are topics that were summarized and thoroughly discussed by Brustad et al. (2008b).

The process of communicating the risks and benefits associated with traditional food is a central aspect of risk management strategies. Communication that focuses solely on risks is unlikely to have the intended result and instead may be damaging to individuals and communities. In fact, one of the key lessons learned is that risk communication on its own creates unnecessary fear, anxiety, and confusion. There are a number of potentially negative impacts of poor communication on contaminant issues (Furgal et al., 2005; Chan et al., 2006): adverse impacts on health and behavior (physical, mental and social); increased anxiety and stress; decreased hunting and fishing activity; decreased consumption of traditional foods; socio-economic impacts of changes in consumption patterns; increased exposure to new risks; and growing distrust among communities of scientific information.

Traditional foods are a crucial cultural anchor and play a vital nutritional role in health and well-being. To further complicate the issue, food substitutes may not be readily available and there is no guarantee that they would be culturally acceptable, nutritional, or affordable. The issues surrounding human exposure to environmental contaminants from traditional food (i.e., its role in health, culture, society, and economy) need to be considered in order to construct messages that inform residents while minimizing potentially negative impacts on northern lifestyles and social well-being. Risk communication should place the message within the broader public health context and be done in a way that is culturally appropriate (Furgal et al., 2005; Chan et al., 2006).

Risk communication is a process which constantly evolves. The amount of communication material and the number of messages sent to northern communities has, in general, decreased. This is an important step because frequent information about contaminants may overwhelm communities. Communication about the issue may be more efficient if messages are built into exiting public health messages. Another notable change is that there has been a shift from a focus strictly on contaminants to a focus on situating the contaminants of concern within a broader public health context (Furgal et al., 2005).

9.3. Risk perception

Differences in the perception of risks between members of the public and scientific or other technical experts have been extensively studied (Rowe and Wright, 2001; Sjöberg, 2002). Often, for a given risk, there is disagreement with regard to the threat posed to individuals or communities, even among experts (Sjöberg, 2002). Risk perception has been shown to be influenced by a variety of factors including age, gender, education, occupation, language, world view, and culture (Jardine et al., 2003; Myers and Furgal, 2006). However, not only do the characteristics of the individuals influence perception, but also a number of factors related to the hazard itself. For example, the voluntary or involuntary nature of the exposure, uncertainty about probabilities or consequences of exposure, lack of personal experience with the risk (fear of the unknown, lack of acceptance of the significance of the risk), effects of exposure delayed in time, genetic effects (effects on the next generation), accidents related to human activity (anthropogenic, not 'natural' causes), unequal distribution of risks and benefits, and the ease of perception of the associated benefits. Risk perception is a combination of personal and collective factors that influence the way in which an individual understands issues, and to which one reacts and takes action at the individual level (personal behaviors).

Understanding and perception of risk among people is much more complex than originally thought and reflects legitimate concerns that are often omitted from formal risk assessment processes (Furgal et al., 2005; Donaldson et al., 2006). Assessments of the response to risk communication (e.g., health advisories) indicate that individuals who adapt and respond to environmental or other health advisories within the context of limited socio-economic resources demonstrate more passive strategies or are less inclined to comply with advice than people with better socio-economic resources. This is likely to be very important in the context of compliance or reaction to advisories or advice around contaminants in traditional foods in the Arctic where sometimes only limited resources, or alternatives to minimize risk, exist. Therefore, it is important not just to understand individual or population perceptions of contaminant risks in the north but also to understand their relationship with and attitudes to traditional foods and a number of socio-demographic factors which may influence their ability to respond or take action (Burger, 2004). For these reasons, the perceptions of those involved and affected by a hazard must be considered because these perceptions directly influence the effectiveness of any risk management decisions and actions (including communications) taken to minimize risks and maximize the benefits of, in this case, consuming traditional foods.

9.4. National recommendations and advisory activities

Unfortunately, for various reasons, not all Arctic countries were able to contribute to this overview of risk communication strategies. Nevertheless, those that did gave a good insight into what is happening in the Arctic, providing a good balance in terms of cultural and scientific aspects and the known variety in national strategies.

9.4.1. Canada

9.4.1.1. Overview

The Northern Contaminants Program (NCP) was established in 1991 in response to concerns about human exposure to elevated levels of contaminants in fish and wildlife species that are important in the traditional diets of Aboriginal peoples living in the Canadian Arctic. Under the NCP, risk communication about contaminants involves a consideration of the quantitative results of risk calculations and the qualitative benefits of traditional food use and how risk is perceived by the public. Risk communication messages developed under the program are typically presented visually within a community context and by someone who is trusted by the residents of the community.

Typically, the focus of communication efforts in the Canadian Arctic has been to answer basic public health questions such as "is my food safe to eat?" An effective answer is formulated by putting the technical information about the risks of contaminants into a message that is understood by the target group. Canadian Arctic communities are culturally heterogeneous. Each culture in the Canadian Arctic holds a particular system of knowledge and a distinct way of understanding based on their history and the history of their relationship with their surroundings. Communication strategies should be adaptable and reflect the uniqueness of each target group (Chan et al., 2006). As such, the most effective risk communication messages tend to be those that are tailored to the specific cultural groups present in the North including Inuit, Dene, Yukon First Nation, and Métis.

9.4.1.2. Specific examples

The NCP and Regional Contaminants Committees (groups working in the Canadian Arctic) and others are making significant efforts to enhance capacity development among northerners to understand, make decisions, and take action on the contaminants issue. These efforts have focused on equipping health and environment representatives in the Canadian Arctic with the understanding, skills, and access to information, knowledge, and training about

contaminants which enable them to effectively conduct risk management and communication activities. Education and training of frontline workers will continue to build capacity in the north. Specific activities promoted by the NCP, to date, include courses for Regional Contaminants Coordinators, training courses for frontline workers, community tours, Elder-scientist retreats, and the production of educational materials for the elementary and high school curriculum. Since 1997, there have been four retreats where elders, scientists, and youth were able to build relationships. In addition, school curriculum materials have been developed and used in elementary and high schools in the North West Territories and Yukon. These efforts are making significant progress towards involving northerners in risk communication activities in a meaningful way (Furgal et al., 2005).

In 2004, as part of the replication of the initial Nunavik Regional Inuit Health Survey in 1992, the status of health risk perceptions and concerns and activities regarding traditional foods were reassessed (NCP, 2003). The survey found that traditional foods, and the activities of hunting and fishing, were still important aspects of everyday life in Nunavik communities today. Despite the social, cultural, economic, and political changes that have taken place in Nunavik, and the apparent concern over contaminants in the food chain, hunting, fishing, gathering, and sharing of wild resources are still regularly practiced in the community. Nearly half (45%) of the Nunavik population goes hunting frequently throughout the year; one third (33%) goes fishing regularly, which is once a week or more in at least two seasons; half (48%) of the population participates in berry collecting at least once a month during berry picking season; and more than half (57%) regularly share their catch with other members of the community. Traditional food items were still used by nearly one third of the population (28%) for their medicinal properties. The results of the 2004 questionnaire were similar to the results reported in1992, most (62%) of people reported that they had heard about contaminants in the environment (NCP, 2008). Familiarity with specific contaminants (mercury, polychlorinated biphenyls [PCBs] and lead) was reported (by 57%, 47%, and 38% of participants, respectively) and was lowest among young females. After learning about chemical contaminants in traditional foods, one quarter (25%) of the population reported having changed some aspect of their diet, however, only a very small number said that they had stopped eating traditional food items altogether. Less than one-quarter (23%) of hunters said that they had rejected or thrown away an animal in the 12 months previous to the survey due to safety concerns. However, these decisions were more closely associated with the presence of visible anomalies rather than concerns related to chemical contaminants in wildlife. These responses are often related to knowledge of visible anomalies in wildlife and personal experience of them, such as parasites (e.g., trichinella worm) in traditional foods (e.g., walrus) that can be transmitted to humans and cause illness (Bruneau et al., 2001; Proulx et al., 2002). The results of recent research in the region highlight the continued importance of traditional food resources and potentially, the limited impact of the concern over contaminants on hunting and fishing activities and food consumption behavior among the Inuit of Nunavik (NCP, 2008).

Myers and Furgal (2006) conducted a survey in two Nunavut and two Labrador communities to evaluate the degree to which residents had received and understood information regarding contaminants in traditional foods. The survey also served as a tool for assessing residents' perception of traditional food and contaminants issues. On average, 69% of participants across the four communities had heard of the term 'contaminants'. However, when asked, over 40% included substances other than chemical or natural compounds in their definition of a 'contaminant' and 15% could not identify what they thought a 'contaminant' was, identifying an issue with regard to actual comprehension of messages previously disseminated in these and perhaps, other regions. Local sources (e.g., garbage, old military sites, oil drums) were the most commonly identified causes of contamination in the traditional food chain and wildlife in the regions and significant percentages of the populations responded that they were not sure whether there were contaminants in traditional foods in their area. This uncertainty was higher among respondents in the Nunavut communities than the Labrador communities and in general, the greatest uncertainty on this issue was expressed among the elderly and women. The majority of individuals (61%) who participated in the Myers and Furgal (2006) survey, said that they did not have any concerns about the safety of their traditional foods, however among those that did, more hunters (55%) than women (30%) reported concerns. Among those who expressed concern, the primary issues identified were wildlife health, physical abnormalities, and contaminants. Responses indicated that individuals are primarily relying on visual cues to discern whether or not there are contaminants in traditional foods and whether or not these foods are safe for consumption. Finally, the predominant perception was that individuals themselves had not been exposed to contaminants (73%), and the majority of Nunavut respondents (65%) said that they would never change their diet because of concern about contaminants. In contrast, the majority of Labrador participants (60%) said they would alter their diet.

