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Exposure and effects assessment of persistent organohalogen contaminants in arctic wildlife and fish ☆

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ABSTRACT

Persistent organic pollutants (POPs) encompass an array of anthropogenic organic and elemental substances and their degradation and metabolic byproducts that have been found in the tissues of exposed animals, especially POPs categorized as organohalogen contaminants (OHCs). OHCs have been of concern in the circumpolar arctic for decades. For example, as a consequence of bioaccumulation and in some cases biomagnification of legacy (e.g., chlorinated PCBs, DDTs and CHLs) and emerging (e.g., brominated flame retardants (BFRs) and in particular polybrominated diphenyl ethers (PBDEs) and perfluorinated compounds (PFCs) including perfluorooctane sulfonate (PFOS) and perfluorooctanic acid (PFOA) found in Arctic biota and humans. Of high concern are the potential biological effects of these contaminants in exposed Arctic wildlife and fish. As concluded in the last review in 2004 for the Arctic Monitoring and Assessment Program (AMAP) on the effects of POPs in Arctic wildlife, prior to 1997, biological effects data were minimal and insufficient at any level of biological organization. The present review summarizes recent studies on biological effects in relation to OHC exposure, and attempts to assess known tissue/body compartment concentration data in the context of possible threshold levels of effects to evaluate the risks. This review concentrates mainly on post-2002, new OHC effects data in Arctic wildlife and fish, and is largely based on recently available effects data for populations of several top trophic level species, including seabirds (e.g., glaucous gull (*Larus hyperboreus*)), polar bears (*Ursus maritimus*), polar (Arctic) fox (*Vulpes lagopus*), and Arctic charr (*Salvelinus alpinus*), as well as semi-captive studies on sled dogs (*Canis familiaris*). Regardless, there remains a dearth of data on true contaminant exposure, cause–effect relationships with respect to these contaminant exposures in Arctic wildlife and fish. Indications of exposure effects are largely based on correlations between biomarker endpoints (e.g., biochemical processes related to the immune and endocrine

Abbreviations: ALB, thyroid hormone binding albumin; AMAP, Arctic Monitoring and Assessment Program; BDE-209, 2,2′,3,3′,4,4′,5,5′-decabromodiphenyl ether; BFR, brominated flame retardant; BGS, brain growth spurt; BMD, bone mineral density; BMR, basal metabolic rate; CHL, chlordane; Con A, concanavalin; CP, chloroparaffin; CYP, cytochrome P450; CBz, chlorobenzene; DNA, deoxyribonucleic acid; E_2, 17β-estradiol; EDC, endocrine disrupting compound; EFI, epithelial follicular index; EHV, herpes virus; EIV, influenza virus; FA, fluctuating asymmetry; FABP, fatty acid binding protein; FSH, follicle stimulating hormone; GH, growth hormone; GST, glutathione-S-transferase; HBCD, hexabromocyclododecane; HCH, hexachlorocyclohexane; Hg, mercury; HP, haptoglobin; HPT, hypothalamus–pituitary–thyroid; IGF-I, insulin-like growth factor I; IgG, immunoglobulin G; IgM, immunoglobin M; LH, luteinizing hormone; LOEL, lowest observed effect level; MeO-, methoxyl-; $MeSO_2$-, methylsulfonyl-; mRNA, messenger ribonucleic acid; OC, organochlorine; OHC, organohalogen contaminant; 25 OHD, 25-hydroxy-vitamin D3; OH-, hydroxyl-; 4-OH-HpCS, 4-hydroxy-heptachlorostyrene; P4, progesterone; PAH, polycyclic aromatic hydrocarbon; PBDE, polybrominated diphenyl ether; PCB, polychlorinated biphenyl; PCDD, polychlorinated dibenzo-*p*-dioxin; PCDF, polychlorinated dibenzofuran; PCP, pentachlorophenol; PFC, perfluorinated compound; PFCA, perfluorinated carboxylic acid; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonate; PFSA, perfluorinated sulfonate; PHA, phytohemagglufinin; POP, persistent organic pollutant; *p,p′*-DDD, bis(*p*-chlorophenyl)-1,1-dichloroethane; *p,p′*-DDE, bis(*p*-chlorophenyl)-1,1-dichloroethene; *p,p′*-DDT, bis(*p*-chlorophenyl)-1,1,1-trichloroethane; PRC, prolactin; REO, reovirus; SLE, St. Lawrence river estuary; T, testosterone; T_4, thyroxine; T_3, 3,3′,5-triiodo-L-thyronine; TBBPA, tetrabromobisphenol A; TBG, thyroid binding globulin; TCDD, 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin; TEF, toxic equivalency factor; TEQ, toxic equivalent; TET, tetanus toxoid; TH, thyroid hormone; TTR, transthyretin.

☆ This paper is a contribution to the AMAP POPs assessment.

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system, pathological changes in tissues and reproduction and development) and tissue residue levels of OHCs (e.g., PCBs, DDTs, CHLs, PBDEs and in a few cases perfluorinated carboxylic acids (PFCAs) and perfluorinated sulfonates (PFSAs)). Some exceptions include semi-field studies on comparative contaminant effects of control and exposed cohorts of captive Greenland sled dogs, and performance studies mimicking environmentally relevant PCB concentrations in Arctic charr. Recent tissue concentrations in several arctic marine mammal species and populations exceed a general threshold level of concern of 1 part-per-million (ppm), but a clear evidence of a POP/OHC-related stress in these populations remains to be confirmed. There remains minimal evidence that OHCs are having widespread effects on the health of Arctic organisms, with the possible exception of East Greenland and Svalbard polar bears and Svalbard glaucous gulls. However, the true (if any real) effects of POPs in Arctic wildlife have to be put into the context of other environmental, ecological and physiological stressors (both anthropogenic and natural) that render an overall complex picture. For instance, seasonal changes in food intake and corresponding cycles of fattening and emaciation seen in Arctic animals can modify contaminant tissue distribution and toxicokinetics (contaminant deposition, metabolism and depuration). Also, other factors, including impact of climate change (seasonal ice and temperature changes, and connection to food web changes, nutrition, etc. in exposed biota), disease, species invasion and the connection to disease resistance will impact toxicant exposure. Overall, further research and better understanding of POP/OHC impact on animal performance in Arctic biota are recommended. Regardless, it could be argued that Arctic wildlife and fish at the highest potential risk of POP/OHC exposure and mediated effects are East Greenland, Svalbard and (West and South) Hudson Bay polar bears, Alaskan and Northern Norway killer whales, several species of gulls and other seabirds from the Svalbard area, Northern Norway, East Greenland, the Kara Sea and/or the Canadian central high Arctic, East Greenland ringed seal and a few populations of Arctic charr and Greenland shark.

1. OHC exposure in Arctic wildlife and fish

The circumpolar Arctic includes land masses and waters within the political boundaries of Canada, Greenland (Denmark), Norway, Sweden, Finland, the Russian Federation and Alaska (United States of America) (Fig. 1). There have been minimal direct use within the circumpolar Arctic of chemical substances classified as persistent organic pollutants (POPs), and those used have been comprised largely of organohalogen (chlorinated, brominated and fluorinated) compounds (OHCs). However, long-range atmospheric transport, and to a lesser general extent via ocean currents and rivers, to the Arctic occurs for POPs (and/or precursors and degradation products) sourced in more southerly latitudes (Braune et al., 2005; de Wit et al., 2004, 2006). As a consequence, lipophilic POPs accumulate in organisms within especially marine food webs and thus there is a concern for the health of exposed wildlife and fish as well as for humans who consume country foods.

The last AMAP assessment of POPs and associations and relationships between OHC exposure and biomarkers of effects in Arctic biota (including wildlife and fish) included any new published information up to approximately 2004 (Braune et al., 2005; Fisk et al., 2005; de Wit et al., 2004, 2006). Within the last 4 to 5 years there has been a considerable amount of new effects information published on OHCs in Arctic wildlife and fish, and is the subject of the present review. As will be summarized, data on OHC levels and effects in fish in the Arctic is, for example, scarce in comparison with animals living in marine (mainly coastal) environments such as polar bear (*Ursus maritimus*) and glaucous gull (*Larus hyperboreus*), which are apex species in the Arctic marine food web. Regardless, POP and effects studies on animals living in polar environments are hampered due to challenging, difficult and/or expensive logistics. Furthermore, there are numerous natural (e.g., ecological and physiological) and anthropogenic factors (e.g., Arctic warming in relation to introduction of new species and pathogens to the Arctic, and changes in the food web and prey–predator interactions) that can influence and/or confound the exposure to and effects of OHCs in many Arctic animals and in particular those that exhibit strong seasonal adaptations at various levels of biological organization (e.g., cellular, organ, whole organism and population). This includes temporal changes in bioenergetics between periods of fat accumulation and fat mobilization, which in turn can influence the toxicokinetics of POPs and the corresponding, tissue-specific effect sensitivity toward POPs. Changes in POP toxicokinetics include factors such as altered deposition and mobilization. Long periods of emaciation, and associated fat mobilization and redistribution of accumulated POPs, seems to make these animals particularly sensitive to POPs. Also, enzyme-catalyzed metabolism can occur in which the POP can be detoxified or toxified to metabolites that can also be persistent and subject to unique toxicokinetics in the exposed organism including unique tissue-specific toxicities.

In (marine) wildlife species feeding at higher levels of the Arctic food web, and as will be discussed in this review, POP/OHC exposure can be high enough to exceed putative threshold levels that have been previously estimated for non-target and non-Arctic species (Fisk et al., 2005). In these non-target species studies, e.g., on captive or non-Arctic species, exposure to specific POPs/OHCs have been shown to result in deleterious and observable effects via mode(s) of action and mechanisms that are a function of the contaminant type and treatment level. However, difficulties in extrapolation relating to differences in sensitivity for animal groups (e.g., comparative toxicology) not living in the Arctic are well appreciated. This raises the question as to whether documented effects observed in non-Arctic species investigated in laboratory studies can be directly transferred and applied to Arctic species. Equally importantly, such laboratory studies often expose captive animals to a single POP or OHC (or technical products) at high doses for short periods of time and use non-food routes of administration (not orally ingested). This makes it difficult to extrapolate these effects seen at high acute doses to possible adverse effects at lower but more chronic (multi-generational) exposures as is the case for Arctic wildlife and fish. Also, free-ranging wildlife and fish as exposed to a complex cocktail of known POPs/OHCs as opposed to simple mixtures or compounds generally used in experimental, lab-based designs.

Among the possible mechanisms that legacy and novel OHCs may elicit effects, e.g., endocrine and immune disruptive potentials, have been reported for OHCs that biomagnify to relatively high concentrations in Arctic wildlife and fish (de Wit et al., 2004; Fisk et al., 2005). Thus, there is great cause for concern that the health, reproduction potential and survival of exposed species may be affected (Fisk et al., 2005). For example, the vulnerability of offspring (fetus and neonate) in highly exposed cohorts of Arctic wildlife where contaminant transfer from the mother is occurring at a time of critical (and sensitive) developmental sensitivity to stressors. In addition, depending on the time period Arctic wildlife and fish are likely coping with other additional anthropogenic stressors such as Arctic warming and the subsequently complex impacts on ecosystems.

An intensely focused environmental stress element in the Arctic is climate change caused by global warming and/or temperature

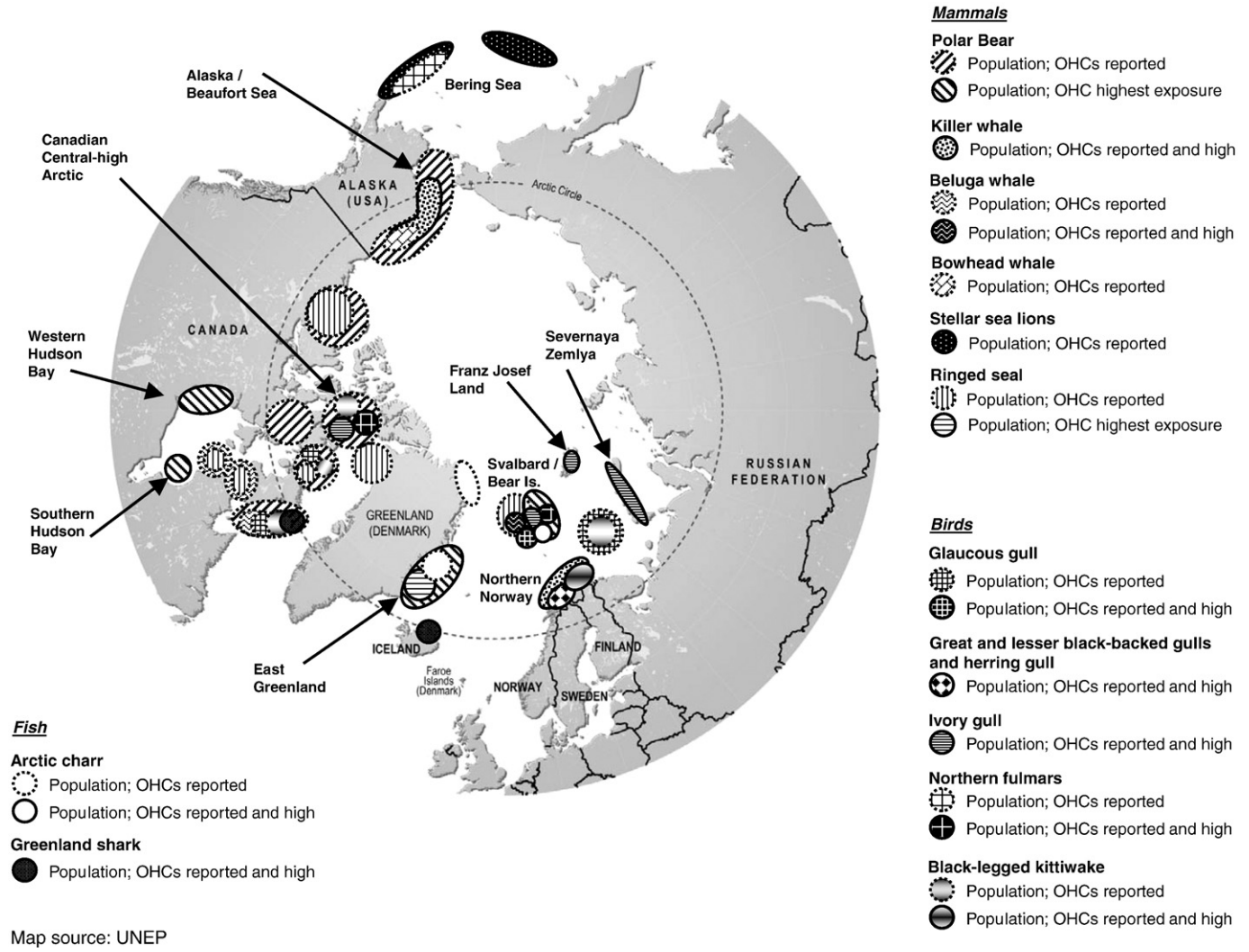

Fig. 1. Map of the circumpolar showing Arctic wildlife and fish species and populations where there is OHC exposure information available in the last 7 years. For a given species, the shaded areas indicate exposure "hotspots". See Tables 1–4 for listings and references of OHC concentration levels.

changes (Graversen et al., 2008). There is an established link between recent climate change and phenological, geographical and compositional changes to ecosystems across many regions of the world (Parmesan and Yohe, 2003). Although the magnitude of warming is regionally variable, it has been reported that for the Arctic the magnitude is nearly twice that of the global average (Johannessen et al., 2004; Graversen et al., 2008). A changing environment can affect wildlife populations under abnormal and possibly increased stressor conditions that are outside of cyclic/seasonal conditions, ranging from habitat loss and alteration to new and more virulent diseases. Climate-related change that will influence OHCs and other POPs may result in increased levels, and at the minimum perturbations, of contaminant exposure at various levels of the food web. This modulation in both contaminant exposure and health status could be deleterious in that certain Arctic wildlife and fish species are challenged by stressors beyond their capacity to tolerate chemical exposures that elicit a biological response or worse a toxicological effect (Jenssen, 2006).