Findings showed that the information previously disseminated through efforts associated with the NCP and other research and education programs had not been as broadly received as expected. In particular, that a key population group, women of childbearing age, did not appear to have received and / or did not understand much of the previously disseminated information on contaminants, health, and traditional foods in the two regions at a level proportional to the efforts invested to disseminate this information. The authors argued that public comprehension of this information did not reflect the importance of the issue or the effort put into previous communications on the subject. Although not critical at that time, it was argued that there was direct risk minimization advice to be given in Nunavut and Labrador in the future; researchers and

health professionals probably did not understand the dynamics of perception and comprehension among a key target group well enough to be prepared to communicate and elicit desired responses from key groups among the population. Issues that were likely to influence the communication of this information in Arctic communities include: 1) disparate views between scientists and northern Aboriginal residents on the environment and traditional foods; 2) differences in language and communication patterns; 3) differences in knowledge systems; and 4) basic characteristics of northern communities that create challenges for widespread communication (Myers and Furgal, 2006).

In many regions, despite strong belief in the health and safety of traditional foods, concern has been raised about the presence and potential effects of contaminants in animals and human health. There is also some concern over the activities used to investigate these issues in wildlife. Previous studies are also supported by the findings of Furgal et al. (2005) in more recent surveys throughout the north. In regional surveys conducted in 2003 in the Yukon, Inuvialuit Settlement Region, Nunavut, and Labrador involving over 700 participants in total, more concerns were expressed among Yukon residents for health and wildlife (66% versus 44% for all Inuit regions combined) than among Inuit residents. However, in all regions, the most commonly cited concerns were associated with chronic diseases in people, general food quality, garbage on the land, and water quality. Approximately 10% (or less for some regions) of respondents identified environmental contaminants in traditional foods as one of these concerns. However, among those expressing concerns with regard to traditional foods, 'contaminants and industrial pollution' were the top concerns in each region, followed by 'abnormalities and animal health'. In all regions, there was generally a high level of awareness of basic contaminants messages, which had previously been delivered under the NCP. The lowest level of recall and awareness for these messages was reported by women of childbearing age in nearly all regions, and many participants' understanding of 'environmental contaminants' reflected the same confusion between chemical phenomena and visible wildlife anomalies reflected by other studies (see above). These results further support Furgal et al.'s (2005) and Myers and Furgal's (2006) argument that the invisible phenomenon of chemical contamination in the traditional food chain is a significant challenge to traditional knowledge systems and understandings of food safety, which have historically been based on observation and personal experience of illness. These results are indicative of the understanding that contaminants and industrial pollution in the food chain are issues to northerners, if people are specifically asked. However, contaminants are of lesser concern than expected when considered relative to all health and environmental concerns affecting daily lifestyles and choices.

The results of another general health and environment perception survey, conducted among Dene of the Yellowknife area and Inuit of two Nunatsiavut communities by Jardine and Furgal, further support the previous findings (Jardine et al., 2003). The study involved a survey and a qualitative research technique known as 'photovoice' to investigate the understanding and awareness of known and theoretical or potential environmental risks to health in northern Aboriginal communities. With both data collection methods used, the importance of socio-cultural variables and place in the identification of risks of concern, to residents in the communities, was evident. Many of the health concerns reported by individuals were related to aspects of their social environment and personal behaviors, more so than their physical environment. In a risk-ranking activity undertaken as part of this study, contaminants and the threat of contamination in the environment ranked very low among all risks identified by the participants. The most important concerns or health risks identified through responses to various questions include activities involving alcohol, drugs, and smoking (Jardine et al., 2003). However, participants did express concern regarding contamination of their land from anthropogenic sources, although to a lesser extent than lifestyle-related risks. Participants' understanding of these risks varied. In general, participants understood and recognized visible changes in their local environment but had difficulties reporting clear understanding of more 'invisible' phenomena, such as arsenic and PCB contamination of the land, water, and animals. According to Jardine et al. (2003) residents in the four communities appeared to understand the nature and magnitude of the risks to their health, associated with lifestyle and basic physical and environmental risks. They showed indications of having received, understood, and accepted information on these risks; yet, often did not modify their behaviors as might be expected to minimize the risks to their health.

9.4.1.3. **Future directions**

There are a number of important future directions for risk communication around the issue of contaminants and health in the Canadian Arctic (NCP, 2003). In order for risk communication to evolve within the NCP, evaluations of prior risk communications about contaminants should be conducted in collaboration with appropriate public health authorities to assess what factors influence the success and effectiveness of communication activities, and to determine the appropriate context for their delivery. This would support communicators and regional health authorities in their efforts to develop culturally appropriate messages and to ensure more effective delivery, through consideration of these factors, in the future. Furthermore, efforts to enhance capacity may be the best strategy to improve future communication efforts with the community rather than developing more educational material. The NCP has the important role of fostering relationships and promoting researchers to build capacity development initiatives into their research. The development of local capacity will be essential in the future, not only to address contaminant challenges, but also as communities are faced with increasing research activity and continued environmental, social, political, and economic change.

9.4.2. **Greenland**

The traditional diet in Greenland is largely based on marine animals and fish. The Greenlandic diet is currently a mixture of traditional food and imported food, and has been for some generations (see Chapter 3). Owing to the climate in Greenland, most of the fresh food comes from wild animals and fish. Greenland has some lamb production and a limited supply of vegetables but most produced foods are imported. A large proportion of the diet is currently based on seafood, fish, and marine mammals, but imported foods are expected to provide an increasing proportion of energy consumed (Mulvad et al., 2007).

How food is produced, how it is prepared, and how it is consumed are important in any community, both to the individual and to social groups; food represents more than just the necessary nutrition, it is also an essential component for social life and the ways in which families function (Mulvad et al., 2007).

As imported foods form an increasingly significant proportion of the diet, arriving either complete or in partially manufactured forms, the general nutritional quality of the diet changes. This affects public health as well as the social aspects of preparing and eating meals. The traditional diet is still very important, both culturally and financially, and is also an important source of nutrients, because in many places imported foods are of relatively poor quality. However, high levels of contaminants carried into the Arctic via long-range transport have been well documented by AMAP, and in Greenland high levels of such contaminants have been found in people and in the species forming parts of the traditional diet. This pollution has reached a level of concern. Nevertheless, the replacement of traditional foods by substandard, imported food is a significant concern. In 2006, Danish and Greenlandic members of the AMAP Human Health Assessment Group presented an advisory memorandum on food policy to the Greenlandic Home Rule Government. It was stressed, however, that this advice should be seen in context with the overall health policy (Grønlands Ernæringsråd, 2006).

In a comprehensive report by Hansen et al. (2008) the 'Greenlandic Dilemma' forms the basis for certain suggestions to the Greenlandic Nutrition Advisory Council. In order to improve the quality of food and to reduce exposure to contaminants through food, there seems to be an urgent need for some degree of intervention directed toward the Arctic populations experiencing rapid dietary and cultural transition. Efforts to decrease contaminant exposure need to be integrated into lifestyle/dietary advice aimed at reversing the development of increasing bodyweight. This is a global health problem, and one which is also an increasing issue in Greenland. In fact, increasing bodyweight has now become one of the major public health concerns in Greenland. Any plan for intervention must include appropriate consideration of the possible consequences for cultural and dietary traditions in the regions (Hansen et al., 2008).

The increase in obesity is primarily related to the quantity of food eaten in relation to energy expenditure. Therefore, energy balance considerations should take into account a certain level of physical activity. The quality of the food and the balance between individual nutrients are equally important (Hansen et al., 2008).

9.4.2.1. **Risk management**

On the basis that energy balance is a prerequisite for maintaining normal body weight (or a negative balance in the case of a weight loss regime), the following recommendations can be made (Hansen et al., 2008):

- Fat – the intake of saturated fat should be restricted to a minimum. When necessary, monounsaturated fat (e.g., olive oil) should be used. The intake fish oil (n-3) should in general be promoted to ensure an n-3 : n-6 ratio of over 0.2. Blubber intake from top-predatory marine mammals should be reduced.
- Carbohydrates – the intake of refined sugars, especially fruit sugar (fructose) should be restricted to a minimum, and refined starches should be eaten in moderation. In contrast, vegetables and fruit intake should be increased.
- Protein – the majority should be derived from lean meat from terrestrial game and from fish.
- Marine mammals – because of their contaminant load, meat, blubber, and organs from top-predatory marine mammals should be eaten in moderation, especially by children and people in the fertile age group.

A reduction in the level of dietary exposure to environmental contaminants is necessary because several Arctic populations have exposures in excess of internationally accepted guidelines for safe intake. High exposure levels are closely related to intake of food derived from top-predatory marine mammals. In Greenland, this exposure has been shown to be related to negative health indicators, such as disturbed sex-hormone balance/activity and to reduced sperm quality (Bonde et al., 2008). Also, recent data have indicated that exposure to persistent organic pollutants is related to an increased proportion of triglycerides in blood lipids; an indicator of increased risk for development of cardiovascular diseases. The effect was only noticeable in obese persons. This underscores that even if exposure levels themselves are not high enough to induce measurable changes in the risk factors in normal-weight individuals, in obese individuals with an increased risk, contaminants can aggravate the risk (Hansen et al., 2008). These observations demonstrate that contaminant exposure and life-style related obesity should be addressed simultaneously in a general food policy.

Human exposure to hazardous contaminants should be reduced in two ways (Hansen et al., 2008):

1. Agree measures such as international conventions to eliminate or reduce production and use of the most dangerous chemicals. This is important but, however, only effective over a generational perspective.
2. Implement intermediate intervention strategies locally, as a quick and effective first action to protect the most exposed populations. In the Arctic, the main source of anthropogenic contaminants of concern

is marine mammal consumption. Consequently, the most efficient way to reduce human exposure is to replace consumption of highly-contaminated marine mammals by fish and terrestrial mammals.

Since the Second World War, the proportion of marine mammals in the traditional diet has steadily declined. Once a major staple food, marine mammals now account for, on average, less than 10% of energy intake in the larger communities. This development is especially pronounced among young people. Some older people still regard marine mammals as part of the traditional food and their cultural integrity. However, because the risk to a normal-weight person over reproductive age of continuing their traditional eating habits is negligible, they should not be recommended to change their diet. In contrast, younger people may need education and guidance towards a more healthy lifestyle (Hansen et al., 2008).

Eating traditions are an integrated part of a culture. Cultures are not static but must constantly develop and adapt to the changing world – as must dietary habits. Nowadays, no generation eats exactly as its parents' generation did and eating habits change with the changing culture. The present tendency to follow a 'western' lifestyle, with increasing consumption of fast food products will by no means promote an improvement in the general health situation. The time has come when it is necessary to implement a general public health policy which, through proper education of the younger generations, may improve living conditions for Arctic peoples within their cultural traditions, and still recognizing the value of local food resources (Hansen et al., 2008).

As part of the risk management in Greenland, the Greenland Home Rule Government and the Greenlandic Board of Food Safety have implemented dietary recommendations by the Greenlandic Nutrition Advisory Council (Grønlands Ernæringsråd, 2006). The concerns/issues listed include that a change in diet and lifestyle toward western food may result in a decreased intake of vitamins, minerals, and other biologically active substances; however the intake of contaminants will also decrease, as will the significance of the diet's connection to cultural, occupational, and social conditions. Furthermore, that incorrect preparation and storage of Greenlandic food can entail risk of food-borne infectious diseases.

The targeted goals were that: 1) the Greenlandic food items should be included in the public institutions' food choices; 2) increased general knowledge about which food items are healthy must be emphasized; 3) increased general knowledge about food hygiene (correct storage and handling) must be encouraged; and 4) increased general knowledge about preparation methods that foster variation and fulfill culinary and nutritional needs must be sought.

The recommendations were that: 1) local and international initiatives that lower emission of pollutants to the environment should be implemented; 2) infrastructure which promotes the use of Greenlandic foods in homes, retail, institutions and other social settings should be established; 3) information and education about food hygiene, storage and preparation of both Greenlandic and imported food should be provided; 4) guidance and education about how Greenlandic and imported food should be included in a diet which fulfils the nutritional recommendations must be stimulated; and 5) local initiatives that increase security about food (i.e. concerning storage and preparation) must be implemented.

Pregnant and nursing women can continue to eat varied Greenlandic food, but should be cautious with polar bear, toothed whales, seabirds, and long-lived seals. These foods can be substituted by fish and land-based (terrestrial) mammals. Children and young people should follow the same advice as pregnant women. It is recommended that everybody follows the dietary advice from the Greenlandic board of Food Safety. Courses should be arranged to secure local knowledge on counseling and communication about nutrition and health (Grønlands Ernæringsråd, 2007).

9.4.3. **Faroe Islands**

9.4.3.1. **Local risk assessment**

Efforts to reduce the high mercury exposure of the Faroese population have been ongoing for about three decades, mainly based on the results of biomonitoring and epidemiological studies (Grandjean et al., 1992).

The authorities first informed the people of the Faroe Islands about high mercury concentrations in the meat and kidneys of pilot whales (*Globicephala melas*) in 1977. People were recommended to limit their consumption of whale meat in accordance with international guidelines on maximum recommended exposure. However, the recommendations in these international guidelines were based on mercury poisoning incidents in Japan and Iraq and not on prospective studies based on populations with low levels of exposure, such as those with hair mercury concentrations of below 20 ppm. In 1985, a pilot study from the Faroese village of Leirvik showed that women of childbearing age had relatively high mercury concentrations in hair samples of over 20 ppm (Grandjean et al., 1992). It was therefore decided, without delay, to examine whether prenatal mercury exposure of pregnant women in the Faroe Islands had any adverse impact on offspring later in life.

Grandjean et al. (1997) assessed seven-year old children that had been exposed to mercury *in utero*, and found that the development of their nervous system had been adversely affected by the mercury exposure. The examinations also revealed significant effects on psychological domains such as memory and reaction time. A correlation between prenatal mercury exposure and blood pressure in the seven-year old children was also found. Further, neurophysiological changes were established at the examinations with evoked potentials after stimulation through the ears. In 1998, these findings caused the Faroese health authorities to revise their recommendations on the consumption of pilot whales (Weihe et al., 2003, see Box 9.2).

Box 9·2. Faroe Island recommendations regarding consumption of pilot whales (Weihe et al., 2003)

Blubber. High PCB contents in blubber mean that adults should consume pilot whale blubber once or twice a month at most. However, that the best way to protect fetuses against the potentially harmful effects of PCBs is for girls and women not to eat blubber until after having given birth to their children.

Meat. The mercury content of pilot whale meat is high and one of the main sources of mercury. Therefore it is recommended that adults eat no more than one to two meals 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 never be eaten.

The marine diet was, and still is, based on fish such as cod and haddock. Studies showed that cod and haddock contain about 0.02 ppm mercury, whereas concentrations in pilot whale meat (muscle) are about 2 ppm. As a result, the health authorities decided to focus on the main source of exposure; meat from pilot whales. Studies have also shown that pilot whale blubber contains high levels of chlorinated organic substances such as PCBs and DDE. When examining the seven-year old children, Grandjean and co-workers found that a minor effect of PCB exposure could be traced in some of the psychological tests, but that the effects were insignificant compared to the impacts of mercury. Nevertheless, the Faroese health and environmental authorities decided to include blubber in their recommendations on the consumption of pilot whales (Weihe et al., 2003).

9.4.3.2. **Risk communication**

To a large extent, risk communication related to contaminants in the marine diet has been performed through the actual scientific work on the projects disclosing possible adverse impacts. Since 1985, cohort studies have included so many families that all corners of the islands have been reached with extensive information about the potential risks regarding adverse impacts of contaminants. This means that about 2000 families have received invitations to participate in examinations, some of them several times. Also, many meetings have been held with associations and educational institutions; the press coverage has been intensive, including interviews with television, newspapers, periodicals, and journals several times a year. The information has been focused on the adverse impacts of mercury and persistent organic pollutants and how to avoid them. It has been stressed several times that common fish species, such as cod, haddock, and pollack, contain only limited amounts of mercury. The population has therefore had a range of alternative dietary choices, and adjustments have been easy to implement (Weihe et al., 2003).

Compared to the other circumpolar countries, the situation in the Faroe Islands is unique in that the sources of marine contaminants are related to a single food item, the pilot whale. It has therefore been relatively easy to communicate a message with the intention of reducing exposure.

However, initially, the risk communication process was competing against cultural resistance to external pressure aimed at stopping the Faroe Islanders whaling. On many occasions over the years, environmental organizations such as Sea Sheppard have tried to pressurize the Faroese to stop whaling. However, it has been fundamental to the Faroe Islanders that catching all species of fish and marine animals be permitted, as long as these species are not threatened. The pilot whale is not a threatened species; there are large populations of pilot whales in the North Atlantic (Weihe et al., 2003). In response to the international pressures against whaling, a natural counter-reaction was seen in the Faroe Islands, where killing and consuming pilot whales became an overt manifestation of the principal attitude to the issue. Communicating a message to abstain from consuming pilot whale meat and blubber based on health risks could easily be misunderstood and confused with the attitudes of those opposed to whaling. As a result, it has been of paramount importance over the last 20 years, to emphasize that the dietary recommendations are health-related and are totally unrelated to the opposition to whaling. In the communication processes, researchers have been asked by individuals as well as by the media about their personal attitudes to whaling, which the individual researcher has had to account for. This illustrates the level of involvement needed when communication is intensive and persistent (Weihe et al., 2003).

9.4.3.3. **Assessment of the efficiency of risk communication**

To examine whether the dietary habits of pregnant women, considered an especially vulnerable group, had changed in relation to the consumption of pilot whale meat and blubber, a detailed diet study involving 148 women was conducted in 2000 and 2001 (Budtz-Jørgensen et al., 2007). The study comprised 24-hour dietary recall interviews and prospective recordings, for six days, as well as a retrospective food-frequency interview. The examination showed dramatic changes in the dietary habits of pregnant women. Results showed the average daily consumption of pilot whale blubber in 2000/2001 was 0.5 – 1.5 g, compared to 7 – 12 g in 1981. Tests showed a corresponding decrease in blood mercury level to about 1 μg/L. As a comparison, between 1986 and 1987, the median level in cord blood was 22 μg/L. However, surprisingly, there was no corresponding decrease in the levels of PCB congeners over this period. This may be due to the long half-life of PCBs, but could also be due to alternative sources of PCBs such as seabirds and their eggs; one source of PCBs could be adult fulmars.

In a recent study (Budtz-Jørgensen et al., 2007), 200 seventy-year old people were asked about their dietary

habits pertaining to pilot whale meat and blubber in their childhood, as middle-aged adults, and now. Results showed that intake peaked during childhood and adolescence, but had reduced considerably over recent years. Some individuals said that their reason for reduced consumption was due to harmful substances in the meat, while others said that it was difficult to get pilot whale meat and blubber.

9.4.3.4. **Beneficial compounds of a marine diet**

Renewed analysis of the mercury examinations for the cohorts established in 1986–86 and 1994–95 respectively, show that if adjusted for fish meals, the negative effect of mercury is increased (Budtz-Jørgensen et al., 2007; Choi et al., 2008). In other words, there are compounds in fish such as cod, haddock, and pollack which reduce the effect of mercury. Moreover, this is not related to selenium because, in the Faroese studies, selenium is present in a molar surplus ten times that of mercury. Statistical analyses do not support the hypothesis of any special beneficial effects from selenium (see also Chapter 7).

The official dietary recommendations in the Faroe Islands do not include a special focus on fish, but the general recommendations issued by Danish health authorities recommend the intake of fish several times a week, and these recommendations are also followed in the Faroe Islands (Weihe et al., 2003). Furthermore, the Faroese Board of Public Health has stressed that the Faroese population should continue its traditionally-large fish intake. However, there are indications that fish intake is decreasing. In 1981, an islands-wide dietary survey showed that each inhabitant consumed on average 78 g of fish per day, while pregnant women in the 2000–01 dietary survey reported an average intake of only 38 g per day. However, it is unlikely that the decrease in fish intake is because fish are considered polluted. The most likely explanation is the easy availability of food items such as chicken, pizza, and inexpensive meat from land mammals.

9.4.3.5. **Conclusions and risk management**

In the Faroe Islands, risk communication has resulted in a significant change in dietary habits, particularly among pregnant women, who are considered one of the most vulnerable groups. One of the factors that has supported the change in dietary habits is that the contaminant sources are related to a single mammal, the pilot whale, another is the easy access to unpolluted fish from the ocean. New recommendations have now been implemented, based on practical, common sense advice.