Among the other biological and physiological factors that are important in interpreting contaminant and effect data and the health of Arctic wildlife and fish are life history parameters and lipid content (Ylitalo et al., 2001). Lipid content is critical for assessing health and plays a key role in the tissue dynamics of many lipophilic OHCs, and is commonly oversimplified from a biological and health perspective. For example, Krahn et al. (2001) evaluated OCs and lipid profiles in blubber of gray whales (*Eschrichtius robustus*) from the eastern North Pacific stock (hunter-killed in the Arctic, biopsied free ranging, and stranded whales). Significantly higher lipid levels were found in the blubber of subsistence animals (Arctic) that were sampled following summer feeding in the Bering and Chukchi Seas, compared to lipid levels in the biopsied and stranded animals. Lipid class profiles from blubber of presumably healthy gray whales (i.e. from subsistence and biopsy sampling) contained primarily triglycerides and were very different from those of stranded animals that showed lipid decomposition (increased proportions of free fatty acids, cholesterol and phospholipids). Higher concentrations of OC contaminants were found in stranded juvenile gray whales, compared to juvenile subsistence whales, and were thought to result from retention of OCs in blubber of the stranded animals as lipid stores are mobilized for energy and total lipid levels decrease, rather than from a difference in diet or feeding areas. OC concentrations in various tissues (blubber, liver, kidney, muscle, and brain) were similar on a lipid weight basis, except for brain, which had lower lipid-adjusted OC concentrations because the blood–brain barrier can limit contaminant transfer (Krahn et al., 2001). Alternately, delayed OC transfer to the brain hypothetically does not explain lower brain OC levels with respect to pseudo-equilibrium concentrations established across the blood–brain barrier. Lower brain concentrations are likely related to the

higher polarity of brain lipids (e.g., phospholids) compared to e.g., adipose tissue. Regardless, assessing toxicokinetic distribution is important especially for target organs (e.g., brain).

The overall goal of the present AMAP exercise is to review the state-of-the-science with respect to what new information has been published in approximately the last 7 years on effects and responses in key, target Arctic wildlife and fish species and populations (Fig. 1), and in relation to exposure to OHCs and precursors, as well as their degradation and/or metabolism byproducts. This also includes, in the case of seabirds, those species and populations that seasonally migrate into and out of the Arctic region for at least part of the year. For both marine and terrestrial (and marine-feeding terrestrial) mammals there presently remains a bias for effects oriented studies in key species from "hotspot" Arctic areas where OHC exposure data has historically been shown to be more plentiful and shown to be higher relative to species from other circumpolar regions (Letcher et al., 2000b; Braune et al., 2005; de Wit et al., 2004, 2006). In the following sub-section we review reports from over approximately the last decade as to the type and highest levels of classes of known OHCs and degradation and metabolite products in Arctic wildlife and fish. Extensive reviews of specific OHCs (and other POPs) in Arctic biota are beyond the scope of the present review and are discussed in OHC class-specific reviews being published in the present special AMAP issue.

1.1. Ursids and canids

Prior to about 7 years ago, East Greenland, Svalbard and the Kara Sea regions of the Arctic had been documented as having the highest levels of OHCs and degradation products in the tissues of ursids and canids (Norstrom et al., 1998; de Wit et al., 2004; Braune et al., 2005). Listed in Table 1, from data available over the last decade, are the maximum exposure concentrations reported for the sum (Σ) of chlorinated, brominated and/or fluorinated OHCs in the tissues and the main body compartment, blood, of free-ranging mammalian wildlife within the Arctic. With respect to ursids and canids essentially, all of the OHC data presently reported for polar bears (Tables 1 and 2 and summarized from references therein) are from populations spanning the circumpolar Arctic with the exception of the vast territory of the Russian Arctic region (Fig. 1). Some miminal data exists for perfluorinated compounds (PFCs), perfluorinated sulfonates (PFSAs) and perfluorinated carboxylates (PFCAs) in mink (*Mustela vison*) from the Yukon Territory and Arctic fox (*Vulpes lagopus*) from Western Hudson Bay. The ΣPFSA concentration in the liver of the Arctic fox is as high as 250 ng/g (ww). For polar bears regardless of population, the general order of tissue concentrations are Σpolychlorinated biphenyl (PCB) ≈ Σchlordanes (CHL) ≈ ΣPFSA (essentially all PFOS) > ΣDDT (i.e., *p,p′*-DDT (bis(*p*-chlorophenyl)-1,1,1-trichloroethane), *p,p′*-DDE (bis(*p*-chlorophenyl)-1,1-dichloroethene) and *p,p′*-DDD (bis(*p*-chlorophenyl)-1,1-dichloroethane), and in some cases *o,p′*-DDT, *o,p′*-DDE and/or *o,p′*-DDD) > Σchlorobenzene (CBz) ≈ Σhexchlorocyclohexane (HCH) ≈ ΣToxaphene ≈ ΣPFCA > Σpolybrominated diphenyl ether (PBDE) > hexabromocyclododecane (HBCD) flame retardant. In the case of ΣPCB, ΣCHL and ΣPFSA, these concentrations exceeded 1 ppm (ww) in bears from reported populations. Mainly for East Greenland bears, and to a lesser extent Svalbard bears, levels of Σhydroxylated (OH)-PCB, Σmethylsulfonyl (CH_3SO_2 = $MeSO_2$)-PCB, 3-$MeSO_2$-*p,p′*-DDE metabolites have been reported (Table 2), and at levels comparable to ΣDDTs and ΣCBzs (Table 1). In contrast levels of ΣOH-PBDEs, Σmethoxylated(MeO)-PBDEs, pentachlorophenol (PCP) and 4-OH-heptachlorstyrene (4-OH-HpCS) are at very low ppb levels or below detection (Table 2).

For polar bears from the East Greenland and Svalbard regions there are substantial reports on OHC concentration associations with changes in various (e.g., endocrine- and immune-related) biomarker responses, although these do not directly establish cause–effect relationships (e.g., Oskam et al., 2003, 2004a; Haave et al., 2003; Braathen et al., 2004; Lie et al., 2004, 2005; Sonne et al., 2004, 2005a,b,c, 2006a,b, 2007a,b, 2008a; Fisk et al., 2005; Kirkegaard et al., 2005; Verreault et al., 2008a; Muir et al., 2006). In some Svalbard and/or Russian investigations, effect studies have been restricted to studying health variables that can be analyzed in blood (plasma or serum) in relation to OHC content in plasma and/or adipose biopsies. This is because the polar bear is especially protected in these regions. All circumpolar bear populations are protected as per the international polar bear treaty of 1973, although only some populations are subject to aboriginal hunts. Samples were obtained during the handling of polar bears in connection with research activities, i.e., chemical immobilization and deployment of satellite collars or conventional tags. A substantial amount of information has been achieved from these studies. This includes correlative relationships and suggested associations between OHC levels and hormone levels, vitamins and immune status as well as associations with contaminant levels and polar bear movements.

For the East Greenland region, it was possible to obtain samples from a large number of organ tissues from polar bears obtained from the traditional hunt. Histopathological investigations on polar bears were started in East Greenland in 1999. These studies have provided a unique opportunity to investigate the potential organ-specific effects by assessments of OHC exposure in relation to changes in biomarker measurements. However, these studies are also based on correlational and descriptive analyses. To improve the understanding and disentangling the potential effects of the cocktail of exposure to contaminants and food stress, experimental exposure studies have been performed using sledge (or sled) dogs (*Canis familiaris*) and domesticated Arctic fox, which are possible surrogate model species for other *Canidae* species including polar bears. In captive sled dog and to a lesser extent Arctic fox studies, which included a cohort fed a naturally POP contaminated diet of minke whale (*Balaenoptera acutorostrata*) blubber, it has been possible over recent years to define and compare OHC exposed and unexposed (reference) groups in direct relation to an array of effects, e.g. reproductive organs and other internal organs, the skeletal system, immune and endocrine systems, and POP dietary accumulation, biotransformation and toxicokinetics (and associated enzyme systems) (e.g., Sonne et al., 2006c, 2007c,d, 2008b,c,d,e,f, 2009a,b,c; Kirkegaard et al., 2010a,b,c; Verreault et al., 2008a,b, 2009a,b,c). To our knowledge, there are no studies that have examined the possible effects of POPs/OHCs on free-living canids, including Arctic foxes. However, a contaminant exposure study has been reported using domesticated (farmed) Arctic foxes (Hallanger, 2006; Rogstad, 2007).

1.2. Marine mammals

Arctic cetaceans and pinnipeds in this review focuses mostly on marine mammals were new OHC-related effects information exists; bowhead whale (*Balaena mysticetus*), beluga whale (*Delphinapterus leucas*), harbour porpoise (*Phocoena phocoena*) and ringed seal. These species are selected based on their 1) circumpolar distribution, 2) potential as models for other species (e.g., ringed seal for ice seals, bowhead for mysticetes, beluga whales for odontocetes), 3) available POPs/OHC data (Tables 1 and 2), 4) physiologic and pathologic data (enzymology, endocrinology, lesions noted, etc.) evaluated in context of OHCs and ecology (e.g., biomagnification and trophodynamics), and 5) use as subsistence species in indigenous communities. Among marine mammals, understanding dose–response relationships for aquatic mammals have been attempted especially for the adverse health effects of PCB exposure (Kannan et al., 2000) and the toxicokinetics and trends of PCBs in beluga whales (Hickie et al., 1999, 2000). Enzyme-catalyzed metabolism of POPs has been shown to have an apparently small influence on the concentrations and

Table 1
A comprehensive selection of recently reported, highest exposure levels of major classes of persistent halogenated organic contaminants in free-ranging mammalian wildlife species within the Arctic: geometric or arithmetic means of concentrations (or ranges of means) in major storage tissues (fat, liver or muscle).[a]

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣPCB[b]				
Bowhead whale (*Balaena mysticetus*) (F + M)	Alaska	Fat	451	Hoekstra et al. (2003a)
Killer whale (*Orcinus orca*) (F + M; transients)	Alaska	Fat	230,000 (lw)	Ylitalo et al. (2001)
Killer whale (M)	Northern Norway	Fat	26,940 (lw)	Wolkers et al. (2007)
Beluga whale (*Delphinapterus leucas*) (F + M)	Hudson Strait (Canadian Arctic)	Fat	661–3690 (lw)	Kelly et al. (2008a)
Beluga whale (F + M)	Western Hudson Bay (Canadian Arctic)	Liver	1737 (lw)	McKinney et al. (2006b)
Beluga whale (M)	Svalbard, Norway	Fat	3198–10075 (lw)	Andersen et al. (2001)
Ringed seal (*Phoca hispida*) (F + M)	Svalbard, Norway	Liver/Plasma	45/22 (lw)	Routti et al., (2008a,b)
Ringed seal (M)	Hudson Strait (Canadian Arctic)	Fat	602 (lw)	Kelly et al. (2008a)
Ringed seal (F + M)	West Greenland	Fat	200 (lw)	Vorkamp et al. (2008)
Ringed seal (F + M)	East Greenland	Fat	1370 (lw)	Rigét et al. (2006); Letcher et al. (2009); Vorkamp et al. (2004)
Stellar sea lions (*Eumetopias jubatus*) (F + M; all pups)	Alaska–Bering Sea	Blood	3692–7797 (lw)	Myers et al. (2008)
Stellar sea lions (F + M; all pups)	Russia–Bering Sea	Blood	4600–18000 (lw)	Myers et al. (2008)
Polar bear (*Ursus maritimus*) (F + M)	East Greenland	Fat	7818 (lw)	Dietz et al. (2004); Gebbink et al. (2008a,b); Verreault et al. (2005a); Sandala et al. (2004)
Polar bear (F + M)	East Greenland	Liver	2354 (ww)	Gebbink et al. (2008a,b)
Polar bear (F)	Svalbard, Norway	Fat	5972 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Greenland, Denmark	Fat	5414–9100 (lw)	Dietz et al. (2004); Verreault et al. (2005a)
Polar bear (F + M)	Locations across Canadian Arctic	Fat	1138–2802 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Alaska	Fat	2174 (lw)	Verreault et al. (2005a); Bentzen et al. (2008)
ΣCHL[b]				
Killer whale (M)	Northern Norway	Fat	6565 (lw)	Wolkers et al. (2007)
Beluga whale (F + M)	Western Hudson Bay (Canadian Arctic)	Liver	808 (lw)	McKinney et al. (2006b)
Beluga whale (M)	Svalbard, Norway	Fat	2099–6143 (lw)	Andersen et al. (2001)
Ringed seal (F + M)	Svalbard, Norway	Liver/Plasma	13/3 (ww)	Routti et al. (2009a)
Ringed seal (F)	Northern Baffin Bay, Canadian Arctic	Fat	194 (ww)	Borgå et al. (2005)
Ringed seal (F + M)	East Greenland	Fat	400 (lw)	Vorkamp et al. (2004)
Polar bear (F + M)	East Greenland	Fat	1776 (lw)	Dietz et al. (2004); Gebbink et al. (2008a,b); Verreault et al. (2005a); Sandala et al. (2004)
Polar bear (F + M)	East Greenland	Liver	4114 (ww)	Gebbink et al. (2008a,b)
Polar bear (F)	Svalbard, Norway	Fat	1517 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Locations across Canadian Arctic	Fat	1819–2457 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Alaska	Fat	2007 (lw)	Verreault et al. (2005a); Bentzen et al. (2008)
ΣDDT[b]				
Killer whale (F + M; transients)	Alaska	Fat	320000 (lw)	Ylitalo et al. (2001)
Beluga whale (F + M)	Hudson Strait (Canadian Arctic)	Fat	520–2521(lw)	Kelly et al. (2008a)
Beluga whale (F + M)	Western Hudson Bay (Canadian Arctic)	Liver	284 (lw)	McKinney et al. (2006b)
Beluga whale (M)	Svalbard, Norway	Fat	3272–6770 (lw)	Andersen et al. (2001)
Ringed seal (F + M)	East Greenland	Fat	1200 (lw)	Vorkamp et al. (2004)
Ringed seal (F + M)	West Greenland	Fat	220 (lw)	Vorkamp et al. (2008)
Ringed seal (M)	Hudson Strait (Canadian Arctic)	Fat	413 (lw)	Kelly et al. (2008a)
Stellar sea lions (F + M; all pups)	Alaska–Bering Sea	Blood	2127–5464 (lw)	Myers et al. (2008)
Stellar sea lions (F + M; all pups)	Russia–Bering Sea	Blood	3600–15000 (lw)	Myers et al. (2008)
Polar bear (F + M)	East Greenland	Fat	309 (lw)	Dietz et al. (2004); Gebbink et al. (2008a,b); Verreault et al. (2005a); Sandala et al. (2004)
Polar bear (F)	Svalbard, Norway	Fat	209 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Greenland, Denmark	Fat	309–559 (lw)	Dietz et al. (2004); Verreault et al. (2005a)
Polar bear (F + M)	Locations across Canadian Arctic	Fat	65–210 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Alaska	Fat	165 (lw)	Verreault et al. (2005a); Bentzen et al. (2008)
ΣCBz[b]				
Killer whale (F + M; transients)	Alaska	Fat	127,000 (lw)	Ylitalo et al. (2001)
Beluga whale (F + M)	Hudson Strait (Canadian Arctic)	Fat	112–377 (lw)	Kelly et al. (2008a)
Ringed seal (F + M)	East Greenland	Fat	16 (lw)	Vorkamp et al. (2004)
Ringed seal (F + M)	West Greenland	Fat	10 (lw)	Vorkamp et al. (2008)
Ringed seal (M)	Hudson Strait (Canadian Arctic)	Fat	78 (lw)	Kelly et al. (2008a)
Polar bear (F + M)	East Greenland	Fat	79–187 (lw)	Dietz et al. (2004); Gebbink et al. (2008a,b); Verreault et al. (2005a); Sandala et al. (2004)
Polar bear (F + M)	East Greenland	Liver	12 (ww)	Gebbink et al. (2008a,b)
Polar bear (F)	Svalbard, Norway	Fat	105 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Locations across Canadian Arctic	Fat	98–191 (lw)	Verreault et al. (2005a)
Polar bear (F + M)	Alaska	Fat	118 (lw)	Verreault et al. (2005a); Bentzen et al. (2008)
ΣHCH[b]				
Beluga whale (F + M)	Hudson Str. (Canadian Arctic)	Fat	95–119 (lw)	Kelly et al. (2008a)
Beluga whale (F + M)	Western Hudson Bay (Canadian Arctic)	Liver	45 (lw)	McKinney et al. (2006b)
Beluga whale (M)	Svalbard, Norway	Fat	68–510 (lw)	Andersen et al. (2001)
Ringed seal (F + M)	East Greenland	Fat	67 (lw)	Vorkamp et al. (2004)
Ringed seal (F + M)	West Greenland	Fat	40 (lw)	Vorkamp et al. (2008)
Ringed seal (M)	Hudson Strait (Canadian Arctic)	Fat	145 (lw)	Kelly et al. (2008a)