9.4.4. **Norway**

9.4.4.1. **Strategies**

In Norway, considered one of the low risk countries for contaminants, risk communication is based on reports from the State Pollution Control, the National Institute of Public Health, and The Norwegian Food Control Authorities, with only sporadic public attention. There are two ways to communicate with the public: through the local public health officers and through the media. If specific health concerns are addressed by the media, a special committee with national experts is often created, with the aim to clarify whether there is a link between a specific cause and a specific health outcome. A typical example is the Norwegian–Russian Health Commission (Smith-Sivertsen et al., 2000), which assessed the health situation in the Russian–Norwegian border zone. The organization 'Stop the Death Clouds' organized public meetings with health experts and toxicologists, discussing rumors about up to 70% malformations in newborn babies on the Kola Peninsula. There was a lot of public attention, which ended quickly when no alarming results were discovered, and no associations between the pollution and any health effects could be documented.

9.4.4.2. **Report design**

Reports after such evaluations are prepared both with a 'common language' synopsis for the media and the general population, as well detailed information for scientific purposes. Use of the media is a powerful tool, and the information given out is often highly biased, before public attention has even developed. If the results indicate serious health concerns, the public health community doctor must act, often through invitations to public meetings and by inviting national experts. This is a development that belongs more to the modern media world than to a professional risk communication strategy. A recent report by Brustad et al. (2008a) addressed the importance of keeping the good childhood diet in relation to Saami and Norwegian ethnicity in northern and mid-Norway (Brustad et al., 2008a). The Norwegian Food Control Authorities issued a dietary advisory in March 2003 stating that all women of childbearing age and children were advised to stop eating cod liver and commercial products derived from it. The latter did not include the cod liver oil that has been distilled and purified to remove impurities. This dietary advice did not mention the positive health effects of cod liver and no alternatives were provided that people might eat to maintain the proper intake of vitamins and n-3 fatty acids (Norwegian Food Control Authority, 2003).

9.4.5. **Russia**

9.4.5.1. **Communication issues**

Communication issues became very urgent when the assessment of persistent toxic substances, food security, and indigenous peoples of the Russian North was published in 2004 (AMAP, 2004b). One of the most discussed findings was that besides the contamination of traditional foods through long-range and regional transport of pollutants into the Russian Arctic, there are other significant sources of food contamination, and correspondingly – additional sources of exposure

to persistent organic pollutants (POPs) in indigenous people. Results obtained from a targeted survey of dwellings, comparative analyses of POPs levels in fresh and ready-to-eat local food, and dietary pattern analyses, suggest that contamination of food during storage, souring, processing, and cooking might contribute significantly to the total POPs exposure of indigenous populations in the Russian Arctic (Dudarev and Chaschin, 2008). A comparison of POPs concentrations in local foods sampled from indigenous residencies with those measured in fish species, reindeer meat, and marine mammal tissues sampled in the natural environment showed that both the occurrence and levels of contaminants may well be increased during food storage/processing/preparation at home. 100% of indoor environment samples were polluted by DDTs, hexachlorocyclohexane (HCH), PCBs, and other POPs. Home-made alcohol-containing drinks and fermented meat from ground pits were highly polluted by PCBs and DDTs. Some insecticides contained considerable concentrations of POPs.

According to Dudarev and Chaschin (2008) the main pathways of additional food contamination are: 1) pollution of soil and water in and around settlements; 2) poorly controlled use of toxic insecticides for the treatment of farmed animals; 3) uncontrolled household use of insecticides and other chemicals for combating insects and pests; 4) uncontrolled use of technical oils and liquids for imbuing of wood and other construction materials; 5) uncontrolled second-hand use of waste technical containers and barrels for souring plants and vegetables, home-made alcohol fermentation, and water keeping; and 6) food contamination specifically associated in some northern regions with prolonged fermentation of meat and fish in ground pits that are not protected from accidental contamination by leakage of drainage waters and contaminated soils due to poor sanitation and general environmental neglect of indigenous communities.

The particular conditions of soils in the Arctic (enhanced precipitation of pollutants from the atmosphere, restricted mobility of soil solutions and surface waters due to widespread permafrost, and as a result limited soil self-cleaning), mean that soil pollution in the Russian Arctic is a potential source of exposure to persistent toxic substances (PTS). Soils as the first step in the POPs food chains is typical for most small settlements in the Russian Arctic due to the closeness and general intermingling of, on the one hand, residential buildings, schools, kindergartens, hospitals, water supply stations, food stores, shops, and on the other, industrial facilities (heat and power plants, garages, maintenance facilities, disposal dumps, and abandoned barrels and other rubbish). This creates the very real threat of POPs moving from soil to drinking water and food, and to direct physical contact with pollutants (particularly for children) (Dudarev and Sychov, 2005a).

Permafrost in the Russian Arctic is a distinctive feature which prevents the extraction of artesian waters and makes construction and use of sewerage and water supply systems more complicated and expensive. Most small settlements in the Russian North have no centralized water systems. Many are connected by pipes to the nearest lake or river, quite a few are supplied with drinking water by truck (in winter – stabbed ice); sewerage and water purifying systems in such settlements are generally absent. Some settlements where average annual temperatures are well below zero, have a mixed system of heating and water supply, where all buildings within the settlement are provided with hot water supplied directly into both heating radiators and water pipelines; this is the water used by people for drinking and cooking food. Technical 'decisions' of this nature, result in the exposure of the population to any number of pollutants.

Another feature specific to Russian northern settlements is the abundance of cockroaches everywhere indoors. Insecticides have been used extensively over the years in an attempt to eliminate these pests. These have been applied in many forms (powders, sprays, pastes) to walls, tables, cabinets, food storage areas, and cooking surfaces. Significant levels of indoor pollution could be explained by the presence of POPs in most of these insecticides, the majority of which were produced in China.

9.4.5.2. **Risk management**

Important and urgent remedial actions were recommended to minimize environmental contamination by these persistent toxic substances, with the aim of reducing exposure and the risk of hazardous health effects in indigenous communities, including:

- an end to the manufacture and use of materials which are associated with the release of PTS;
- a ban on the supply of materials containing PTS to the northern regions, and concerted efforts to identify, catalogue, collect, transport, store and remove existing materials containing PTS;
- taking responsibility for environmental security and the safety of personnel involved in activities to prevent the release of such pollutants;
- construction of depositories for wastes containing PTS, in accordance with the rules on sanitation;
- collection of abandoned barrels (empty or not), metal wreckage, building materials and other PTS-contaminated materials and their transportation to depositories;
- disassembling of old buildings containing materials contaminated by PTS (PCB-containing wood impregnation oils);
- removal of relevant indoor wall materials (lead-containing plasters and paints);
- use of effective and safe systems for incinerating liquid and paste-like wastes, as well as solid wastes of organic origin contaminated by PTS;

- safe transport of old transformers, other PCB-containing sets, and solid non-organic wastes to special yards designated for the isolation of dangerous wastes;
- use of effective recultivation methods and PTS-decontamination of soils in and around settlements, lawn-and-garden areas, and reindeer-herding, fishing and hunting locations;
- establishment of safe (for people and environment) systems of water supply;
- use of safe and effective chemical control measures in domestic and occupational situations for protecting rooms, animals, and plants against insects, rodents, and microbes;
- use of effective systematic control of PTS levels in food raw materials and food products (especially for local traditional foods);
- implementation of recommendations on restricting the consumption of those local food products where levels of PTS exceed allowable limits, and the dissemination of this information to the population;
- implementation of recommendations on methods of cooking and preserving food, that can lower PTS concentrations in ready-to-eat products;
- informing local people of recommendations on the ban on tar originally made from chemical or technical liquids and oils – for conserving food products, producing home-made alcohol, and storing water, and also the ban on the use of ground pits for making 'kopalkhen' (stored food in the ground); and
- informing local people of recommendations on the ban on lead-containing items in the home, use of leaded gasoline for boats, snowmobiles and other vehicles, and the substitution of lead shot by steel bullets and other ammunition for hunting and fishing.

On the basis of this information, guidelines were prepared for and approved by the Ministry of Health Care and Social Development (Dudarev and Chaschin, 2008) and information brochures about traditional nutrition in the far north of Russia were drawn up for indigenous peoples living inland (Dudarev and Sychov, 2005a) and in coastal communities (Dudarev and Sychov, 2005b). These brochures reported the concentrations of persistent toxic substances in local food products and calculated the maximum permissible daily intakes based on Russian values of maximum permissible concentrations for the main contaminants in humans (see Figure 9.2).

The first example of a good working partnership between indigenous residents and the authorities in dealing with the problems of persistent toxic substances in Arctic Russia, is the start of waste clean-up activities in the Chukotka Autonomous Okrug (see Chapter 2). Two villages, Lavrentiya and Lorino, were identified as having serious problems with leaking and abandoned

Зелёный цвет Потребление не ограничено	*Нерпа* 	*Лахтак* 	*Морж* 	*Кит* 	*Олень* 
Жёлтый цвет Потребление лучше сократить до 300-400 г/сутки	Мясо	Мясо	Мясо	Мясо	Мясо
	Жир	Жир	Жир	Жир	Жир
	Печень	Печень	Печень	Печень	Печень
	Почки	Почки	Почки	Почки	Почки
РоЗовый цвет Потребление лучше сократить до 100 г/сутки	*Заяц* 	*Рыба лососевая* 	*Рыба морская* 	*Уткц уси* 	*Тунбровые птицы* 
Красный цвет Этот продукт цучше заменить другой пищей	Мясо	Мясо	Мясо	Мясо	Мясо
	Жир	Жир	Жир	Жир	Жир
	Печень	Печень	Печень	Печень	Печень
	Почки				

Figure 9.2. Visual presentation of advice concerning consumption of traditional foods in the Far North of Russia. Source: Dudarev and Sychov (2005a). *Нерпа* – ringed seal; *Лахтак* - bearded seal; *Морж* – walrus; *Кит* – whale; *Олень* – reindeer; *Заяц* – hare; *Рыба лососевая* – salmonoids; *Рыба морская* – marine fish; *Уткц уси* - ducks and geese; *Тунбровые птицы* - tundra birds; *Мясо* – meat; *Жир* – fat; *Пеуень* – liver; *Почки* – kidney. Green: consumption unlimited; Yellow: recommended to limit consumption to 300-400 g/day; Pink: recommended to limit consumption to 100 g/day; Red: recommended to replace with alternative food.

drums – thousands of drums were contaminating soil in and around the villages. These drums were leaking grease, oil, and other wastes, some of which contained persistent toxic substances. Once in the soil these contaminants were migrating into traditional ground pits, and in some cases contaminating food stores. In some areas, drums had been buried in the permafrost and so were temporarily contained. Lectures and training sessions (for residents) were held in both villages during August 2007, with the active participation of representatives of the Northwest Public Health Research Center. Topics addressed included: principles and safe practices for identifying, sampling, handling, labeling and storing drums of discarded hazardous materials in preparation for shipment to a recycling and treatment facility. The clean-up process started in summer 2008 with a group of local people (mainly indigenous people) collecting drums near the Lorino and Lavrentiya settlements for storage at a specially prepared area of a scrap yard. Various organizations are participating in this project: the Arctic Contaminants Action Program (ACAP), the Chukotka Regional Administration, the Northwest Public Health Research Centre (NWPHRC), the Chukotka Red Cross, the Russian Association of Indigenous Peoples of the North (RAIPON), and the U.S. Environmental Protection Agency's Office of International Assistance.