(continued on next page)

Table 1 (*continued*)

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣHCH[b]				
Polar bear (F+M)	East Greenland	Fat	137–263 (lw)	Dietz et al. (2004); Gebbink et al. (2008a,b); Verreault et al. (2005a); Sandala et al. (2004)
Polar bear (F+M)	East Greenland	Liver	7 (ww)	Gebbink et al. (2008a,b)
Polar bear (F)	Svalbard, Norway	Fat	71 (lw)	Verreault et al. (2005a)
Polar bear (F+M)	Locations across Canadian Arctic	Fat	260–498 (lw)	Verreault et al. (2005a)
Polar bear (F+M)	Alaska	Fat	490 (lw)	Verreault et al. (2005a); Bentzen et al. (2008)
ΣToxaphene				
Killer whale (M)	Northern Norway	Fat	8206 (lw)	Wolkers et al. (2007)
Beluga whale (F+M)	Eastern Hudson Bay (Canadian Arctic)	Fat	497–473 (lw)	Kelly et al. (2008a)
Beluga whale (M)	Svalbard, Norway	Fat	11,447 (lw)	Andersen et al. (2006)
Ringed seal (F+M)	East Greenland	Fat	38 (lw)	Vorkamp et al. (2004)
Ringed seal (M)	Hudson Strait (Canadian Arctic)	Fat	157 (lw)	Kelly et al. (2008a)
Ringed seal (F+M)	Svalbard, Norway	Liver/Plasma	3/<1 (ww)	Routti et al. (2009a)
Polar bear (F+M)	Alaska	Fat	490 (lw)	Bentzen et al. (2008)
ΣPBDE[b]				
Killer whale (M)	Northern Norway	Fat	475 (lw)	Wolkers et al. (2007)
Beluga whale (F+M)	Hudson Strait (Canadian Arctic)	Fat	16–34 (lw)	Kelly et al. (2008b)
Beluga whale (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	53 (lw)	McKinney et al. (2006b)
Beluga whale (F+M)	Western Canadian Arctic	Fat	12 (lw)	Tomy et al. (2008)
Narwhal (*Monodon monoceros*) (F+M)	Western Canadain Arctic	Fat	18 (lw)	Tomy et al. (2008)
Ringed seal (F+M)	White, Barents+Kara Seas (Russia)	Fat	10 (lw)	Vorkamp et al. (2008)
Ringed seal (F+M)	West Greenland)	Fat	6 (lw)	Vorkamp et al. (2008)
Ringed seal (F+M)	East Greenland	Fat	149 (lw)	Rigét et al. (2006); Letcher et al. (2009)
Ringed seal (F+M)	Svalbard, Norway	Fat	18 (lw)	Wolkers et al. (2004)
Ringed seal (F+M)	Svalbard, Norway	Liver/Plasma	1/<1 (ww)	Routti et al. (2009b)
Ringed seal (F+M)	Eastern Hudson Bay (Canadian Arctic)	Fat	11–14 (lw)	Kelly et al. (2008b)
Polar bear (F+M)	East Greenland (F+M)	Fat	68–75 (lw)	Dietz et al. (2007); Gebbink et al. (2008a,b); Muir et al. (2006)
Polar bear (F+M)	East Greenland	Liver	40 (ww)	Gebbink et al. (2008a,b)
Polar bear (F)	Svalbard, Norway	Fat	50 (lw)	Muir et al. (2006); Sørmo et al. (2006)
Polar bear (F)	Svalbard, Norway	Plasma	6 (ww)	Verreault et al. (2005b)
Polar bear (F+M)	Locations across Canadian Arctic	Fat	12–22 (lw)	Muir et al. (2006)
Polar bear (F+M)	Alaska	Fat	80 (lw)	Muir et al. (2006); Bentzen et al. (2008)
HBCD[b]				
Beluga whale (F+M)	Western Canadian Arctic	Fat	2 (lw)	Tomy et al. (2008)
Narwhal (F+M)	Western Canadian Arctic	Fat	2 (lw)	Tomy et al. (2008)
Walrus (*Odobenus rosmarus*) (M)	Western Canadian Arctic	Fat	2 (lw)	Tomy et al. (2008)
Ringed seal (F+M)	East Greenland	Fat	38 (lw)	Letcher et al. (2009); Vorkamp et al. (2004)
Polar bear (F+M)	East Greenland	Fat	44 (lw)	Gebbink et al. (2008a,b); Muir et al. (2006)
Polar bear (F+M)	Svalbard, Norway	Fat	50 (lw)	Muir et al. (2006); Sørmo et al. (2006)
Polar bear (F+M)	Alaska	Fat	<1 (lw)	Muir et al. (2006)
ΣPFSA[b]				
Beluga whale (M)	SE Baffin Is. (Canadian Arctic)	Liver	13 (ww)	Tomy et al. (2004)
Narwhal (M)	SE Baffin Is. (Canadian Arctic)	Liver	11 (ww)	Tomy et al. (2004)
Walrus (F+M)	SE Baffin Is. (Canadian Arctic)	Liver	2 (ww)	Tomy et al. (2004)
Ringed seal (F+M)	Alaska	Liver	8 (ww)	Quakenbush and Citta (2008)
Bearded seal (*Erignathus barbatus*) (F+M)	Alaska	Liver	5 (ww)	Quakenbush and Citta (2008)
Bearded seal (F+M)	Beaufort Sea, NWT, Canada	Liver	3 (ww)	Powley et al. (2008)
Spotted seal (*Phoca largha*) (F+M)	Alaska	Liver	8 (ww)	Quakenbush and Citta (2008)
Ribbon sea (*Histriophoca fasciata*) (F+M)	Alaska	Liver	7 (ww)	Quakenbush and Citta (2008)
Ringed seal (F+M)	Locations across Canadian Arctic	Liver	10–88 (ww)	Martin et al. (2004); Butt et al. (2007, 2008)
Ringed seal (F+M)	Beaufort Sea, NWT, Canada	Liver	25 (ww)	Powley et al. (2008)
Ringed seal (F+M)	East Greenland	Liver	95 (ww)	Bossi et al. (2005a)
Ringed seal (F+M)	West Greenland	Liver	28 (ww)	Bossi et al. (2005a)
Polar bear (F+M)	East Greenland	Liver	3000 (ww)	Smithwick et al. (2005); Dietz et al. (2008)
Polar bear (F)	Svalbard, Norway	Blood	4240 (ww)	Smithwick et al. (2005)
Polar bear (F+M)	Locations across Canadian Arctic	Liver	1200–1430 (ww)	Smithwick et al. (2005)
Polar bear (F+M)	Southern Hudson Bay, Nunavut	Liver	2800 (ww)	Smithwick et al. (2005)
Polar bear (F+M)	Alaska	Liver	850 (ww)	Smithwick et al. (2005)
Arctic fox (*Alopex lagopus*) (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	250 (ww)	Martin et al. (2004)
Mink (*Mustela vison*) (F+M)	Yukon Territory, Canada	Liver	9 (ww)	Martin et al. (2004)
ΣPFCA[b]				
Ringed seal (F+M)	Alaska	Liver	14 (ww)	Quakenbush and Citta (2008)
Bearded seal (F+M)	Alaska	Liver	7 (ww)	Quakenbush and Citta (2008)
Bearded seal (F+M)	Beaufort Sea, NWT, Canada	Liver	3 (ww)	Powley et al. (2008)
Spotted seal (F+M)	Alaska	Liver	15 (ww)	Quakenbush and Citta (2008)
Ribbon seal (F+M)	Alaska	Liver	21 (ww)	Quakenbush and Citta (2008)
Ringed seal (F+M)	Locations across Canadian Arctic	Liver	9–83 (ww)	Martin et al. (2004); Butt et al. (2007, 2008)
Ringed seal (F+M)	Beaufort Sea, NWT, Canada	Liver	15 (ww)	Powley et al. (2008)
Ringed seal (F+M)	East Greenland	Liver	14 (ww)	Bossi et al. (2005a)
Ringed seal (F+M)	West Greenland	Liver	7 (ww)	Bossi et al. (2005a)

Table 1 (*continued*)

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣPFCA[b]				
Polar bear (F + M)	East Greenland	Liver	500 (ww)	Smithwick et al. (2005); Dietz et al. (2008)
Polar bear (F)	Svalbard, Norway	Blood	320 (ww)	Smithwick et al. (2005)
Polar bear (F + M)	Locations across Canadian Arctic	Liver	304–630 (ww)	Smithwick et al. (2005)
Polar bear (F + M)	Southern Hudson Bay, Nunavut	Liver	515 (ww)	Smithwick et al. (2005)
Polar bear (F + M)	Alaska	Liver	285 (ww)	Smithwick et al. (2005)
Arctic fox (F + M)	Western Hudson Bay (Canadian Arctic)	Liver	53 (ww)	Martin et al. (2004)
Mink (F + M)	Yukon Territory, Canada	Liver	24 (ww)	Martin et al. (2004)

[a] More details on the concentration levels and patterns of individual organohalogen contaminants in the present wildlife and fish species can be found in contaminant specific reviews in the present issue of STOTEN. Female (F) and/or male (M) adults unless specified otherwise. The mean concentrations are the highest reported for a given species or location within generally the last 10 years.

[b] PCB: polychlorinated biphenyl congeners, CBz: polychlorinated benzenes, CHL: Chlordane compounds, DDT: dichlorodiphenyldichloroethylene (*p,p′*-DDE) and dichlorodiphenyldichloroethane (*p,p′*-DDT), HCH: hexachlorocyclohexane isomers, CP: polychlorinated paraffin congeners, PBDE: polybrominated diphenyl ether congeners (mainly BDE47, 99 and 100), HBCD: hexabromocyclododecanes isomers (essentially all α-HBCD), PFSA: perfluorinated sulfonates (mainly perfluorooctane sulfonate (PFOS) and in some cases perfluorohexane sulfonate (PFHxS)), PFCA: perfluorinated carboxylates (mainly C_8 to C_{13} perfluorohydrocarbon chain lengths).

[c] Concentrations reported as means or ranges of means on either a wet weight (ww) or lipid weight (lw) basis.

congener-specific patterns of some POPs such as PCBs in northern Alaskan bowhead whales via apparent PCB metabolism to persistent and retained OH- and $MeSO_2$-PCBs (Hoekstra et al., 2003a).

With respect to marine mammals most of the recent OHC (exposure) data is for beluga whale (Hudson Strait, southest Baffin Bay) and ringed seal (Canadian Arctic locations, East Greenland and Svalbard), and much lesser so for killer whale (*Orcinus orca*), bowhead whale and Stellar sea lion (*Eumetopias jubatus*) (Northern Norway, Alaska–Beaufort Sea and/or Alaska–Russian Bering Sea only) (Tables 1 and 2; Fig. 1). Generally, for all marine mammals, the general order (and similar to polar bears) of tissue concentrations are ΣPCB > ΣCHL ≈ ΣDDT ≈ ΣPFSA > ΣCBz ≈ ΣHCH ≈ ΣToxaphene ≈ ΣPFCA > ΣPBDE > HBCD. Extremely high levels of OHCs, i.e., ΣPCB, ΣCHL, ΣDDT, ΣCBz, ΣToxaphene and/or ΣPBDE have been reported for Alaskan and Northern Norway killer whales relative to other Arctic marine mammals and populations. In the case of Alaskan killer whales, ΣPCB, ΣCHL and ΣCBz levels in fat were >100 ppm (lw), and for Northern Norway animals levels of ΣPCB, ΣCHL and ΣToxaphene in fat were 27, 7 and 8 ppm (lw), respectively (Table 1).

For pinnipeds, in the blubber of ringed seal from East Greenland, levels of ΣPCB, ΣCHL and ΣDDT exceeded or approached 1 ppm (lw). The ringed seal is an iconic circumpolar ice seal that is an important prey item for wildlife and humans. The importance of the ringed seal in the arctic ecosystem has led the AMAP to suggest that the ringed seal be included as a target (indicator) species for arctic environmental monitoring (de Wit et al., 2004). The available OHCs data for ringed seal is not geographically uniform across the Arctic range of this seal species but there is a relatively large OHC database over space and time (Braune et al., 2005) (Tables 1 and 2). Many recent studies have reported OHCs in tissues of ringed seals. We list reports of OHCs in ringed seal only over the past 7 years (Tables 1 and 2 and references therein); however, in addition to recent Svalbard, Greenland, Canadian Arctic and Alaska reports, locations across the Arctic reported prior to 7 years ago have included the White Sea and Baltic Sea (e.g., Weis and Muir, 1997; Letcher et al., 1998; Muir and Norstrom, 2000; Sandau et al., 2000; Kucklick et al., 2001, 2006; Hoekstra et al., 2003b; Hickie et al., 2005; Letcher et al., 2009). For Alaska, Kucklick et al. (2006) highlighted the use of a tissue archive in that since 1987 the Alaska Marine Mammal Tissue Archival Project (AMMTAP) has collected tissues.

Exceptionally high ΣPCB levels (4 to 10 ppm lw) were recently reported in the blood of Stellar sea lion pups from the Alaskan–Russian Bering Sea areas (Table 1). For bowhead whale from Alaska (Beaufort Sea), beluga whales from Western Hudson Bay and ringed seals from East Greenland and Norway. Levels of ΣOH-PCB and $\Sigma MeSO_2$-PCB metabolites have been reported (Table 2), but at levels much lower than ΣPCBs (Table 1). Levels of the *p,p′*-DDE metabolite 3-$MeSO_2$-*p,p′*-DDE were much lower than for *p,p′*-DDE and/or ΣDDT in East Greenland and Svalbard ringed seal and Western Hudson Bay beluga whale. Levels of ΣOH-PBDE, PCP and 4-OH-HpCS in East Greenland ringed seals and Western Hudson Bay and/or Hudson Strait beluga whale were essentially not detectable. ΣMeO-PBDE levels in the fat and/or liver were higher than ΣOH-PCB and $\Sigma MeSO_2$-PCB, and comparable to ΣCHL and ΣCBz concentrations in Hudson Strait and Bay beluga whales (Tables 1 and 2).