9.4.5.3. **Risk communication**

Results of the various studies and activities have been reported at meetings attended by representatives of state authorities, local self-governments, health care organizations, educational institutions, non-governmental organizations, indigenous communities and the general public, and have served as a basis for decision-making in Murmansk province, and the Nenets, Taymir and Chukotka autonomous okrugs. A summary of the Russian Arctic data (AMAP, 2004b) was presented to the special council, headed by Artur Chilingarov, vice-chairman of the Russian State Duma Committee in 2004. Several meetings with indigenous groups took place in capital cities and particular settlements in each of the four regions, and with the participation of RAIPON representatives. Especially significant were efforts to make this information available to local physicians, ecologists, economic managers, businessmen, trades people, school teachers, pre-school workers, historians, and gamekeepers, who would be able to translate the scientific results into a form that was understandable to the indigenous people with whom they had contact, thus helping to support the safety, well-being and health of current and future generations of indigenous people.

The media also played an active role; interviews took place via local radio, television, and newspapers in each of the four regions. A television program about persistent toxic substances in the Russian North was made by Channel 11 of St-Petersburg TV, representatives of which also participated in field expeditions with scientists. The film was distributed in the communities together with a summary of the report (AMAP, 2004b) and the information brochures.

An educational program for schools (a methodological manual for teachers of 5-9 classes of Russian northern regions secondary schools) was published under the auspices of the Arctic Council Indigenous Peoples Secretariat (Chaschin et al., 2006).

9.5. **Discussion**

Brustad et al. (2008b) concluded that 'Health advice to the public can, due to its complex nature, never be an exact science. However, a common system and principles in formulating advice would most likely facilitate a clearer massage to the public. Consideration of the criteria currently employed for grading evidence not only shows the complexity of this field, but also provides evidence that a consensus is building.' Both risks and benefits must be acknowledged. Risk assessment analysis alone cannot justify dietary recommendations. The authors suggested that advice is most appropriately formulated within the context of risk management, of which both epidemiological evidence and risk assessment are essential components (Brustad et al., 2008b).

9.5.1. **AMAP and risk communication**

AMAP was established by the Arctic Council to investigate the spread and effects of pollution from the industrial regions in the temperate zones to the Arctic. AMAP's main role has been to harmonize the compilation of data to establish the levels and extent of contamination in the circumpolar area and also to initiate research into the correlation between contaminants and the health status of these areas.

Because all Arctic circumpolar areas are represented within the Arctic Monitoring and Assessment Programme, the present assessment provides a reasonably reliable picture of the status of human exposure to heavy metals and legacy POPs within the Arctic. Furthermore, because the exposure measurements have been repeated over time, it is possible to comment on the development of trends with regard to pollution in many areas. Effects studies have also been undertaken. By comparing documented levels of exposure to the effect studies from the Arctic area, and the toxicological literature in general, it may be concluded that in several places it is possible that exposure via food has adverse implications on the health of populations. Studies have demonstrated that the main source of exposure to contaminants in the Arctic is traditional food, especially marine animals.

The benefit / risk management process for traditional foods in circumpolar countries has been challenged by the issue of environmental contaminants entering the Arctic food chain for many decades. Although a framework for risk management has been adopted in many countries no common process to integrate all benefits and risks, qualitative and quantitative

information, to assess and direct decision-making on this topic has yet been developed.

In societies with a wide range of alternative dietary choices and broad cultural means of existence, dietary adjustments are easy to implement. This is not the case in the Arctic area, however, where communities depend heavily on marine food, especially marine mammals. Many populations in the circumpolar area experience real food insecurity. Will there be enough food? Will the healthy food be available? Many Arctic people still experience periods of starvation (CNF, 2007).

Marine mammals are the focus for many Arctic cultures. It has been possible to achieve some significant reductions in exposure to heavy metals and organic chlorines by eliminating the most contaminated species and organs from the diet. It is feared, however, that a change in food choices and lifestyle will alter community culture to such a degree that some of the cultures will not survive. Another reason for caution when communicating adverse effects of certain pollutants is that, theoretically, contaminated food also contains compounds that have a positive impact on health, such as marine fatty acids (see Chapters 3 and 7).

All these considerations constitute 'The Arctic Dilemma', that traditional food items have both positive and negative properties and that the management and communication of this dilemma is complicated and dependant on geographic, demographic, cultural, and social conditions (Chapters 3 and 7).

Dietary guidelines for individual communities are principally the responsibility of the national/local health authorities. The aim of the communication is to provide balanced information allowing people to make informed rational choices about how to reduce their exposure to toxic substances and at the same time ensure that their food has satisfactory nutritional and aesthetic properties. Information alone is not enough, however. There is also an obligation on local authorities to make healthy food available even in small communities, so that people can actually carry out these informed rational dietary choices. This is more of a political and logistic issue.

Because AMAP is able to contribute data and information on exposure status in local areas over time and because such information is of general interest to populations living in the Arctic, it has to some extent initiated and participated in public health assessments of both the beneficial and adverse effects resulting from the various sources of exposure, such as marine mammals.

9.5.2. Communication strategies and problems in the Arctic

Information presented in this chapter highlights how risk communication has been conducted differently in different countries and regions. In most countries, risk communication has been undertaken by national authorities, seldom or never by communication professionals. Communication of information resulting from AMAP's activities has been given much consideration from the start, and on some occasions professional communicators have been used to ensure that the information is communicated as effectively as possible. Nevertheless, the goal of giving clear but nuanced information on the sometimes complicated conclusions arising from its work has not been totally satisfactory in all cases. This may be partly due to none of the Arctic countries having an official strategy for the communication of the results.

In the Faroe Islands, risk communication has had measurable positive effects on both the food choices of target groups (children and young woman) and health parameters (Weihe et al., 2003). In Norway, Sweden, Finland, and Iceland, human health issues resulting from the accumulation of contaminants from Arctic food chains have been very limited and so the need for dietary advice to the populations has also been limited (Brustad et al., 2008a).

It is communities in northern Alaska, Canada, Russia and Greenland that are subject to 'The Arctic Dilemma' where risk communication has been complicated and often unsuccessful. The difficulty is to convey insights to all citizens of exposed populations that will enable them to weigh the benefits against the drawbacks in their dietary choices.

One particular difficulty has been in identifying the receiver for the risk communication. Is it the health professionals of a given country or is it the entire, affected population? Another difficulty is the form of the communication. A simple message may be easy to communicate, but equally easy to misunderstand, for example, that all seafood is considered contaminated. On the other hand, balanced and targeted risk communication would only reach a specific and narrow receiver population.

Another difficulty has been that toxicological terms are relatively alien to the general population. It is assumed that the majority of a population wants questions about the negative impacts of contaminants answered by a yes or no and not by a number of statistical variations which they can interpret to fit their own personal preferences. However, it is likely that a substantial proportion of the communicated messages with regard to contaminants in the circumpolar area have not been fully understood.

Risk perception research has been valuable in showing the local perspectives and understanding of the issue; surveys and other qualitative assessments have shown that while the majority of the population is aware of the issue of 'contaminants', some confusion with regard to the 'chemical only' nature of the use of terms by the research community exists and may create barriers to understanding the messages given out by northern health professionals and researchers.

In the Canadian Arctic, it appears that women of childbearing age have received and understood the least regarding this issue, yet may be the most at risk to contaminant exposure because of the sensitivity of the

developing fetus. This is therefore the most important target audience around which to develop risk reduction strategies and messages (Kuhnlein et al., 2000).

Research conducted in the Canadian Arctic indicates that contaminants are not direct determinants influencing food choice among northern residents, however, indirect impacts of food choice and hunting catch rejection may be taking place in some regions (NCP, 2003).

9.6. Recommendations

Communication of risk needs to embrace the right-to-know and other fundamental human rights, as well as the precautionary principle.

Regular monitoring of food consumption behavior, food safety perspectives, and concerns and determinants of food choice should continue to support the development and provision of information that aids in 'informed decision making' by northern residents.

Communication of AMAP results on human health issues should be undertaken in a more professional manner, with the help of professional communicators. There is a need for more comprehensive tools and strategies for communication of AMAP results, both for the general population groups, public health purposes and decision makers, and specifically for the most vulnerable indigenous population groups. It is important that governmental authorities give more focus to professional communication strategies and that AMAP should use national authorities to develop communication strategies for this issue.

The benefits of traditional food consumption should be communicated along with the results of technical risk assessments to support the provision of information to residents in these regions; to help residents make informed decisions about food and health has become critical to successful risk communication processes.

Risk communication must be carried out with great care and respect toward the receiver culture. This does not mean, however, that recommendations should not be given. Recommendations should always be based on a combination of evidence, experience, and common sense. Pre-testing of messages and an evaluation of the risk perception by the public might be beneficial.

The anticipated communication channels, audiences, communities, general public, health officials, or government officials should be identified as well as the question of who should communicate advice to the public, scientists, national experts, physicians, public health officers, health staff, bureaucrats, local politicians, and indigenous organizations.