The bowhead whale is an ice associated whale and is harvested for food (subsistence) and other uses by Russians, Canadians and Alaskans. This whale is nearly circumpolar with the most robust population inhabiting the Bering, Chukchi and Beaufort Seas. Other populations are found in eastern Canada, Greenland, Svalbard, and Okhotsk Sea. Most data for POPs/OHCs (Table 1) on this species have been derived from samples collected from the subsistence harvest in northern Alaska. The most recent studies evaluating OHCs in bowhead whales are those of Hoekstra et al. (2002a,b,c, 2003a,b) and Rosa et al. (2007a,b). These efforts evaluated the chemical feeding ecology, metabolism and some biomarkers for bowhead whales.

Due to its low trophic position, the bowhead whale is predicted to have a relatively low exposure to POPs compared to many marine mammals of the Arctic. This has proven to be the case with a few notable exceptions. Hoekstra et al. (2002a) studied the Bering–Chukchi–Beaufort Sea population of bowhead whale muscle stable carbon ($\delta^{13}C$), nitrogen ($\delta^{15}N$), and sulfur ($\delta^{34}S$) isotope ratios. This study described that seasonal differences (spring versus fall) in $\delta^{13}C$ values were not associated with seasonal changes in $\delta^{15}N$ values, suggesting that bowhead whales maintain a consistently lower trophic position relative to other marine mammals. Hoekstra et al. (2002b) evaluated blubber and liver during seven consecutive subsistence harvests. The rank order of organochlorine (OC) group concentrations in bowhead blubber samples were toxaphene; ΣPCBs, ΣDDT, ΣHCHs, and ΣCBz. In liver, ΣHCH was the most abundant OC group, followed by ΣPCBs, ΣToxaphene, ΣCHL, ΣCBz, and ΣDDT. Tissue-specific differences in OC patterns in blubber and liver may be attributed to variation of tissue composition and the relatively low capacity of this species to biotransform various OCs. Principal component analysis of contaminant levels in bowhead blubber samples suggest that proportions of OCs, such as ΣHCH, fluctuate with seasonal migration of this species between the Bering, Chukchi, and Beaufort Seas.

1.3. Marine and terrestrial birds

There are reports of various OHCs and metabolite products in a variety of (mainly marine and fish-eating) birds across the western

Table 2
A comprehensive selection of recently reported, highest exposure levels of classes of metabolites, degradation products or related compounds of persistent organohalogen contaminants reported in free-ranging wildlife and fish species within the Arctic: geometric or arithmetic mean concentrations in major storage tissues (fat, liver or blood).[a]

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣOH-PCB[b]				
Glaucous gull (*Larus hyperboreus*) (F+M)	Bear Is. (Svalbard), Norway	Liver/Blood	28/52 (ww)	Verreault et al. (2005c, 2007a)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	<1 (ww)	Verreault et al. (2005c)
Bowhead whale (*Balaena mysticetus*) (F+M)	Alaska	Plasma	2 (ww)	Hoekstra et al. (2003a)
Beluga whale (*Delphinapterus leucas*) (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	3 (lw)	McKinney et al. (2006b)
Ringed seal (*Phoca hispida*) (F+M)	Svalbard, Norway	Plasma	<1 (ww)	Routti et al. (2008a,b)
Polar bear (*Ursus maritimus*) (F+M)	East Greenland	Fat	59 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Liver	322 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Blood	827 (ww)	Gebbink et al. (2008a,b); Sandala et al. (2004)
Polar bear (F)	Svalbard, Norway	Plasma	173 (ww)	Verreault et al. (2005b)
ΣMeSO$_2$-PCB[b]				
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Liver/Blood	25/2 (ww)	Verreault et al. (2005c, 2007a)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	92 (lw)	Verreault et al. (2005c)
Bowhead whale (F+M)	Alaska	Fat	7 (ww)	Hoekstra et al. (2003a)
Beluga whale (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	77 (lw)	McKinney et al. (2006b)
Ringed seal (F+M)	East Greenland	Fat	36 (lw)	Letcher et al. (2009)
Ringed seal (F+M)	Svalbard, Norway	Liver	2 (ww)	Routti et al. (2008a,b)
Polar bear (F+M)	East Greenland	Fat	214 (ww)	Gebbink et al. (2008a,b); Sandala et al. (2004)
Polar bear (F+M)	East Greenland	Liver	322 (ww)	Gebbink et al., (2008a,b)
Polar bear (F+M)	East Greenland	Blood	107 (ww)	Gebbink et al., (2008a,b); Sandala et al., (2004)
3-MeSO$_2$-p,p′-DDE[b]				
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Liver/Blood	1/<1 (ww)	Verreault et al. (2007a)
Ringed seal (F+M)	East Greenland	Fat	2 (lw)	Letcher et al. (2009)
Beluga whale (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	22 (lw)	McKinney et al. (2006b)
Polar bear (F+M)	East Greenland	Fat	6 (ww)	Gebbink et al. (2008a,b); Sandala et al. (2004)
Polar bear (F+M)	East Greenland	Liver	29 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Blood	1 (ww)	Gebbink et al. (2008a,b); Sandala et al. (2004)
BCPS[b]				
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Plasma	20–26 (lw)	Verreault et al. (2005c)
PCP[b]				
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Plasma	<1 (ww)	Verreault et al. (2005c)
Ringed seal (F+M)	East Greenland	Fat	1 (ww)	Letcher et al. (2009)
Ringed seal (F+M)	Svalbard, Norway	Blood	<1 (ww)	Routti et al., (2008a,b)
Polar bear (F+M)	East Greenland	Fat	1 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Liver	4 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Blood	<1 (ww)	Gebbink et al. (2008a,b); Sandala et al. (2004)
4-OH-HpCS[b]				
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Plasma	<1 (ww)	Verreault et al. (2005c)
Polar bear (F+M)r	East Greenland	Fat	1 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Liver	8 (ww)	Gebbink et al. (2008a,b)
Polar bear (F+M)	East Greenland	Blood	10 (ww)	Gebbink et al. (2008a,b); Sandala et al. (2004)
ΣOH-PBDE[b]				
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Liver/Blood	4/4 (ww)	Verreault et al. (2005b, 2007a)
Beluga whale (F+M)	Hudson Strait (Canadian Arctic)	Fat, Blood	<1 (lw)	Kelly et al. (2008a)
Beluga whale (calves)	Hudson Strait (Canadian Arctic)	Fat	<1 (lw)	Kelly et al. (2008a)
Beluga whale (M)	Hudson Strait (Canadian Arctic)	Liver	<1 (lw)	Kelly et al. (2008a)
Beluga whale (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	<1 (lw)	McKinney et al. (2006b)
Ringed seal (F+M)	Svalbard, Norway	Plasma	<1 (ww)	Routti et al. (2009b)
Ringed seal (F+M)	East Greenland	Fat	1 (lw)	Letcher et al. (2009)
Polar bear (F+M)	East Greenland	Fat	1 (ww)	Gebbink et al., (2008a,b)
Polar bear (F+M)	East Greenland	Blood	3 (ww)	Gebbink et al., (2008a,b)
Polar bear (F)	Svalbard, Norway	Plasma	<1 (ww)	Verreault et al. (2005b)
ΣMeO-PBDE[b]				
Polar cod (*Boreogadus saida*) (F+M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	10 (lw)	Kelly et al. (2008a)
White-winged scoter (*Melanitta deglandi*) (F+M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	2 (lw)	Kelly et al. (2008a)
Common eider (*Somateria mollissima*) (F+M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	1 (lw)	Kelly et al. (2008a)
Glaucous gull (F+M)	Bear Is. (Svalbard), Norway	Liver/Blood	32/3 (ww)	Verreault et al. (2005b, 2007a)
Beluga whale (F+M)	Hudson Strait (Canadian Arctic)	Fat	62–100 (lw)	Kelly et al. (2008a)
Beluga whale (F+M)	Hudson Strait (Canadian Arctic)	Blood	10–31 (lw)	Kelly et al. (2008a)
Beluga whale (M)	Hudson Strait (Canadian Arctic)	Liver	310 (lw)	Kelly et al. (2008a)
Beluga whale (calves)	Hudson Strait (Canadian Arctic)	Fat	310 (lw)	Kelly et al. (2008a)
Beluga whale (F+M)	Western Hudson Bay (Canadian Arctic)	Liver	100 (lw)	McKinney et al. (2006b)
Ringed seal (F+M)	East Greenland	Fat	5 (lw)	Letcher et al. (2009)
Ringed seal (M)	Hudson Strait (Canadian Arctic)	Fat	7 (lw)	Kelly et al. (2008a)
Polar bear (F+M)	East Greenland	Fat/Blood	4/<1 (ww)	Gebbink et al., (2008a,b)
Polar bear (F+M)	East Greenland	Fat	1 (ww)	Gebbink et al., (2008a,b)
Polar bear (F)	Svalbard, Norway	Plasma	<1 (ww)	Verreault et al. (2005b)

hemispheric Arctic but largely in the muscle, liver, plasma and/or egg of black-legged kittiwake (*Rissa tridactyla*) from Northern Norway, Canadian high Arctic areas and Barents Sea, northern fulmar (*Fulmarus glacialis*) from the Canadian high Arctic, Alaska (Aleutian Archipelago) and Svalbard (Bear Is.), and glaucous gull from Northern Baffin Bay but mainly from Svalbard (Bear Is.) (Tables 2 and 3). Other recent reports of OHCs in birds include those from Northeastern Hudson Bay (white-winged scoter (*Melanitta deglandi*) and common eider (*Somateria mollissima*)), South (peregrine falcon (*Falco peregrinus*)) and East (black guillemot (*Cepphus grylle*)) Greenland and Svalbard (Arctic tern (*Sterna paradisaea*). Generally, for all Arctic birds, the general order of tissue (or egg) concentrations are ΣPCB > ΣCHL ≈ ΣDDT ≈ ΣToxaphene ≈ ΣCP (chlorinated paraffins) > ΣCBz ≈ ΣHCH ≈ ΣPFSA > ΣPBDE ≈ HBCD > ΣPFCA. Higher levels of ΣPCB of > 1 ppm (lw or ww) have been reported for black-legged kittiwake, great (*Larus marinus*) and lesser (*Larus fuscus*) black-backed and herring (*Larus argentatus*) gulls (Northern Norway), glaucous (Bear Is.) and ivory (Canadian central-high Arctic) gulls, and northern fulmars (Bear Is. and Canadian central-high Arctic). For the last three bird species/populations, levels of ΣCHL and ΣDDT have also been reported to be > 1 ppm (lw or ww). Higher OHC concentrations have also been recently reported in the eggs of ivory gulls from Svalbard, and Frans Josef Land and Severnaya Zemlya in the Russian arctic (Miljeteig et al., 2007). ΣDDT levels > 1 ppm have also been reported for black-legged kittiwakes (Northern Norway). High levels of ΣPBDE (> 1 ppm) were recently reported in the liver of northern fulmars (Bear Is.).

ΣOH-PCB, ΣMeSO$_2$-PCB, 3-MeSO$_2$-*p,p′*-DDE, ΣOH-PBDE, PCP, 4-OH-HpCS and ΣMeO-PBDE concentrations have only been reported in the liver, plasma and/or egg of glaucous gull (Svalbards, Bear Is.) (Table 2). The only exception is the recent report of ΣMeO-PBDE levels in the muscle of white-winged scoter and common eider (Northeastern Hudson Bay) (Table 2). Of these contaminant classes, ΣOH-PCB, ΣMeSO$_2$-PCB and ΣMeO-PBDE levels were in to 2 to 52 ng/g (ww) range, ΣOH-PBDE around 4 ng/g (ww), and the remainder at very low to sub-ppb levels in the liver or plasma of glaucous gull (Bear Is.). ΣOH-PCB and ΣMeSO$_2$-PCB levels were at least 3 orders of magnitude lower than ΣOH-PCBs in the glaucous gull liver (Table 1).

OHC exposure-effects related studies have mainly been on the marine seabird the glaucous gull. There have been limited studies on OHC exposure-related effects in terrestrial birds having a seasonal or annual distribution within the Arctic. Among the effect studies carried out with terrestrial birds in the last 7 years, the species of focus has been the American kestrel (*Falco sparverius*) and peregrine falcon (*Falco peregrinus*). These two species were selected for the purpose of the present review as they also have a northern distribution in Europe and North America.

Marine birds migrating (mainly for breeding) or based permanently in the Arctic and Subarctic regions have received particular research attention with respect to the effects of environmental chemical pollution. Since 2002, an impressive number of studies have been published on a wide range of species spanning Europe and North America and including predatory, fish-eating and bottom-feeding species. However, most of the investigations conducted thus far have been on species from Europe, creating an important contaminant effect knowledge gap for species in North America (de Wit et al., 2004; Fisk et al., 2005).

In a recent study on terrestrial grey sparrows (*Passer dometicus*) from North-Norway (Helgeland) very high levels of the PBDE congener 2,2′,3,3′,4,4′,5,5′-decabromoDE (BDE-209) were reported in liver samples of the birds (Ciesielski et al., 2008). These sparrows nested at farms, and this may indicate that the high levels were associated with living in an environment heavily impacted by human activity. In contrast, very low levels were reported in livers of willow (*Lagopus lagopus*) and rock ptarmigans (*Lagopus mutus*) (Ciesielski et al., 2008).

1.4. Marine and freshwater fish

Levels of POPs, including OHCs, have historically been reported to be generally low in Arctic fish (de Wit et al., 2006; Braune et al., 2005). In a few species/populations with high contaminant levels, PCBs have generally been the dominant contaminant class, whereas levels of *p,p′*-DDT are known to normally be somewhat lower (de Wit et al., 2004; Evenset et al., 2005). Recent reports (roughly in the last 7 years) have reported various OHC classes in the muscle, liver and to a much lesser extent whole body, of mainly Arctic charr (*Salvelinus alpinus*) (Bear Is. and East and Northern Greenland) and polar cod (*Boreogadus saida*) (Barents Sea, Northeastern Hudson Bay and Northeastern Baffin Bay) (Table 4). OHCs have also been reported in the liver of Atlantic cod (*Gadus morhua*) (Barents Sea), a few species of marine flatfish (Barents Sea, West Greenland and Southeastern Baffin Bay), and three species of freshwater fish from Northern Québec (Canada) (Table 4). Finally, OHCs have been reported in the liver and/or muscle of Greenland shark (*Somniosus microcephalus*) (Iceland and Southeastern Baffin Bay). Generally, for all fish reported, the order of tissue concentrations are ΣPCB > ΣCHL ≈ ΣCP > ΣDDT ≈ ΣToxaphene ≈ ΣCBz ≈ ΣHCH ≈ ΣPBDE ≈ ΣPFSA ≈ ΣPFCA > HBCD (Table 4). High levels of ΣPCB of > 1 ppm (lw or ww) have been reported in the muscle and/or liver for two species and populations of long-lived fish, Arctic charr (Bear Is.) and Greenland shark (Iceland and Southeastern Baffin Bay). For the same charr population levels of ΣCP have been reported to be > 1 ppm. For Southeastern Baffin Bay, Greenland shark levels of ΣCHL and ΣDDT have also been reported to be > 1 ppm. There are no known reports of ΣOH-PCB, ΣMeSO$_2$-PCB, 3-MeSO$_2$-*p,p′*-DDE, ΣOH-PBDE, PCP, 4-OH-HpCS and ΣMeO-PBDE concentrations in Arctic fish. The lone exception is for MeSO$_2$-PCBs and -*p,p′*-DDEs, which were not detected (< 0.01 ng/g lw) in whole body homogenates of Arctic cod samples collected in 1993 from the Resolute Bay area (Letcher et al., 1998). The only known exception is one recent study that reported ΣMeO-PBDE levels of about 10 ng/g (lw) in the muscle of polar cod from Northeastern Hudson Bay (Table 2), and was exceedingly low relative to other major OHC classes in polar cod but comparable to ΣPBDE, ΣPFSA, ΣPFCA and HBCD levels (Table 4).