The language used for communication is important. The choice of terms, such as 'seafood' rather than 'food from the sea' or a distinction between fish and marine mammals, should be carefully decided. Precise wording is necessary for clear useful messages. A glossary might be useful.

It is crucial to involve the populations affected as well as external stakeholders (e.g., indigenous organizations) in the communication and evaluation processes in order to build trust and credibility. Good cooperation with the media is also very important.

Communication effort should be evaluated systematically and incorporated into AMAP's future monitoring program. In addition, communication strategies should be developed to optimize transfer of knowledge from scientists to national authorities and then to citizens. It should be considered to what extent it is possible and useful to develop compatible communication strategies in all circumpolar countries, even if the culture and socio-economic conditions are totally different.

Both northern residents and public health professionals require or request more information and support to interpret the implications of such technical risk assessment guidelines, viable risk optimization strategies, and risk communication processes and emerging issues in environmental health and toxicological research.

Effect studies of communication should be part of future assessments in AMAP.

A circumpolar assessment of communication efficiency should be established. New studies on risk communication result in new materials for better communication. More work is, however, needed on the effectiveness and effects of risk-benefit communication. The dissemination of AMAP assessment reports and information, both to the public and to health authorities in the Arctic, should be improved.

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 (AMAP, 2003).

9.7. Policies on contaminants

As levels of legacy contaminants decline, levels of emerging substances are increasing, raising new concerns. There will be changes in human exposures, as well as changes in the physiological behavior of contaminants (see Chapter 5).

AMAP cannot provide specific public health advice in local and regional situations, but can evaluate the work of local health authorities in developing and disseminating advice.

Human contaminant levels are too high, especially in the Arctic, and there is a need for strongly restricting the use and emissions of chemicals that are persistent, toxic and able to accumulate in food chains. A forum for initiatives on this topic should be the Stockholm Convention.

Chapter 10

Conclusions and Recommendations

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10.1. Introduction

The mandate given by the Arctic Council to the AMAP Human Health Assessment Group for the five-year assessment undertaken from 2003 to 2008 was to continue monitoring exposure levels of contaminants and their effects in Arctic populations in order to provide scientific advice on actions to be taken by Arctic governments in their efforts to take remedial and preventive actions relating to contaminants.

Evaluations of individual and population-based impacts of contaminants must be placed within the context of the general health status and vulnerability of indigenous people living in the Arctic. Indigenous people often have less access to health care and have poorer health as indicated by major health disparities (see Chapter 8). Changing economies, climate change, and social structure within the circumpolar region also play a significant role in health and well-being (see Chapter 2). In general, the conclusions and recommendations published in the AMAP 2002 assessment are still valid. However, new monitoring data, especially from Arctic Russia and new scientific evidence have lead to a strengthening of the previous conclusions and to new ones.

The purpose of this chapter is to integrate the information and conclusions provided in the preceding chapters of this assessment on human health in the Arctic to clearly identify what has changed over the last five years in knowledge of contaminant-health interactions and to provide recommendations for consideration by public health practitioners, health and environment policy makers, and governments.

The main conclusions of the present assessment are:

- Human exposure to most legacy persistent organic pollutants (POPs) and mercury is declining across much of the Arctic, but remains high among some populations. Further monitoring of these contaminants is needed in all Arctic regions to determine whether the declining trends continue. Additional studies are needed to better understand recently observed health effects and risks associated with current levels of exposure in the Arctic.
- Additional, emerging compounds have been recently measured in human tissues from the Arctic, but there are inadequate data to conclude whether levels are increasing, declining, or remaining steady. Neither are there adequate spatial data to indicate where on an Arctic-wide basis, levels are changing. The toxicological effects of these substances are poorly understood. The levels of these newer (emerging) contaminants need to be monitored across the Arctic region and their effects better understood.
- A major dietary shift from traditional to imported foods is underway in most of the Arctic, with significant health implications primarily due to increased intake of saturated fats and sugars.
- The global obesity epidemic and associated diseases such as diabetes now also affect Arctic populations. Diabetes and insulin-resistance are a major public health issue and a major source of morbidity at every stage of life. Recent scientific evidence shows that POPs exposure, at levels observed in the Arctic, independently increases the risk of diabetes. The dietary causes of obesity in the Arctic, changes in exposure to POPs, and the combined effects of obesity and POPs require further study.
- Development of dietary advice can be complex due to varying contaminant levels in different traditional foods and different areas of the Arctic, limited access to, or choice of, imported foods in remote communities, and shifting food preferences among Arctic populations. Communicating the risks and benefits associated with dietary choices of both traditional and imported foods must therefore be done carefully, taking into account a wide range of factors (social, economic, cultural), and in collaboration with communities to ensure advice is culturally appropriate.
- Interactions between climate change and contaminant transport and behavior have the potential to change human exposure in the Arctic significantly. Current understanding is inadequate to determine the likelihood and magnitude of the health impacts of exposure changes. Continued monitoring is required to detect trends in environmental levels of contaminants. Predictive models of contaminant transport and behavior need to be improved to take changing climate into account.

Specific conclusions and recommendations are provided in the sections that follow and are grouped under a series of headings.

10.2. Key findings from this assessment

Health disparities between indigenous and non-indigenous populations and between population groups in different Arctic regions continue to be significant.

- Health studies have shown that in some areas of the Arctic, indigenous peoples have similar health status to non-indigenous populations. However, in many areas their health is significantly poorer. Among indigenous people, suicides and injuries remain a significant cause of death in some parts of the circumpolar region.

- Arctic populations are in a process of rapid dietary transition from a traditional to a westernized diet. This has adversely influenced the health status of some populations.
- Lifestyle-related conditions, such as obesity, diabetes, and circulatory diseases, all of which are elements of metabolic syndrome, are more prevalent than previously reported. The development of metabolic diseases is related to consumption of imported foods high in saturated fats and sugars and to low physical activity.

Levels of legacy POPs in human tissues are declining in many regions of the circumpolar Arctic. New sources and patterns are being seen in Arctic Russia.

- Owing to new monitoring in Arctic Russia this is the first AMAP assessment that allows a comparison of all Arctic regions. Some Arctic populations have been sampled only once or twice, while other populations have had several sampling periods, allowing for more definitive conclusions on time trends to be made for these populations.
- This assessment indicates that legacy POPs such as polychlorinated biphenyls (PCBs), DDE, and oxychlordane, have decreased in many populations included in previous AMAP assessments. Concentrations of PCBs and oxychlordane in Inuit mothers and adults in eastern Canada and Greenland that eat marine mammals continue to be two to ten times higher than levels seen in other Arctic populations.
- Recent data for Arctic Russia have also indicated elevated levels of oxychlordane and PCBs in indigenous coastal peoples from Chukotka. These levels have been linked to consumption of marine mammals by these coastal peoples.
- DDE, the major metabolite of the pesticide DDT, is now found at the highest concentration in Arctic Russia. In Russia, DDE is found at elevated levels in all populations from inland, coastal, and urban non-indigenous populations. This indicates that the likely source is recent use of DDT in Russian agriculture or as a pesticide in northern communities rather than through atmospheric transport and local accumulation in the marine mammal food chain.

Levels of mercury in human tissues are declining in several Arctic regions. Inuit continue to have the highest exposure levels of mercury in the Arctic and most often exceed blood guidelines.

- Mercury levels are declining in many populations across the Arctic; however, Inuit who consume marine mammals continue to have blood mercury levels which are three to ten times higher than populations who consume imported foods, as determined in the previous two assessments (AMAP, 1998, 2003). This finding is especially prominent in Greenland and parts of Arctic Canada. The pattern in Russia is different: even in areas with relatively high levels of POPs, mercury concentrations are low. A decreasing proportion of Inuit women of childbearing age are exceeding guidelines for blood mercury.
- Dietary changes due to social, cultural, and economic changes, plus people's responses to risk management recommendations in the Arctic, are likely to be the reasons for these decreases in human body burdens, which are in contrast to the increasing levels of mercury seen in many marine species.

New evidence indicates that POPs, mercury, and lead can affect the health of people and especially children at lower levels of exposure than previously thought.

- Current human exposure to existing levels and mixtures of contaminants in the Arctic influences the health of some Arctic populations in a negative manner and exerts additive effects on lifestyle related diseases. Subtle effects have been demonstrated to be present at a sub-clinical level with only minimal exposure:
  - Negative effects from prenatal PCB exposure and mercury on human growth and gestation have been observed in Arctic populations, despite the beneficial effects of n-3 fatty acids from the traditional diet.
  - Recent epidemiological studies in Arctic Quebec support previous results from other locations showing that prenatal exposure to PCBs is related to a relatively specific profile of cognitive impairments in children.
  - There is also additional evidence that POPs exposure among some Arctic populations is associated with alterations in the immune system.
  - New data from the Arctic support previous findings that mercury may be a risk factor for cardiovascular disease, mainly through its action on blood pressure. These effects appear to occur at exposure levels currently observed in many Arctic populations.
  - There is epidemiological evidence that methyl-mercury decreases paraoxonase (PON-1) activity. PON-1 is an anti-oxidant, and decreases in its activity may indicate increased cardiovascular risk.
  - There is evidence to show that non-coplanar PCBs have a pro-oxidative effect and may aggravate signs of metabolic syndrome, primarily induced by lifestyle factors.
  - Preliminary analysis of the extended Russian Arctic cohort adds evidence to the findings identified earlier (AMAP, 2004) that higher levels of maternal blood serum PCBs might be associated with more frequent occurrences of low birth weight, premature births, stillbirths, and menstrual irregularities. These possible adverse reproductive health effects of POPs and metals, as well as their potential influence on the sex-ratio of newborns, will require more in-

depth evaluation. Detailed analyses of all available data and systematic epidemiological studies, which take into account relevant confounders and other contaminants, must be undertaken before conclusive statements can be made.