2. Biological effects in relation to OHC levels in Arctic wildlife and fish

As illustrated in Fig. 1 and discussed in Section 1, based on OHC data summarized in Tables 1–4, recent reports on OHCs in Arctic wildlife and fish indicate that there are several “hotspot” species and populations with respect to exposure, which should be considered to be at heightened risk of possible OHC-mediated effects. In general,

Notes to Table 2:

[a] More details on the concentration levels and patterns of metabolites, degradation products or related compounds of organohalogen contaminants in the present wildlife and fish species may be found in contaminant specific reviews in the present issue of STOTEN. Female (F) and/or male (M) adults unless specified otherwise. The mean concentrations are the highest reported for a given species or location within about the last 7 years.

[b] OH-PCB: hydroxylated polychlorinated biphenyl congeners, PCP: pentachlorophenol, 4-OH-HpCS: 4-hydroxy-heptachlorostyrene, MeSO$_2$-PCB: methylsulfone-PCB congeners, 3-MeSO$_2$-*p,p′*-DDE: 3-methylsulfone-dichlorodiphenyldichloroethylene, BCPS: bis(4-chlorophenyl)sulfone, OH-PBDE: hydroxylated polybrominated diphenyl ether congeners, MeO-PBDE: methoxylated-PBDE congeners.

[c] Concentrations reported as means or ranges of means on either a wet weight (ww) or lipid weight (lw) basis.

Table 3
A comprehensive selection of recently reported, highest exposure levels of major classes of persistent halogenated organic contaminants in free-ranging avian wildlife species within the Arctic: geometric or arithmetic means of concentrations (or ranges of means) in major storage tissues (fat, liver or muscle).[a]

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣPCB[b]				
White-winged scoter (*Melanitta deglandi*) (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	2500 (lw)	Kelly et al. (2008a)
Common eider (*Somateria mollissima*) (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	287 (lw)	Kelly et al. (2008a)
Common eider (hatchlings)	Svalbard, Norway	Egg yolk	262 (lw)	Murvoll et al. (2007)
Dovekie (or Little auk) (*Alle alle*) (F + M)	Barents Sea	Liver	130 (ww)	Borgå et al. (2005)
Dovekie (or Little auk) (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	14 (ww)	Borgå et al. (2005)
Black guillemot (*Cepphus grylle*) (F + M)	Barents Sea	Liver	100 (ww)	Borgå et al. (2005); Haukås et al. (2007)
Black guillemot (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	47 (ww)	Borgå et al. (2005)
Black guillemot	East Greenland	Egg	6410 (lw)	Vorkamp et al. (2004)
Common guillemot (or murre) (*Uria aalge*)	Northern Norway	Egg	2300 (lw)	Helgason et al. (2008)
Thick-billed murre (*Uria lomvia*) (F + M)	Barents Sea	Liver	49 (ww)	Borgå et al. (2005)
Thick-billed murre (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	33 (ww)	Borgå et al. (2005)
Thick-billed murre	Canadian central high Arctic	Egg	120 (ww)	Braune (2007)
Thick-billed murre (hatchlings)	Svalbard, Norway	Egg yolk	2429 (lw)	Murvoll et al. (2007)
Black-legged kittiwake (*Rissa tridactyla*) (F + M)	Barents Sea	Liver	492 (ww)	Borgå et al. (2005)
Black-legged kittiwake (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	123 (ww)	Borgå et al. (2005)
Black-legged kittiwake	Canadian central high Arctic	Egg	177 (ww)	Braune (2007)
Black-legged kittiwake (hatchlings)	Svalbard, Norway	Egg yolk	24,536 (lw)	Murvoll et al. (2006a)
Black-legged kittiwake	Northern Norway	Egg	7254–7938 (lw)	Helgason et al. (2008)
Northern fulmar (*Fulmarus glacialis*) (F + M)	Bear Is. (Svalbard), Norway	Liver/Blood	7273/8106 (lw)	Knudsen et al. (2007)
Northern fulmar	Canadian central high Arctic	Egg	163 (ww)	Braune (2007)
Northern fulmar (F + M)	Canadian central high Arctic	Liver	1383–3637 (lw)	Mallory et al. (2006)
Northern fulmar (F + M)	Aleutian Archipelago, Alaska	Liver	622 (ww)	Ricca et al. (2008)
Atlantic puffin (*Fratercula arctica*)	Northern Norway	Egg	2535–4594 (lw)	Helgason et al. (2008)
Tufted puffin (*Fratercula cirrhata*) (F + M)	Aleutian Archipelago, Alaska	Liver	265 (ww)	Ricca et al. (2008)
Glaucous gull (*Larus hyperboreus*) (F + M)	Bear Is. (Svalbard), Norway	Plasma	31646–49894 (lw)	Verreault et al. (2005b,c)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	11,786 (lw)	Verreault et al. (2005c)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Liver	20,114 (ww)	Verreault et al. (2007a)
Glaucous gull (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	1680 (ww)	Borgå et al. (2005); Haukås et al. (2007)
Ivory gull (*Pagophila eburnea*)	Canadian central high Arctic	Egg	4877 (lw)	Braune et al. (2007)
Herring gull (*Larus argentatus*)	Northern Norway	Egg	8786–11,596 (lw)	Helgason et al. (2008)
Great black-backed gull (*Larus marinus*) (F + M)	Northern Norway	Blood	95 (ww)	Helberg et al. (2005)
Lesser black-backed gull (*Larus fuscus*) (F + M)	Northern Norway	Blood	28 (ww)	Bustnes et al. (2008b)
Lesser black-backed gull	Northern Norway	Egg	1342 (ww)	Bustnes et al. (2006b)
Glaucous-winged gull (*Larus glaucescens*) (F + M)	Aleutian Archipelago, Alaska	Liver	1083 (ww)	Ricca et al. (2008)
Peregrine falcon (*Falco peregrinus*)	South Greenland	Egg	55 (lw)	Vorkamp et al. (2009)
ΣCHL[b]				
Dovekie (or Little auk) (F + M)	Barents Sea	Liver	24 (ww)	Borgå et al. (2005)
Dovekie(or Little auk) (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	5 (ww)	Borgå et al. (2005)
Black guillemot (F + M)	Barents Sea	Liver	14 (ww)	Borgå et al. (2005)
Black guillemot (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	12 (ww)	Borgå et al. (2005)
Black guillemot	East Greenland	Egg	960 (lw)	Vorkamp et al. (2004)
Common guillemot (or murre)	Northern Norway	Egg	47–89 (lw)	Helgason et al. (2008)
Thick-billed murre (F + M)	Barents Sea	Liver	5 (ww)	Borgå et al. (2005)
Thick-billed murre (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	4 (ww)	Borgå et al. (2005)
Thick-billed murre	Canadian central high Arctic	Egg	30 (ww)	Braune (2007)
Black-legged kittiwake (F + M)	Barents Sea	Liver	38 (ww)	Borgå et al. (2005)
Black-legged kittiwake (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	15 (ww)	Borgå et al. (2005)
Black-legged kittiwake	Northern Norway	Egg	336–605 (lw)	Helgason et al. (2008)
Black-legged kittiwake	Canadian central high Arctic	Egg	45 (ww)	Braune (2007)
Northern fulmar	Canadian central high Arctic	Egg	112 (ww)	Braune (2007)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver/Blood	3363/1556 (lw)	Knudsen et al. (2007)
Northern fulmar (F + M)	Aleutian Archipelago, Alaska	Liver	93 (ww)	Ricca et al. (2008)
Atlantic puffin	Northern Norway	Egg	383–870 (lw)	Helgason et al. (2008)
Tufted puffin (F + M)	Aleutian Archipelago, Alaska	Liver	17 (ww)	Ricca et al. (2008)
Glaucous gull (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	82 (ww)	Borgå et al. (2005)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Plasma	2086–2721 (lw)	Verreault et al. (2005c)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Liver	1399 (ww)	Verreault et al. (2007a)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	969 (lw)	Verreault et al. (2005c)
Ivory gull	Canadian central high Arctic	Egg	3240 (lw)	Braune et al. (2007)
Herring gull	Northern Norway	Egg	744–1125 (lw)	Helgason et al. (2008)
Lesser black-backed gull (F + M)	Northern Norway	Blood	8 (ww)	Bustnes et al. (2008b)
Lesser black-backed gull	Northern Norway	Egg	30 (ww)	Bustnes et al. (2006b)
Glaucous-winged gull (F + M)	Aleutian Archipelago, Alaska	Liver	68 (ww)	Ricca et al. (2008)
ΣDDT[b]				
White-winged scoter (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	565 (lw)	Kelly et al. (2008a)
Common eider (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	179 (lw)	Kelly et al. (2008a)
Dovekie (or Little auk) (F + M)	Barents Sea	Liver	32 (ww)	Borgå et al. (2005)
Dovekie (or Little auk) (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	9 (ww)	Borgå et al. (2005)
Black guillemot (F + M)	Barents Sea	Liver	32 (ww)	Borgå et al. (2005); Haukås et al. (2007)
Black guillemot (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	52 (ww)	Borgå et al. (2005)
Black guillemot	East Greenland	Egg	1340 (lw)	Vorkamp et al. (2004)

Table 3 (*continued*)

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣDDT[b]				
Common guillemot (or murre)	Northern Norway	Egg	962–1117 (lw)	Helgason et al. (2008)
Thick-billed murre (F + M)	Barents Sea	Liver	25 (ww)	Borgå et al. (2005)
Thick-billed murre (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	32 (ww)	Borgå et al. (2005)
Thick-billed murre	Canadian central high Arctic	Egg	103 (ww)	Braune (2007)
Black-legged kittiwake (F + M)	Barents Sea	Liver	98 (ww)	Borgå et al. (2005)
Black-legged kittiwake (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	56 (ww)	Borgå et al. (2005)
Black-legged kittiwake	Northern Norway	Egg	806–1562 (lw)	Helgason et al. (2008)
Black-legged kittiwake	Canadian central high Arctic	Egg	43 (ww)	Braune (2007)
Northern fulmar	Canadian central high Arctic	Egg	124 (ww)	Braune (2007)
Northern fulmar (F + M)r	Bear Is. (Svalbard), Norway)	Liver	1289 (lw)	Knudsen et al. (2007)
Northern fulmar (F + M)	Aleutian Archipelago, Alaska	Liver	15 (ww)	Ricca et al. (2008)
Atlantic puffin	Northern Norway	Egg	1104–1569 (lw)	Helgason et al. (2008)
Tufted puffin (F + M)	Aleutian Archipelago, Alaska	Liver	4 (ww)	Ricca et al. (2008)
Glaucous gull (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	2380 (ww)	Borgå et al. (2005); Haukås et al. (2007)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Plasma	10,245–15076 (lw)	Verreault et al. (2005c)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	3559 (lw)	Verreault et al. (2005c)
Ivory gull	Canadian central high Arctic	Egg	10,744 (lw)	Braune et al. (2007)
Herring gull	Northern Norway	Egg	2241–4184 (lw)	Helgason et al. (2008)
Great black-backed gull (F + M)	Northern Norway	Blood	30 (ww)	Helberg et al. (2005)
Lesser black-backed gull (F + M)	Northern Norway	Blood	16 (ww)	Bustnes et al. (2008b)
Lesser black-backed gull	Northern Norway	Egg	652 (ww)	Bustnes et al. (2006b)
Glaucous-winged gull (F + M)	Aleutian Archipelago, Alaska	Liver	15 (ww)	Ricca et al. (2008)
Peregrine falcon	South Greenland	Egg	40 (lw)	Vorkamp et al. (2009)
ΣCBz[b]				
White-winged scoter (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	71 (lw)	Kelly et al. (2008a)
Common eider (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	48 (lw)	Kelly et al. (2008a)
Black guillemot	East Greenland	Egg	400 (lw)	Vorkamp et al. (2004)
Ivory gull	Canadian central high Arctic	Egg	586 (lw)	Braune et al. (2007)
Black-legged kittiwake	Canadian central high Arctic	Egg	18 (ww)	Braune (2007)
Thick-billed murre	Canadian central high Arctic	Egg	32 (ww)	Braune (2007)
Northern fulmar	Canadian central high Arctic	Egg	14 (ww)	Braune (2007)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver/Blood	602/583 (lw)	Knudsen et al. (2007)
Northern fulmar (F + M)	Aleutian Archipelago, Alaska	Liver	82 (ww)	Ricca et al. (2008)
Tufted puffin (F + M)	Aleutian Archipelago, Alaska	Liver	48 (ww)	Ricca et al. (2008)
Glaucous-winged gull (F + M)	Aleutian Archipelago, Alaska	Liver	116 (ww)	Ricca et al. (2008)
Peregrine falcon	South Greenland	Egg	<1 (lw)	Vorkamp et al. (2009)
ΣHCH[b]				
White-winged scoter (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	9 (lw)	Kelly et al. (2008a)
Common eider (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	15 (lw)	Kelly et al. (2008a)
Herring gull	Northern Norway	Egg	15–32 (lw)	Helgason et al. (2008)
Black-legged kittiwake	Northern Norway	Egg	20–34 (lw)	Helgason et al. (2008)
Black-legged kittiwake	Canadian central high Arctic	Egg	8 (ww)	Braune (2007)
Thick-billed murre	Canadian central high Arctic	Egg	11 (ww)	Braune (2007)
Black guillemot	East Greenland	Egg	170 (lw)	Vorkamp et al. (2004)
Common guillemot (or murre)	Northern Norway	Egg	14 (lw)	Helgason et al. (2008)
Northern fulmar	Canadian central high Arctic	Egg	6 (ww)	Braune (2007)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver	16 (lw)	Knudsen et al. (2007)
Northern fulmar (F + M)	Aleutian Archipelago, Alaska	Liver	48 (ww)	Ricca et al. (2008)
Atlantic puffin	Northern Norway	Eggs	15–29 (lw)	Helgason et al. (2008)
Tufted puffin (F + M)	Aleutian Archipelago, Alaska	Liver	24 (ww)	Ricca et al. (2008)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Plasma	74–109 (lw)	Verreault et al. (2005c)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	48 (lw)	Verreault et al. (2005c)
Ivory gull	Canadian central high Arctic	Egg	175 (lw)	Braune et al. (2007)
Glaucous-winged gull (F + M)	Aleutian Archipelago, Alaska	Liver	80 (ww)	Ricca et al. (2008)
Peregrine falcon	South Greenland	Egg	<1 (lw)	Vorkamp et al. (2009)
ΣToxaphene				
White-winged scoter (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	119 (lw)	Kelly et al. (2008a)
Common eider (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	192 (lw)	Kelly et al. (2008a)
Black guillemot	East Greenland	Egg	1350 (lw)	Vorkamp et al. (2004)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver	406 (lw)	Knudsen et al. (2007)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway)	Plasma	1800–2400 (lw)	Verreault et al. (2005c)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	1829 (lw)	Verreault et al. (2005c)
ΣCP[b]				
Dovekie (or Little auk) (M)	Bear Is. (Svalbard), Norway	Liver/Muscle	2600/1100 (lw)	Reth et al. (2006)
Black-legged kittiwake (F + M)	Bear Is. (Svalbard), Norway	Liver/Muscle	970/500 (lw)	Reth et al. (2006)
ΣPBDE[b]				
Arctic tern (*Sterna paradisaea*)	Svalbard, Norway	Egg	41 (lw)	Jenssen et al. (2007)
White-winged scoter (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	71 (lw)	Kelly et al. (2008a)
Common eider (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	20 (lw)	Kelly et al. (2008a)
Common eider (hatchlings)	Svalbard, Norway	Egg yolk	2 (lw)	Murvoll et al. (2007)