  - Recent monitoring has found that levels of lead in pregnant women in Arctic Canada, Greenland, and Sweden are declining. The use of lead shot for hunting is a significant source of lead exposure in some areas. Small proportions of pregnant women in Greenland and the Russian eastern Arctic continue to exceed the blood guidelines for lead, which are based on risks to infant neurodevelopment. Recent results emphasize that behavioral effects of prenatal lead exposure are likely to be observed when testing protocols include sensitive measures of behavior, even at very low concentrations. At these lower concentrations, significant associations have been found with attention in 11-month old Inuit infants and neuro-motor function (reaction time, action tremor) in five-year old Inuit children.

- New methodologies have made it possible to determine the total dioxin-like bioactivity in human serum from the Arctic. The findings in the Arctic provide an independent measure of net biological activity of the actual total congener composition from a mixture of contaminants found in human serum and interactions with health biomarkers and nutrients:

  - In Greenlandic Inuit, complex mixtures of POPs in serum decrease the estrogenic and increase the androgenic bioactivity compared to similar measurements made with European serum. The effects found in Greenlandic Inuit vary with the profile of the contaminants found in populations in different geographical locations.

  - Serum dioxin-like bioactivity of total POPs is a good effect biomarker of sperm DNA damage in Inuit as well as Europeans.

  - Single proxy chemical markers for POPs such as CB153 cannot adequately predict overall serum dioxin-like activity. Dioxin-like congeners such as CB118 should be included in future studies of chemical markers of estimated dioxin-like activity in serum.

Climate change may increase the mobilization of POPs and mercury, and lead to higher releases of contaminants within the Arctic.

- The interaction between global climate, regional weather patterns, ocean processes, and atmospheric processes is very complex and poorly understood. While the impacts of climate change on contaminant exposure are also largely unknown, it is very likely that climate change will have a significant impact on the redistribution of a wide range of contaminants and significant changes in exposure of human populations in the Arctic to contaminants.

- In order to better predict the effects of climate change on contaminant movements, data for transport pathways related to ocean currents, upper atmospheric winds, 'polar sunrise' phenomena, ice-related releases of contaminants, releases from thawing waste sites, and other pathways will need to be collected regularly and utilized in more sophisticated predictive models. Monitoring information for wildlife and human populations will also be needed to corroborate these predictions of how and where contaminants are moving as climate changes.

- Based on monitoring and climate impact modeling outputs, it will become increasingly important to provide dietary advice in the circumpolar region that maximizes nutritional benefit and social-cultural integrity while minimizing contaminant exposures. Research on climate change and contaminant interactions will be essential for regionally appropriate adaptation strategies.

- Climate change may create ice-free passages in the Arctic Ocean. These changes may lead to increased transport by ship of Arctic oil and gas and other resources. Spills, vessel accidents, and ballast-water release in a warmer Arctic may increase contaminant releases in the Arctic and increase exposure of circumpolar residents.

Several emerging compounds have recently been detected in the Arctic and in human tissues and have not been adequately evaluated.

- Recent monitoring of polybrominated diphenylethers (PBDEs) in Arctic populations has found these compounds in the traditional foods and the blood of Arctic peoples. Levels of PBDEs are comparable or lower in the Arctic peoples compared to southern peoples of most circumpolar countries. An exception is Alaska where the levels are elevated and comparable to the levels in the U.S. general population, where levels of PBDEs are higher than in most other countries. However, there is inadequate information for any conclusions on trends in the levels of PBDEs in Arctic peoples. Despite the lack of trends these compounds are expected to further increase in the Arctic peoples. Only very limited toxicological, epidemiological, and monitoring data are available for PBDEs so definitive conclusions on health risks cannot be made at this time.

- Various perfluorinated compounds such as perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are also being found in the Arctic environment, animals, and peoples. The levels of perflourinated compounds such as PFOS in human plasma often exceed the levels of legacy POPs. The levels of PFOS and PFOA determined in Arctic people are comparable with concentrations found in southern peoples.

Traditional foods are an important source of nutrients for many Arctic residents. These foods are also the main source of exposure to contaminants. Dietary advice should take into account contaminant concentrations in local foods in order to reduce the exposure level.

- Traditional food is a good source of vitamins and essential trace elements. Marine food is also rich in polyunsaturated fatty acids which are associated with health benefits for the cardiovascular system, metabolic function, and fetal growth and development especially of the central nervous system.
- Traditional food is also a fundamental component of the culture of many Arctic peoples. Its use is often important to the identity of a people; the sharing of traditional food plays a role in the maintenance of social norms and expectations. The activities of gathering and hunting have significant physical health benefits. Given the high cost of living in most Arctic communities, traditional food saves many families money and promotes health and well-being.
- Communities consuming large amounts of marine predators have a dietary exposure to contaminants that is higher than that of communities which eat land mammals and fish. Polar bears, toothed whales, turbot, Greenland shark, and birds like marine gulls and fulmars (including their eggs) are marine predators and have high levels of contaminants. However, there are regional differences in levels found in these species.
- Combined, these aspects illustrate and confirm the 'Arctic Dilemma' described first in the second AMAP assessment of human health in the Arctic (AMAP, 2003); traditional food is nutritionally, culturally, economically, and spiritually important but is also the major source of exposure to POPs and metals. Nevertheless, the results of this assessment support the importance of promoting the consumption of traditional food after providing information which allows informed choice.
- Because the diet and local food sources, their role, amount consumed, and levels of contaminants in the biota vary to a large extent within and between populations and areas of the circumpolar Arctic, it is not feasible to provide specific dietary recommendations that apply to all Arctic populations. In general, traditional foods should be recommended and dietary advice about this food should be based upon local conditions and knowledge of contaminant levels.

Imported store-bought foods have lower contaminant levels, but many of these foods commonly consumed in the Arctic tend to be high in saturated fats and sugars. An increasing proportion of the Arctic population is consuming unhealthy imported foods.

- Comparable information about nutritional intakes in Arctic Russia is still lacking. Nutritionally, the inadequacies of the diets are not necessarily a question of imported versus traditional foods, but the low nutrient density of imported foods available and consumed.
- Available imported foods tend to have low contaminant levels (POPs and metals) because they come from very short food chains and they can also be an important source of folate and vitamin C. However, imported foods also tend to be high in sugar and saturated fats and sometimes trans-fatty acids, and to have a low density of vitamins and minerals.
- The increased prevalence of obesity and metabolic diseases observed in Arctic populations is associated with current socio-economic changes and a dietary transition which lead to increased consumption of imported foods and less traditional food plus less physical activity.

Lifestyles in much of the circumpolar region are changing. Unhealthy choices can worsen general health and exacerbate responses to contaminant exposures.

- Lifestyles in much of the circumpolar region are continuing to change as Arctic economic opportunities increase. Access to global communication systems provides a wide range of consumption messages, including those which focus on food selections which are unhealthy. Community concerns about consumption of traditional foods, less hunting, a more sedentary lifestyle and other changes in lifestyle are likely to lead to some significant deterioration in individual and population health.
- A dietary transition towards increased use of imported food, and less hunting, gathering and consumption of traditional food is leading to a higher prevalence of obesity and its sequels (metabolic syndrome, diabetes type II, and cardiovascular disease). In many Arctic communities (e.g., in Canada and Greenland) the traditional to imported food ratio has continued to decrease and is especially low among youth. Although relatively low contaminant concentrations are found in the imported food, in general, the decreasing proportion of traditional food in the diet has had a negative impact on the intake of most nutrients.
- Health status is also likely to be affected by factors such as: less trade and barter and more reliance on income from employment to purchase goods (including imported foods); the need for employment outside the community, necessary to generate income to purchase imported foods; and exposure through employment or industry to imported diseases and social pressures.
- Exposure to POPs and methylmercury will aggravate the development of ill health associated with lifestyle changes. Both POPs and mercury are likely, in a dose-dependent way, to increase the severity of

lifestyle-related metabolic disturbances induced by the changes in lifestyle.

Genetic factors influence how individuals and individual populations respond to environmental exposure.

- Gene/environment studies are a new area of research in an Arctic context. Genes are major determinants of the reaction of an organism to environmental exposures. Very little is known about genetics in Arctic populations and there are large gaps in knowledge related to how genetic factors may interact with contaminants to affect disease outcomes.

Quality assessment (QA) and quality control (QC) are essential components of all monitoring programs and must remain robust elements of monitoring activities.

- Inter-comparability of data between different studies and different laboratories is a key element in monitoring and assessments of exposures and risk. QA/QC is now well developed and integrated into the AMAP human health blood monitoring program. The AMAP inter-laboratory comparison program has markedly improved analytical co-operation, data comparability, data reliability, and data accuracy among participating laboratories.

Health risk communication is important but complex. Past experiences can be used to develop effective communication strategies.

- Risk communication must be carried out with great care and must be sensitive to cultural preferences at a community level. Within a community there may be a need for specific and targeted advice to address the potential health risks for a particular subgroup (e.g., women of childbearing age).
- Community involvement in all aspects and phases of the development of risk communication information is critical to ensuring that the advice is appropriate and relevant. It is also crucial to involve other stakeholders such as Indigenous organizations in the communication development process and evaluation processes.
- As contaminant levels change (e.g., a decline in some of the legacy POPs or an increase in an emerging POP) and new scientific information about health impacts becomes available, risk communication will need to evolve to maintain its currency.
- The AMAP Human Health Assessment Group cannot provide specific public health advice in local and regional situations, but can evaluate the circumpolar impacts of efforts by local health authorities to develop and disseminate advice.

Breast-feeding is very important for infant development and health and should still be promoted in conjunction with dietary advice for mothers.

- In 2002, the AMAP Human Health Assessment Group concluded that breast-feeding was important for immune system development, disease prevention, good nutrition, and mother-child bonding (social development). The Group re-affirms this conclusion in 2008, despite the presence of several POPs and metals in the breast milk of Arctic mothers. Studies of prenatal and post-natal exposure confirm that breast-feeding is best for at least six months.

Blood and breast milk are both valuable media for human biomonitoring globally and in the Arctic. However, in the Arctic blood is the preferred media for human biomonitoring.