(*continued on next page*)

Table 3 (*continued*)

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣPBDE[b]				
Black guillemot (F + M)	Barents Sea	Liver	3 (ww)	Haukås et al. (2007)
Black guillemot	East Greenland	Egg	83 (lw)	Vorkamp et al. (2004)
Thick-billed murre (hatchlings)	Svalbard, Norway	Egg yolk	90 (lw)	Murvoll et al. (2007)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver	5255 (lw)	Knudsen et al. (2007)
Glaucous gull (F + M)	Northern Baffin Bay (Canadian Arctic)	Liver	59 (ww)	Haukås et al. (2007)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Liver/Blood	522/52 (ww)	Verreault et al. (2005b, 2007a)
Black-legged kittiwake (hatchlings)	Svalbard, Norway	Egg yolk	461 (lw)	Murvoll et al. (2006a)
Ivory gull	Canadian central high Arctic	Egg	44 (lw)	Braune et al. (2007)
Lesser black-backed gulls (F + M)	Northern Norway	Blood	2 (ww)	Bustnes et al. (2008b)
HBCD[b]				
Arctic tern	Svalbard, Norway	Egg	5 (lw)	Jenssen et al. (2007)
Common eider (hatchlings)	Svalbard, Norway	Egg yolk	6 (lw)	Murvoll et al. (2007)
Thick-billed murre (hatchlings)	Svalbard, Norway	Egg yolk	35 (ww)	Murvoll et al. (2007)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver	15 (lw)	Knudsen et al. (2007)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Liver/Blood	76/3 (ww)	Verreault et al. (2005b, 2007a)
Black-legged kittiwake (hatchklings)	Svalbard, Norway	Egg yolk	118 (lw)	Murvoll et al. (2006a)
Ivory gull	Canadian central high Arctic	Egg	2 (lw)	Braune et al. (2007)
ΣPFSA[b]				
Black guillemot (F + M)	Barents Sea	Liver	14 (ww)	Haukås et al. (2007)
Black-legged kittiwake (F + M)	SE Baffin Is. (Canadian Arctic)	Liver	10 (ww)	Tomy et al. (2004)
Northern fulmar (F + M)	Bear Is. (Svalbard), Norway	Liver	5 (ww)	Knudsen et al. (2007)
Northern fulmar (F + M)	Canadian central high Arctic	Liver	1 (ww)	Martin et al. (2004)
Common loon (F + M)	Northern Québec (Canadian Arctic)	Liver	20 (ww)	Martin et al. (2004)
Glaucous gull (F + M)	Barents Sea	Liver	66 (ww)	Haukås et al. (2007)
Glaucous gull (F + M)	SE Baffin Is. (Canadian Arctic)	Liver	20 (ww)	Tomy et al. (2004)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Plasma	134 (ww)	Verreault et al. (2005d)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Liver	105 (ww)	Verreault et al. (2005d)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	104 (ww)	Verreault et al. (2005d)
Herring gull	Northern Norway	Egg	42 (ww)	Verreault et al. (2007b)
Lesser black-backed gull (F + M)	Northern Norway	Blood	35 (ww)	Bustnes et al. (2008b)
ΣPFCA[b]				
Black guillemot (F + M)	Barents Sea	Liver	1 (ww)	Haukås et al. (2007)
Common loon (F + M)	Northern Québec (Canadian Arctic)	Liver	2 (ww)	Martin et al. (2004)
Glaucous gull (F + M)	Barents Sea	Liver	2 (ww)	Haukås et al. (2007)
Glaucous gull (F + M)	Bear Is. (Svalbard), Norway	Plasma	102 (ww)	Verreault et al. (2005d)
Glaucous gull	Bear Is. (Svalbard), Norway	Egg	42 (ww)	Verreault et al. (2005d)
Herring gulls	Northern Norway	Egg	7 (ww)	Verreault et al. (2007b)
Lesser black-backed gull (F + M)	Northern Norway	Blood	8 (ww)	Bustnes et al. (2008b)

[a] More details on the concentration levels and patterns of individual organohalogen contaminants in the present wildlife and fish species can be found in contaminant specific reviews in the present issue of STOTEN. Female (F) and/or male (M) adults unless specified otherwise. The mean concentrations are the highest reported for a given species or location within generally the last 10 years.

[b] PCB: polychlorinated biphenyl congeners, CBz: polychlorinated benzenes, CHL: Chlordane compounds, DDT: dichlorodiphenyldichloroethylene (*p,p′*-DDE) and dichlorodiphenyldichloroethane (*p,p′*-DDT), HCH: hexachlorocyclohexane isomers, CP: polychlorinated paraffin congeners, PBDE: polybrominated diphenyl ether congeners (mainly BDE47, 99 and 100), HBCD: hexabromocyclododecanes isomers (essentially all α-HBCD), PFSA: perfluorinated sulfonates (mainly perfluorooctane sulfonate (PFOS) and in some cases perfluorohexane sulfonate (PFHxS)), PFCA: perfluorinated carboxylates (mainly C_8 to C_{13} perfluorohydrocarbon chain lengths).

[c] Concentrations reported as means or ranges of means on either a wet weight (ww) or lipid weight (lw) basis.

concentrations of OHCs and/or PCB and *p,p′*-DDE metabolites have been shown to be especially high for polar bears from Western and Southern Hudson Bay, East Greenland and/or Svalbard. For both cetaceans and pinnipeds and among measured OHCs, ΣPCB, ΣCHL and ΣDDT exposure levels continue to be the most substantial, and OHC exposure levels are generally highest for Alaskan and Northern Norway killer whales, Svalbard beluga whales, East Greenland ringed seals and Bering Sea Stellar sea lions. For (marine) birds, among measured OHCs exposure levels, ΣPCBs, ΣCHLs and ΣDDTs continue to generally be the most substantial, and especially for black-legged kittiwake great and lesser black-backed gulls and herring gulls (Northern Norway), glaucous (Bear Is.) and ivory (Canadian central-high Arctic) gulls. High OHC concentrations have also been recently reported in the eggs of ivory gulls from Frans Josef Land and Severnaya Zemlya) gulls, and northern fulmars (Bear Is. and Canadian central-high Arctic). For fish, Arctic charr (Bear Is.) and Greenland shark (Iceland and Southeastern Baffin Bay) are of highest OHC exposure concern.

Since the last Arctic wildlife effects review that focused on Canadian (North American) species (Fisk et al., 2005), there has been a substantial amount of new information on OHC exposure in relation to e.g., endocrine and immune function in free-ranging Arctic wildlife species and populations, specifically Svalbard glaucous gulls and Svalbard and East Greenland polar bears. With respect to endocrine disrupting compounds (EDCs), over the last decade legacy and more recently emerging (brominated and fluorinated) OHCs have demonstrated endocrine disruptive potential in *in vitro* and *in vivo* studies on non-Arctic wildlife and fish. Although the major concern about EDCs are related to exposure and effects in humans, the effects of EDCs on wildlife and ecosystem functions are potentially very large. A good example of an EDC, and one of the classic OHCs, the synthetic pesticide DDT, and in particular *o,p′*-DDT, and the DDT metabolites of *o,p′*-DDE and *p,p′*-DDE have estrogenic effects (Wojtowicz et al., 2007), either by acting as estrogenic receptor agonists (Di Lorenzo et al., 2002) or as androgen receptor agonists (Kelce et al., 1995). Furthermore, there are numerous reports that other insecticides such as β-HCH, *cis*- and *trans*-chlordane, dieldrin, endosulfan, mirex, oxychlordane, toxaphenes and *trans*-nonachlor have reproductive and endocrine effects (Colborn et al., 1993). Several classic industrial chemicals detected in Arctic fish and wildlife, such as polychlorinated dibenzo-*p*-dioxins (PCDDs) and PCBs, have also been reported to have endocrine disruptive properties (Colborn et al., 1993). More recently

it has also been demonstrated that several novel industrial chemicals including several BFRs such as PBDEs and tetrabromobisphenol A (TBBPA) (Hamers et al., 2006, 2008; van der Ven et al., 2006, 2008; Harju et al., 2007; Kuiper et al., 2007; Morgado et al., 2007) and PFCs (Oakes et al., 2005; Liu et al., 2007; Chang et al., 2008; Jensen and Leffers, 2008) have effects on multiple endocrine systems.

For Arctic mammals, several studies have documented associations between OHCs and hormone levels, e.g., plasma hormone levels in Svalbard polar bears and in captive studies on domesticated Arctic fox. In Svalbard bears associations have been shown for thyroid hormones (Skaare et al., 2001; Braathen et al., 2004), cortisol (Oskam et al., 2004a), testosterone (Oskam et al., 2003), and progesterone (Haave et al., 2003). For seabirds, and specifically the top predator, glaucous gull, from Svalbard, there has been several reports showing associations between exposure to OHCs and/or POPs to altered levels of e.g., sex steroid hormones (Verboven et al., 2008a; Verreault et al., 2006, 2008b), thyroid hormones (Verreault et al., 2004, 2007c) and prolactin (Verreault et al., 2008b). In Svalbard Arctic charr and polar bears alterations in cortisol levels have also been associated with POP exposure (Jørgensen et al., 2002a,b; Oskam et al., 2004a). The following sub-sections highlight relatively new reports of OHC exposure and levels and associations with changes in various biomarkers in Arctic wildlife and fish. Regardless, in all but a few cases these are correlative relationships between tissue or blood OHC concentrations and biomarker responses, and thus only suggestive of cause–effect linkages.

2.1. Ursids and canids

OHC-related effects are of most concern in polar bears from "hotspots" of high OHC exposure including Hudson Bay, East Greenland and Svalbard relative to other circumpolar regions such as (Tables 1 and 2, Fig. 1). For example, it has been speculated that polar bears from Svalbard may suffer from OHC/POP exposure-related population effects that could have resulted from reproductive impairment of females, lower survival rates of cubs, or increased mortality of reproductive females (Derocher et al., 2003). The possible reproductive impairment of polar bears at Svalbard is based on the scarcity of females that are 16 years or older and have cubs. However, as will be described, much of the studies reported for East Greenland and Svalbard bears assess correlations between OHC tissue or body compartment residue levels and biomarker-specific measurement among individuals. However, this "weight of evidence" from multiple associative effect-OHC level indicators is compelling and provides strong suggestions of effects.

OHCs have been reported to be relatively high in some populations of Arctic canids (Fuglei et al., 2007; Hoekstra et al., 2003c), and in particular in Arctic foxes at Svalbard which have a marine feeding regime and a diet consisting of mainly seabirds, seabird eggs and carcasses of marine mammals (Fuglei et al., 2007). In free-living Arctic foxes from Svalbard, it was shown that body condition showed a significant inverse relationship with PBDEs, CHLs and HCB levels. The authors suggested that the increased tissue contaminant concentrations were due to depletion of adipose tissue as a consequence of their natural emaciation cycle during the spring and summer (Fuglei et al., 2007). Thus, the relationship between reduced body condition and high adipose tissue levels of POPs is not believed to be caused by the POPs. It should also be noted that foxes that were feeding at high trophic levels had higher tissue contaminant levels (Sonne et al., 2008f). Regardless, more direct evidence is needed that establishes cause–effect relationships with recognized mechanisms, which has been provided to some degree by effects studies using semi-captive sled dogs and Arctic foxes.

2.1.1. Vitamins

Potential effects mechanisms for OHCs and POPs may be on vitamin homeostasis. Vitamin A and E are important anti-oxidants, and are also important for the normal development and health of animals. Vitamin D is an important factor in bone formation and metabolism and eggshell formation. OHCs may also affect the homeostasis of several vitamins, including vitamin A, E and D (Spear and Moon, 1986; Brouwer et al., 1989; Kato et al., 1989; Käkelä et al., 1999; Lilienthal et al., 2000).

A study on Greenland sledge dog cohorts fed a porcine (*Suis scrofa*) fat control diet or exposed to a natural cocktail of OHCs via a minke whale (*Balaenoptera acutorostrata*) blubber diet (up to 21 months) showed that 25-hydroxyvitamin D3 (25OHD), a liver metabolite of vitamin D3, was significantly lower in exposed individuals of the maternal generation, although they had received quantitatively higher amounts of vitamin D3 in the diet than controls (Kirkegaard et al., 2010a). Vitamin D3 and 25OHD in plasma of all whale blubber exposed groups, and also 25OHD in liver of exposed offspring dogs was significantly higher than pork fat fed controls. The study concluded that a natural dietary cocktail of OHCs (and possibly other POPs) from marine mammals in amounts of 50–200 g/day may reduce liver levels of vitamin 25OHD in the sled dogs. For the same sled dog cohort study, Kirkegaard et al. (2010b) also reported that retinol (vitamin A) and α-tocopherol (vitamin E) concentrations were measured to be 66–266 fold and 5 fold higher, respectively, in the whale blubber fed to the exposed dogs compared to the lard fed to the control dogs. Samples taken at the end of the study with exposure varying between 12 to 19 months, showed negative correlations between hepatic retinol and ΣDDT concentrations, and between hepatic vitamin A and ΣPBDE when including all exposed animals. A negative correlation between kidney vitamin E and ΣPCB (measured in adipose tissue) was observed, while positive significant correlations between kidney retinol and ΣCHL and dieldrin were shown as well. Hepatic vitamin E concentrations were significantly lower in the exposed group compared to controls, most likely due to a combination of OHC exposure and high dietary intake of unsaturated fatty acids.

In an exposure study on farmed arctic foxes, where pups were exposed to a diet containing naturally POP contaminated minke whale blubber from weaning (2 months of age), it was reported that at an age of 22 months the exposed animals had lower plasma and vitamin E levels than control animals that were exposed to a diet containing clean pig fat (Rogstad, 2007).