- Both blood and breast milk can be used as human tissues for monitoring contaminants. The preference for blood monitoring in the Arctic is based on a need for information on both males and females, multiple age groups (children, adolescents, adults, and senior citizens), and both metals and POPs. Several studies and data provided in previous AMAP assessments indicate that contaminant concentrations in blood and breast milk are well correlated and inter-comparable. An exception is the perfluorinated compounds, for which serum is needed.
- Using standard laboratory techniques, there is enough lipids in blood to enable the quantitative estimation of all the POPs currently under study. Metals are also readily evaluated in whole blood obtained from the same samples of blood needed for POPs analyses; metals are less readily determined in breast milk.
- Blood can be obtained routinely from mothers in birthing centers pre-partum and enables immediate interventions if considered necessary; breast milk is often only available once birth mothers have returned to their communities and can be expensive to collect and safeguard. In addition, blood sampling is often more socially and culturally acceptable than sampling of breast milk.

10.3. Key recommendations

These recommendations are based on the conclusions from this assessment and the significant knowledge gaps that have been identified.

10.3.1. General

- The human health assessment process initiated through AMAP should be continued with the aim of pursuing a more holistic health impact assessment of the influences of environmental pollution on the health of Arctic peoples and the associated risk factors affecting them. This effort should be coordinated with related public health work initiated through the Sustainable Development Working Group.

- Considering the importance of general health and the influence of changing diets and contaminants on disease outcomes, more effort needs to be made to systematically collect, analyze, and report on the health status of Arctic populations and especially indigenous peoples.
- It is very important to maintain and expand current human population cohorts in the Arctic as identified in this assessment, such as those in Canada, Greenland, and the Faroe Islands. Only long-term prospective studies will provide the information needed to track adverse health outcomes associated with contaminants and changing conditions related to climate change, socio-cultural conditions, and diet.
- Uniform reporting of key health status indicators should occur every three to five years, should include trend information, should be broken down by age and gender, and should be provided by all circumpolar jurisdictions at appropriate regional levels.
- Because genotype may influence responses to contaminants, more knowledge about genetic variability and susceptibility among Arctic peoples is needed. Including genetics in studies that examine lifestyle and contaminant interactions will provide better insight into individual and population vulnerability to contaminants.
- Public health officials should continue to recommend breast feeding among Arctic populations as a healthy practice which optimizes infant growth and development. However, there is a need to reduce contaminant levels in breast milk through national, regional, and international action to reduce pollution and through relevant food advice to women of childbearing age.

10.3.2. **Climate change**

- Monitoring is urgently needed to ensure early detection of climate-induced human health threats related to contaminants. Essential monitoring elements include contaminant levels in humans and wildlife food species, zoonotic diseases in wildlife, and observations of environmental parameters such as water quality, ice, permafrost, and weather.
- Improved predictive models of contaminant transport and behavior in the Arctic are needed to understand the likely impacts of climate change with respect to contaminants. These models require improved comprehensive circumpolar monitoring of environmental matrices integrated with weather and climate data.

10.3.3. **Nutrition**

- More research about determinants of food choices and availability is needed to provide better dietary advice relevant to local conditions and preferences. This research should focus on differences by age and gender.
- Because consumption of imported food is likely to continue increasing in most of the Arctic, health authorities should work vigorously with local and national food agencies to promote the availability and consumption of imported food items with high nutritional value.
- In order to maximize the benefits of traditional food use and to reduce the risks associated with the intake of contaminants in some traditional foods, such as certain marine mammals, health authorities should promote improved access to and consumption of local traditional foods such as fish and terrestrial mammals that have lower levels of POPs and metals and high nutrient values.
- Studies should combine human biomonitoring of contaminants with total diet studies in the Arctic in order to produce better exposure estimates and better dietary advice.

10.3.4. **Health risks posed by contaminants**

- Continued monitoring of legacy POPs, mercury, and lead in humans and traditional foods is needed to obtain valid exposure trends and to track the effectiveness of national, regional, and international actions to reduce releases.
- Polybrominated compounds and perfluorinated compounds need to be included in future routine monitoring in all Arctic countries in order to reveal their sources; because these compounds are not associated with traditional food as are the legacy POPs. Additional sampling and analytical method development, where needed, should be undertaken for other compounds such as short-chain chlorinated paraffins, pentachlorophenol, siloxanes, and parabenes.
- Toxicological studies of polybrominated compounds and perfluorinated compounds need to be undertaken at levels at and above those found in human tissues, to determine the effects of these substances on development, behavior, reproduction, immune function, the nervous system, and organ function.
- Because the exposure level to methylmercury continues to be high in some Arctic populations, continued monitoring of trends is warranted.
- Further research is needed on the relationship between mercury and cardiovascular disease in Arctic populations.
- Contaminant-nutrient interactions should be further investigated in prospective Arctic cohort studies.

10.3.5. **Communication**

- Regional health authorities should collaborate with communities to develop effective, culturally appropriate communication strategies concerning contaminants and human health. Communication efforts should be evaluated with respect to their impacts on the intended audience.
- Dietary advice to Arctic residents should include both the benefits of traditional food consumption and the results of technical risk assessments concerning contaminants.
- Risk perceptions, dietary patterns, and determinants of food choice should be taken into account in the development of communication materials.
- AMAP should improve the distribution and availability of its reports and information to the general public, health authorities, and scientists in or working in the Arctic. Possible steps include greater prominence on the world-wide web's search engines and increasing AMAP's presence at relevant meetings and conferences.

10.3.6. **Political and administrative**

- Taking into account the similarity in properties between polybrominated compounds and perfluorinated compounds and other better known POPs and the long-range transport and bioaccumulation of PFOS in human tissues, these substances should be added to the Stockholm Convention.
- A global agreement to control mercury emissions should be pursued to complement national and regional efforts to reduce environmental mercury concentrations and to lower human exposures to mercury in the Arctic.

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Glossary

α-HCH ..... Alpha-hexachlorocyclohexane
α-TOH ..... Alpha-tocopherol
β-HCH ..... Beta-hexachlorocyclohexane
γ-HCH ..... Gamma-hexachlorocyclohexane / Lindane
AA ..... Arachidonic acid
ADH ..... Alcohol dehydrogenase
AHR / AhR ..... Aryl hydrocarbon receptor
ALA ..... Alpha-linolenic acid
ALDH ..... Aldehyde dehydrogenase
AMAP ..... Arctic Monitoring and Assessment Programme
AO ..... Autonomous Okrug
APOE ..... Apolipoprotein E
AR ..... Androgen receptor
BPA ..... Bisphenol-A
Cd ..... Cadmium
CoQ10 ..... Coenzyme Q10
CRM ..... Certified reference material
CYPs ..... Cytochrome P450 enzymes
DDE ..... Dichloro-diphenyl-dichloro-ethylene
DDT ..... Dichloro-diphenyl-trichloroethane
DEW ..... Distant Early Warning
DGLA ..... Dihomogamma-linolenic acid
DHA ..... Docosahexaenoic acid
DNL ..... De novo lipogenesis
DPA ..... Decosapentaenoic acid
EAR ..... Estimated Average Requirement
ECHA ..... Environmental Chemicals Agency (EU)
EEQ ..... Estimated estradiol equivalence
EFA ..... Essential fatty acid
EPA ..... Eicosapentaenoic acid
EQAS ..... External quality assessment scheme
ER ..... Estrogen receptor
EROD ..... Ethoxyresofurin-O-deethylase
FFQ ..... Food frequency questionnaire
GI ..... Glycemic index
HBB ..... Hexabromobiphenyl
HBCD ..... Hexabromocyclododecane
HCB ..... Hexachlorobenzene
HCH ..... Hexachlorocyclohexane
HDL ..... High density lipoprotein
Hg ..... Mercury
HHAG ..... Human Health Assessment Group (AMAP)
Kow ..... Partition coefficient
LA ..... Linoleic acid
LDL ..... Low density lipoprotein
Lp(a) ..... Lipoprotein(a)
LoA ..... Level of action
LoC ..... Level of concern
LOD ..... Limit of detection
LRTAP ..... Convention on Long-range Transboundary Air Pollution
MDEs ..... Mercury depletion events
MeHg ..... Methylmercury
MOMs ..... Monitoring our Mothers
mtDNA ..... Mitochondrial DNA
NADPH ..... Nicotinamide adenine dinucleotide
NCP ..... Northern Contaminants Program (Canada)
NOEC ..... No observed effect concentration
NWT ..... North West Territories (Canada)
OctaBDE ..... Octabromodiphenyl ether
OH-PCBS ..... Hydroxylated PCBs
PAHs ..... Polyaromatic hydrocarbons
Pb ..... Lead
PBB ..... Polybrominated biphenyl
PBDDs ..... Polybrominated dibenzodioxins
PBDEs ..... Polybrominated diphenylethers
PCBs ..... Polychlorinated biphenyls
PCDD ..... Polychlorinated dibenzo-p-dioxin
PCDF ..... Polychlorinated dibenzo-furan
PCNs ..... Polychlorinated naphthalenes
PCP ..... Pentachlorophenol
PeCB ..... Pentaclorobenzene
PentaBDE ..... Pentabromodiphenyl ether
PFAAs ..... Perfluoroalkyl acids
PFOA ..... Perfluorooctanoic acid
PFOS ..... Perfluorooctane sulfonate
PFHS ..... Perfluorohexanesulfonate
PND ..... Post natal day
POP ..... Persistent organic pollutant
PPARs ..... Peroxisome proliferator activated receptors
PTS ..... Persistent toxic substance
PUFA ..... Polyunsaturated fatty acid
QA ..... Quality assessment
QC ..... Quality control
RAIPON ..... Russian Association of Indigenous Peoples of the North
RDA ..... Recommended Daily Allowance
RFSL ..... Russian Food Safety Limits
RSZ ..... Rescaled sum of z scores
SCCP ..... Short-chained chlorinated paraffins
Se ..... Selenium
SSZ ..... Sum of squared z-scores
TBBPA ..... Tetrabromobisphenol-A
TCDD 2,3,7,8-tetrachlorodibenzo-p-dioxin
TDI ..... Tolerable Daily Intake
TEFs ..... Toxic Equivalency Factors
TEQ ..... Toxic equivalent
TNF ..... Tumor necrosis factor
TTP ..... Time-to-pregnancy
TWI ..... Tolerable Weekly Intake
UNECE ..... United Nations Economic Commission for Europe
UV ..... Ultraviolet radiation