2.1.2. Endocrine system

2.1.2.1. Thyroid hormones. As summarized in Table 5, with respect to effects of OHCs on thyroid hormones (THs), a study on polar bears from the Svalbard area suggested that females appear to be more susceptible than males (Braathen et al., 2004). However, in the Braathen et al. (2004) study it is worth noting that condition, which may strongly influence the TH levels, was not included as a variable in the statistical analysis. In females with cubs-of-the year, negative relationships were found between ΣPCB and free thyroxine (FT_4), free 3,3′,5-triiodo-L-thyronine (FT_3) and the ratios of total thyroxine (TT_4) and total triodothyronine (TT_3) (TT_4:TT_3). In females with older cubs and/or without cubs, ΣPCB was negatively related to TT_4 and positively related to TT_3:FT_3. In males, ΣPCB was negatively related to FT_3 and positively related to FT_4:FT_3. It was also noted that PCB-118 showed opposite relationships between some of the TH variables. Thus, PCB levels have been shown to be correlated with five TH variables in the female Svalbard polar bears (TT_4, FT_4, FT_3, TT_3:FT_3, and TT_4:TT_3), but only two TH variables in males (FT_3 and FT_4:FT_3). T_3 is an active TH form with respect to tissue-/cell-specific, TH-mediated gene expression and activity e.g., metabolism and thermo-regulation. Since FT_3 is an active TH form, the effect on this hormone, and its balance with TT_3 and FT_4 is of particular concern, and also strongly suggests that PCBs may cause physiological related effects in this bear population. This suggests that the effects of OHCs on TH homeostasis

Table 4
A comprehensive selection of recently reported, highest exposure levels of major classes of persistent halogenated organic contaminants in free-ranging fish species within the Arctic: geometric or arithmetic means of concentrations (or ranges of means) in major storage tissues (fat, liver or muscle).[a]

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣPCB[b]				
Arctic charr (*Salvelinus alpinus*) (F + M)	Bear Is. (Svalbard), Norway	Muscle	2700 (ww)	Skotvold et al. (1998)
Arctic charr (F + M)	East Greenland	Muscle	530–870 (lw)	Vorkamp et al. (2004)
Arctic charr (F + M)	North Greenland	Muscle	9 (ww)	Cleemann et al. (2002)
Atlantic cod (*Gadus morhua*) (F + M)	Barents Sea (several locations)	Liver	165–392 (ww)	Stange and Klungsøyr (1997)
Polar cod (*Boreogadus saida*) (F + M)	Barents Sea (several locations)	Liver/Whole body	47–91/3 (ww)	Stange and Klungsøyr (1997); Borgå et al. (2005); Haukås et al. (2007)
Polar cod (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	60 (lw)	Kelly et al. (2008a)
Polar cod (F + M)	Northern Baffin Bay, Canadian Arctic	Whole body	2 (ww)	Borgå et al. (2005)
Long rough dab (*Hippoglossoides platessoides*) (F + M)	Barents Sea (several locations)	Liver	16–57 (ww)	Stange and Klungsøyr (1997)
Greenland halibut (or Greenland turbot) (*Reinhardtius hippoglossoides*) (F + M)	West Greenland	Liver	112 (ww)	Berg et al. (1997)
Greenland halibut (or Greenland turbot) (F + M)	Southeast Baffin Is. (Canadian Arctic)	Muscle	58 (lw)	Fisk et al. (2002)
Greenland shark (*Somniosus microcephalus*) (F + M)	Southeast Baffin Is. (Canadian Arctic)	Liver	3442 (lw)	Fisk et al. (2002)
Greenland shark (F)	Iceland	Liver/Muscle	4400/4100 (lw)	Strid et al. (2007)
ΣCHL[b]				
Arctic charr (F + M)	East Greenland	Muscle	330–430 (lw)	Vorkamp et al. (2004)
Polar cod (F + M)	Barents Sea	Whole body	4 (ww)	Borgå et al. (2005)
Polar cod (F + M)	Northern Baffin Bay (Canadian Arctic)	Whole body	3 (ww)	Borgå et al. (2005)
Polar cod (F + M)	Barents Sea (several locations)	Liver	25–46 (ww)	Stange and Klungsøyr (1997)
Atlantic cod (F + M)	Barents Sea (several locations)	Liver	75–140 (ww)	Stange and Klungsøyr (1997)
Long rough dab (F + M)	Barents Sea (several locations)	Liver	7–18 (ww)	Stange and Klungsøyr (1997)
Greenland halibut (or Greenland turbot) (F + M)	Southeast Baffin Is. (Canadian Arctic)	Muscle	162 (lw)	Fisk et al. (2002)
Greenland shark (F + M)	Southeast Baffin Is. (Canadian Arctic)	Liver	1815 (lw)	Fisk et al. (2002)
ΣDDT[b]				
Arctic charr (F + M)	East Greenland	Muscle	310–500 (lw)	Vorkamp et al. (2004)
Polar cod (F + M)	Barents Sea	Liver/Whole body	21/3 (ww)	Borgå et al. (2005); Haukås et al. (2007)
Polar cod (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	50 (lw)	Kelly et al. (2008a)
Polar cod (F + M)	Northern Baffin Bay (Canadian Arctic)	Whole body	3 (ww)	Borgå et al. (2005)
Polar cod (F + M)	Barents Sea (several locations)	Liver	11–45 (ww)	Stange and Klungsøyr (1997)
Atlantic cod (F + M)	Barents Sea (several locations)	Liver	98–175 (ww)	Stange and Klungsøyr (1997)
Long rough dab (F + M)	Barents Sea (several locations)	Liver	7–30 (ww)	Stange and Klungsøyr (1997)
Greenland halibut (or Greenland turbot) (F + M)	Southeast Baffin Is. (Canadian Arctic)	Muscle	78 (lw)	Fisk et al. (2002)
Greenland shark (F + M)	Southeast Baffin Is. (Canadian Arctic)	Liver	7195 (lw)	Fisk et al. (2002)
ΣCBz[b]				
Arctic charr (F + M)	East Greenland	Muscle	45–53 (lw)	Vorkamp et al. (2004)
Polar cod (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	27 (lw)	Kelly et al. (2008a)
Greenland halibut (or Greenland turbot) (F + M)	Southeast Baffin Is. (Canadian Arctic)	Muscle	55 (lw)	Fisk et al. (2002)
Greenland shark (F + M)	Southeast Baffin Is. (Canadian Arctic)	Liver	52 (lw)	Fisk et al. (2002)
ΣHCH[b]				
Arctic charr (F + M)	East Greenland	Muscle	21–26 (lw)	Vorkamp et al. (2004)
Polar cod (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	10 (lw)	Kelly et al. (2008a)
Greenland halibut (or Greenland turbot) (F + M)	Southeast Baffin Is. (Canadian Arctic)	Muscle	81 (lw)	Fisk et al. (2002)
Greenland shark (F + M)	Southeast Baffin Is. (Canadian Arctic)	Liver	53 (lw)	Fisk et al. (2002)
ΣToxaphene				
Arctic charr (F + M)	East Greenland	Muscle	220–240 (lw)	Vorkamp et al. (2004)
Polar cod (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	33 (lw)	Kelly et al. (2008a)
ΣCP[b]				
Arctic charr (F)	Bear Is. (Svalbard), Norway	Liver/Muscle	400/1440 (lw)	Reth et al. (2006)
Atlantic cod (F)	Iceland/Northern Norway	Liver	150 (lw)	Reth et al. (2006)
ΣPBDE[b]				
Arctic charr (F + M)	East Greenland	Muscle	26–46 (lw)	Vorkamp et al. (2004)
Polar cod (F + M)	SE Baffin Is. + E. Hudson Bay, Canada	Whole body	23 (lw)	Tomy et al. (2008)
Polar cod (F + M)	Svalbard, Norway + Barents Sea	Liver/Whole body	2 (ww)/3 (lw)	Sørmo et al. (2006); Wolkers et al. (2004); Haukås et al. (2007)
Polar cod (F + M)	Northeastern Hudson Bay (Canadian Arctic)	Muscle	10 (lw)	Kelly et al. (2008a)
HBCD[b]				
Polar cod (F + M)	Svalbard, Norway	Whole body	1.9 (lw)	Wolkers et al. (2004); Sørmo et al. (2006)
Polar cod (F + M)	SE Baffin Is. + E. Hudson Bay, Canada	Whole body	2 (lw)	Tomy et al. (2008)

Table 4 (*continued*)

Species	Arctic location	Tissue	Concentration (ng/g)[c]	Reference
ΣPFSA[b]				
Polar cod (F + M)	Beaufort Sea, NWT, Canada	Whole body	1 (ww)	Powley et al. (2008)
Polar cod (F + M)	Barents Sea (F + M)	Liver	2 (ww)	Haukås et al. (2007)
Polar cod (F + M)	SE Baffin Is. (Canadian Arctic)	Liver	2 (ww)	Tomy et al. (2004)
White sucker (*Catostomus commersonii*) (F + M)	Northern Québec (Canadian Arctic)	Liver	8 (ww)	Martin et al. (2004)
Brook trout (*Salvelinus fontinalis*) (F + M)	Northern Québec (Canadian Arctic)	Liver	39 (ww)	Martin et al. (2004)
Lake whitefish (*Coregonus clupeaformis*) (F + M)	Northern Québec (Canadian Arctic)	Liver	12 (ww)	Martin et al. (2004)
ΣPFCA[b]				
Polar cod (F + M)	Beaufort Sea, NWT, Canada	Whole body	1 (ww)	Powley et al. (2008)
Polar cod (F + M)	Barents Sea	Liver	7 (ww)	Haukås et al. (2007)
White sucker (F + M)	Northern Québec (Canadian Arctic)	Liver	15 (ww)	Martin et al. (2004)
Brook trout (F + M)	Northern Québec (Canadian Arctic)	Liver	18 (ww)	Martin et al. (2004)
Lake whitefish (F + M)	Northern. Québec (Canadian Arctic)	Liver	17 (ww)	Martin et al. (2004)

[a] More details on the concentration levels and patterns of individual organohalogen contaminants in the present wildlife and fish species can be found in contaminant specific reviews in the present issue of STOTEN. Female (F) and/or male (M) adults unless specified otherwise. The mean concentrations are the highest reported for a given species or location within generally the last 10 years.

[b] PCB: polychlorinated biphenyl congeners, CBz: polychlorinated benzenes, CHL: Chlordane compounds, DDT: dichlorodiphenyldichloroethylene (*p,p′*-DDE) and dichlorodiphenyldichloroethane (*p,p′*-DDT), HCH: hexachlorocyclohexane isomers, CP: polychlorinated paraffin congeners, PBDE: polybrominated diphenyl ether congeners (mainly BDE47, 99 and 100), HBCD: hexabromocyclododecanes isomers (essentially all α-HBCD), PFSA: perfluorinated sulfonates (mainly perfluorooctane sulfonate (PFOS) and in some cases perfluorohexane sulfonate (PFHxS)), PFCA: perfluorinated carboxylates (mainly C_8 to C_{13} perfluorohydrocarbon chain lengths).

[c] Concentrations reported as means or ranges of means on either a wet weight (ww) or lipid weight (lw) basis.

could be related to a number of factors. Thyroid system EDCs, e.g., those structurally and chemically resembling T_4 and T_3, may target multiple TH control pathways related to the hypothalamic–pituitary–thyroid axis and in a chemical-dependent manner (Boas et al., 2006). Mechanisms of interference could include TH production and metabolism (e.g., TH degradation and interconversion), thyroid receptor binding, cellular uptake and interaction with thyroid hormone binding proteins such as TH binding albumin and transthyretin (TTR) (Ucán-Marín et al., 2010).

In a study on polar bears from the highly OHC exposed East Greenland population, no histological abnormalities were detected in thyroid glands (Kirkegaard et al., 2005). This suggested that the possible effect of OHCs on the TH balance of polar bears was not related to damage of the thyroid gland. Sonne et al. (2009a) very recently reported on the impact from dietary OHC exposure on thyroid gland pathology in farmed male Arctic foxes (*V. lagopus*). The exposed group was fed a diet based on wild minke whale blubber as main fat source in order to mimic the exposure to OHC cocktails in the Artic environment. Among the findings, the study shows that the OHC mixture in minke whale blubber may effect the development of thyroid gland cysts, C-cell hyperplasia and increases in the prevalence of cystic remnants of embryonic ducts. The authors speculated that the mechanism causing these effects could include endocrine disruption of the HPT (hypothalamus–pituitary–thyroid)-axis, a disturbance of the calcium homeostasis/metabolism or energy metabolism or immune suppression.

A study on Greenland sledge dog cohorts fed a porcine fat control diet or exposed to a natural cocktail of OHCs via a minke whale blubber diet (up to 21 months) showed that the exposed dogs had circulating blood concentrations levels of OHCs that were associated with changes in TH levels (Kirkegaard et al., 2010c). Significantly lower FT_3, TT_3, FT_4 and TT_4 in exposed as compared to control bitches across 10–18 months of age, and FT_4 across all observations (6–18 months) was observed. A significantly higher TT_4:FT_4 ratio in exposed as compared to controls, lower thyroid gland weight with increasing ΣDDT and an increase in TT_3 with increasing dieldrin were observed. The data suggested that OHC exposure time of at least 10–18 months may be crucial in low-dose OHC exposure studies, and there may be chronic effects on TH dynamics.

The results of a contaminant exposure study using domesticated (farmed) Arctic foxes was recently completed (Hallanger, 2006; Rogstad, 2007). Reports so far have shown that there were no differences in plasma TH levels in juvenile (6 months old) foxes that had been exposed to the POP contaminated diet containing naturally POP contaminated minke whale blubber, and the control animals given a diet containing clean pig fat (Hallanger, 2006). However, the results showed that in exposed 22 months old foxes the ratio between FT_4 and FT_3 (FT_4:FT_3) was lower in the exposed foxes (Rogstad, 2007).

2.1.2.2. Cortisol. Concerning cortisol, a study on 121 male and 130 female polar bears from the Svalbard area showed that concentrations of OC pesticides combined with PCBs and their interactions could account for over 25% of the variation in the cortisol concentration (Oskam et al., 2004a) (Table 5). Even though the relationships showed that the OC levels related negatively and the PCBs contributed positively to the variation in plasma cortisol, the overall relationship was negative between levels of chlorinated OHCs and plasma cortisol. The authors concluded that despite the complexity of stress responses and the interactions with environmental factors, the study demonstrated that high concentrations of these OHCs in polar bears might alter plasma cortisol concentrations. Since glucocorticoids are necessary for the normal fetal development, it was suggested that disturbances of the regulation of this endocrine system during critical stages in fetal life may induce abnormal neurobehavioural function in adult life (Oskam et al., 2004a; Ropstad et al., 2006).

2.1.2.3. Reproductive hormones. With respect to reproductive hormone effects, correlations between OHCs and sex hormones have been reported in both female and male polar bears. A study on 121 male polar bears from the Svalbard area showed that the combination of OCs and PCBs accounted for 57% of the variation in the plasma testosterone concentration (Oskam et al., 2003). The testosterone concentrations were negatively correlated with both OC and PCB concentrations in the male polar bears. More recently, a study on polar bears from East Greenland confirmed the relationship between chlorinated OHCs and testosterone (Smette, 2007). In this study testosterone was extracted from blood samples taken from immature and adult male polar bears by Greenland hunters. The results suggested that in immature males, contaminants such as *trans*-chlordane, CB118, dieldrin, and CB153 were important determinants for the variation in the blood plasma concentration. In adult males, compounds such as *trans*-chlordane, *p,p′*-DDE, BDE47, and CB128 were suggested to be important determinants in the variation of testosterone. In an experimental study on farmed arctic foxes, it was reported that juvenile (6 months old) foxes that were exposed to POP contaminated feed (naturally POP contaminated minke whale blubber) had significantly lower plasma testosterone levels than control animals (Hallanger, 2006). However, no between-group

Table 5
Summary of correlations between selected biological parameters (retinoid and hormone levels, and immune response) and organohalogen concentrations (blood plasma) reported in free-ranging Svalbard Glaucous gulls and Svalbard and East Greenland polar bears.[a]

Biomarker	Svalbard Glaucous gulls				Svalbard and East Greenland polar bears			
	Both sexes[b]	Males[b]	Females[b]	References	Both sexes[b]	Males[b]	Females[b]	References
Retinoid levels								
Retinol (vitamin A) (liver)	↑↓ (ΣPCBs) ↓ (HCB)			Henriksen et al., (2000)				
Retinol (vitamin A) (plasma)					↓ (ΣPCB, HCB, HCH)	↔	↔	Skaare et al., (2001); Braathen et al., (2004)
Retinyl palmitate (liver)	↔			Henriksen et al., (2000)				
Hormone levels								
Free thyroxine (T_4) (plasma)		↓ (HCB, Oxy)	↔	Verreault et al. (2004)		↔	↓ (ΣPCB)	Braathen et al. (2004)
Total T_4 (plasma)		↓ (HCB, Oxy)	↔	Verreault et al. (2004)		↔	↓ (ΣPCB)	Braathen et al. (2004)
Free triiodothyronine (T_3) (plasma)		↔	↔	Verreault et al. (2004)		↓ (ΣPCB)	↓ (ΣPCB)	Braathen et al. (2004)
Total T_3 (plasma)		↔	↔	Verreault et al. (2004)		↔	↔	Braathen et al. (2004)
Free T_4/T_3 ratios (plasma)		↓ (HCB, Oxy, DDE, ΣPCB)	↔	Verreault et al., (2004), (2007c)		↑ (ΣPCB)	↔	Braathen et al. (2004)
Total T_4/T_3 ratios (plasma)		↓ (HCB, Oxy, DDE, ΣPCB)	↔	Verreault et al., (2004), (2007c)		↔	↓ (ΣPCB)	Braathen et al. (2004)
Total T_3/Free T_3 ratios (plasma)		↔	↔	Verreault et al. (2004)		↔	↑ (ΣPCB)	Braathen et al. (2004)
Total T_4/Free T_4 ratios (plasma)		↓ (Oxy)	↔	Verreault et al. (2004)	↓ (ΣPCB, HCB) ↑ (DDE)	↔	↔	Skaare et al., (2002); Braathen et al., (2004)
Testosterone (T) (plasma)		↔	↔	Verreault et al. (2006)		↓ (ΣPCB) ↓ (ΣOCP)		Oskam et al. (2003)
17β-estradiol (E_2) (plasma)		↔	↔	Verreault et al. (2006)			↔	Haave et al. (2003)
Progesterone (P_4) (plasma)		↑ (ΣPCB, ΣDDT, ΣCHL ΣPBDE)	↔	Verreault et al. (2006)			↑(ΣPCB)	Haave et al. (2003)
Corticosterone (g. gulls)or cortisol (p. bears) (plasma)	↑ (ΣOHC)			Verboven et al. (2009a)	↑ (ΣPCB) ↓ (ΣOCP)			Oskam et al., (2004)
Immune response								
White cell indices (blood)		↑ (Oxy, PCBs)	↑ (HCB, Oxy, DDE, PCBs)	Bustnes et al. (2004)				
Antibody response to *diphtheria toxoid*		↔	↓ (HCB, Oxy)	Bustnes et al. (2004)				
Antibody titre against *influenza virus* (EIV)	↓ (ΣPCB)			Sagerup et al. (2009)	↓ (ΣPCB)			Lie et al. (2004)
Antibody titre against reovirus (REO)	↔			Sagerup et al. (2009)	↓ (ΣPCB)			Lie et al. (2004)
Antibody titre against *tetanus toxoid* (TET)	↔			Sagerup et al. (2009)	↑ (ΣPCB)			Lie et al. (2004)
Immunoglobulin-G and -M (blood)	↓ (ΣPCB)			Sagerup et al. (2009)	↓ (ΣPCB, HCB)			Lie et al. (2004)
Lymphocyte response to Phytohemagglutinin (PHA)	↑ (ΣPCB)			Sagerup et al. (2009)	↓ (ΣPCB, ΣOCP)			Lie et al. (2005)
Lymphocyte response to pokeweed mitogen (PWM)	↔			Sagerup et al. (2009)	↑ (ΣPCB) ↓ (ΣOCP)			Lie et al. (2005)
Lymphocyte response to concanavalin (Con A)	↑ (ΣPCB)			Sagerup et al. (2009)	↓ (ΣPCB)			Lie et al. (2005)
Lymphocyte response to lipopolysaccharid (LPS)					↑ (ΣPCB) ↑ (ΣOCP)			Lie et al. (2005)
Lymphocyte response to mycobacterium *avium paratubercolosis* (PPD)					↑ (ΣPCB) ↓ (ΣOCP)			Lie et al. (2005)

[a] Statistical analyses were conducted separately on males and females and/or on both sexes combined. ↓ : negative correlation; ↑ : positive correlation; ↔ : no change. When specified, the organohalogens (sums or individual compounds) that were negatively or positively correlated with these biological parameters are identified in parentheses.
[b] PCB: polychlorinated biphenyl congeners, HCB: hexachlorobenzene, Oxy.: oxychlordane, DDE: dichlorodiphenyldichloroethylene, DDT: dichlorodiphenyldichloroethane compounds, CHL: chlordane compounds, PBDE: polybrominated diphenyl ether congeners, HCH: hexachlorocyclohexane isomers, OHC: sum of various chlorinated and brominated, persistent organohalogen contaminants (OHCs) as well as their metabolic products, OCP: sum of various organochlorine pesticides.

differences were found in 22 months old foxes (Rogstad, 2007). This may indicate age-related effects of POPs on testosterone in males.

In female polar bears from the Svalbard area, a positive correlation between PCBs and progesterone (P4) has been reported (Haave et al., 2003). One of the effects of P4 is to exert a negative feedback on secretion of gonadotropin-releasing hormone from the hypothalamus, thus inhibiting secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary (Richards, 1996). A PCB-induced increase of P4 may therefore affect FSH/LH-stimulated maturation of follicles in females and prevent normal ovulation from taking place. It has been reported that slightly elevated P4 concentrations in heifers at the time of artificial insemination led to significantly lower fertility (Waldman et al., 2001). Thus, functionally it is possible that PCB-induced rise in P4 concentrations in polar bears may reduce their reproduction (Haave et al., 2003). The estradiol concentrations in the same study were not related to OHC concentrations in female polar bears (Haave et al., 2003).

In a study on Greenland sledge dog cohorts fed a porcine fat control diet or exposed to a natural cocktail of OHCs via a minke whale blubber diet, sledge dog males were followed for up to six months and testosterone concentrations, testes/baculum morphology and bone mineral density (BMD) were determined (Kirkegaard et al., 2010d). Plasma testosterone concentrations were lower in the exposed group relative to the control animals although not significantly.

A goat model, and also a murine model, have been used to evaluate endocrine and reproductive effects of selected chlorinated compounds (Lundberg et al., 2006; Lyche et al., 2004a,b,c, 2006; Oskam et al., 2004b, 2005; Ropstad et al., 2006). In the goat studies, females were exposed to the non-dioxin like PCB-153 and the dioxin-like PCB-126 during gestation and lactation, and effects were examined in their offspring 9 months post-partum. At that time the mean concentrations of PCB-153 and -126 in adipose tissue of the goat kids were 5800 and 0.49 ng/g lipid weight, respectively (Lyche et al., 2004b). These levels are relatively similar to those reported in polar bears (Ropstad et al., 2006). In female

offspring, exposure to PCB-153 during gestation and lactation resulted in significantly lowered offspring prepubertal LH concentrations, delayed puberty, and that concentrations of P were higher during the luteal phase of the estrous cycle (Lyche et al., 2004b; Ropstad et al., 2006). PCB-126 did not cause any marked effects. In male offspring, PCB-153 exposure caused significantly smaller testis diameter. Male offspring exposed to PCB-153 differed significantly from the control group with respect to plama LH and testosterone levels, had a lower ratio of interstitium area to seminiferous tubules area and proportion of diploid cells, and also showed a significantly higher percentage of sperm with damaged DNA (Oskam et al., 2005). Furthermore, maternal exposure to PCB-126 also affected testosterone levels in male offspring (Oskam et al., 2005).

Even though it is difficult to predict any adverse reproductive effects from OHCs based on correlative studies for free-ranging bears, and even more difficult to demonstrate causality, the relationships between the OHCs and reproductive hormones in recent studies strongly suggest that some OHC alone or as complex mixture can modulate the reproductive system in male and female polar bears. This strong suggestion is also supported by results from experimental studies on various model species such as domesticated arctic foxes, mice and goats as surrogates for polar bears (Lundberg et al., 2006; Lyche et al., 2004a,b,c, 2006; Oskam et al., 2004b, 2005; Ropstad et al., 2006; Sonne et al., 2009a). Thus, high OHC levels in male cubs may be a reason for concern since disturbed testis development can lead to subsequent impairment of reproductive health in adulthood. Furthermore, the continuous presence of high concentrations of OHCs and perhaps POPs in general throughout their life could possibly potentiate any reproductive toxicity that may have occurred during fetal and early postnatal development.

2.1.3. Reproductive pathology

The reproductive organs are susceptible to changes in homeostasic function that are induced by OCs (Colborn et al,. 1993; Damstra et al., 2002). The functioning of reproductive organs involves a complex interaction and timing between endocrine (hormonal) and immune parameters. Impaired fertility has been associated with a negative impact from OHCs in both male and female mammals. Among the effects noted are testicular dysfunctions, such as low sperm count and altered spermatozoa morphology in males, and pathological changes such as endometriosis, leiomyomas, occlusions and stenosis in the female reproductive tract (Bergman and Olsson, 1985; Bergman, 1999; Campagna et al., 2001; Damstra et al., 2002). Such effects may lead to a reduction in the number of successful births which, if it occurs at high frequencies, could potentially have an effect at the population level. Pathological problems may also lead to life-long sterility. PCBs are known to have estrogenic properties (e.g. Matthews and Zacharewski, 2000) while some of the OH-PCB metabolites are anti-estrogenic (e.g. Kramer et al., 1997; Moore et al., 1997) and others estrogenic (e.g. Andersson et al., 1999). In laboratory mice and rat studies, prenatal and neonatal oral exposure to various PCB congeners has shown that the most likely severe impact is on the brain growth spurt (BGS) where permanent spontaneous changes in behaviour, learning and memory occurred (e.g. Eriksson and Fredriksson, 1998; Holene et al., 1999). However, prenatal exposure is maternally derived. The toxicity is probably mediated via decreases in brain dopamine concentrations probably due to accumulations of specific PCB congeners in the brain tissue as shown in studies using laboratory rat strains (e.g. Shain et al., 1991; Seegal and Schantz 1994; Kodavanti et al., 1995, 1996; Mariussen et al., 1999). Similar findings have been reported in humans from the Faroe Island Cohort Study (e.g. Grandjean and Landrigan, 2006); however, this was confounded by exposure to Hg.

2.1.3.1. Reproductive organs. Reproductive organs from East Greenland polar bears from 1999–2001 have been examined to investigate potential negative impacts from OHCs (Sonne et al., 2006c). Multiple regression analyses showed a significant inverse relationship between various OHC groups and testes length and baculum length/weight, respectively, in both subadult and adult males. Decreasing baculum bone mineral density (BMD) was significantly correlated with increasing concentrations of CHLs, dieldrin, PCBs, PBDEs and HCB in both subadults and adults. In females, a significant inverse relationship was found between OHCs and ovary and uterine horn length and weight (Sonne et al., 2006c). Sonne et al. (2007b) also investigated the spatial and temporal trends in sexual organ size of polar bears. These results supported the idea that there may be an impact from xenoendocrine contaminants on the size of East Greenland polar bear genitalia. To what extent these findings have an effect on the East Greenland polar bear sperm and ovocyte quality/quantity and uterus and penis size/robustness and hence the reproduction is uncertain.

A clinical survey on East Greenland male sledge dogs revealed a rare congenital malformation of the urethra and penis corresponding to severe third degree perineal and penile *hypospadias* (Sonne et al., 2008a). This effect was related to high dioxin toxic-equivalency (TEQ) values, among others OHCs, and hence teratogenic changes from EDCs in the neonatal environment could not be excluded. Genetic-based defects may also play a role although *hypospadias* is very rare in dogs and such malformation means that the animal will not be able to reproduce. It was suggested that this congenital malformation was due to endocrine organ pathology/tumours of the dam, enzyme/receptor defects (mutation) in the pup and/or *in uteri* exposure to xenoestrogenic OHCs (Sonne et al., 2008a).

In a study on Greenland sledge dog cohorts fed a porcine fat control diet or exposed to a natural cocktail of OHCs via a minke whale blubber diet, sledge dog males were followed for up to six months and testes/baculum morphology were determined (Kirkegaard et al., 2010d). Baculum weight was lower although not significantly in the exposed group. Daily peri- and postnatal exposure to *ca.* 100 g of polluted minke whale blubber resulted in reduction of testes weight in Greenland sledge dogs. The study concluded that the results showed that especially the size of sexual organs may be affected by endocrine disrupting environmental pollutants in sledge dogs.

2.1.3.2. Enlarged clitoris/pseudohermaphorditism. Wiig et al. (1998) reported on four suspected pseudohermaphroditic female polar bears examined during live-capture around Svalbard for the purpose of satellite tagging. It was suggested that the enlarged clitorises were congenital and could have been caused by an enzyme defect (21-hydroxylase deficiency), androgen producing tumour or a high exposure to OHCs during the foetal stage or early development of the reproductive organs. However, the authors did not have access to necropsy/biopsy samples from the individuals and it could therefore not be definitively concluded that this phenomenon in fact corresponded to the patho-anatomical diagnosis of a pseudohermaphrodite. In another study, polar bear sexual organs were collected from 44 East Greenland polar bears from 1999 to 2002, and only one aberrant adult female was identified. The bear had a significantly enlarged clitoris resembling in size, form and colour those of previously reported pseudohermaphroditic polar bears from Svalbard (Wiig et al., 1998; Sonne et al., 2005a). Except for the enlarged clitoris, all dimensions of the external and internal reproductive organs of the bear were similar to a reference group of 23 normal adult female polar bears from East Greenland collected in 1999–2002. The aberrant bear was a female genotype, and macroscopic examination of her internal reproductive organs indicated that she was reproductively functional. The histological examination of the clitoral enlargement revealed intense chronic ulcerative and perivascular clitoriditis similar to acral lick dermatitis frequently seen in domestic dogs. The authors concluded that there were no signs of pseudohermaphroditic hyperplasia of clitoral tissue due to androgenic or antiestrogenic endocrine disruption. The levels of OHCs and dioxin TEQ values were also lower than concentrations

that were considered to be of toxicological risk. It was therefore concluded that some of the previously reported adult female polar bear pseudohermaphrodites from Svalbard (Wiig et al., 1998) may have been misdiagnosed. Wiig et al. (1998) also reported on two yearlings from one of the adult Svalbard females exhibiting enlarged clitorises (*i.e.* all three bears from this family had the same abnormality raising the question of abnormality versus genetic derivation). It is likely that the yearling phenomenon was a teratogenic lesion and explanations for that are similar to those suggested for the above *hypospadias* dog (pathology/tumours of the dam, enzyme/receptor defects (mutation) in the pup and/or *in uteri* exposure to environmental xenoestrogens). These results emphasized that examinations for pseudohermaphrodism in arctic wildlife need to consider that occurrences can be due to natural events via numerous etiologies (Sonne et al., 2005a).

2.1.4. Immune system

Results from studies by Bernhoft et al. (2000) and Lie et al. (2004, 2005) have suggested that serum immunoglobulin G (IgG) levels, and humoral (anti-body response following immunization) and cellular immunity (antigen and mitogen induced lymphocyte proliferation) may be impaired by OHCs in the Svalbard subpopulation of polar bears.

In assessing whether a cause–effect relationship exists with respect to immune toxicity from a typical Greenlandic peoples natural intake of OHCs from marine mammal blubber, results from a controlled study on domestic West Greenland sledge dogs were recently reported (Sonne et al., 2006b). The exposed sledge dog group was fed a diet based on minke whale blubber rich in OHCs and n-3 fatty acids, and with exposure levels similar to those of Inuits and polar bears. The control group was fed a diet based on uncontaminated pork fat. The study documented that a daily intake of 50–200 g of minke whale blubber for 21–52 weeks caused an impairment of both the non-specific and specific cellular immune system in the sledge dogs. Acute phase complement protein and cytokine RNA expression was also studied in the same cohort of sledge dogs after exposure for up to ca. 100 weeks, and suppression was observed for liver haptoglobin (HP) and fatty acid binding protein (FABP) in the exposed group (Sonne et al., 2007b). This study concluded that the combination of OHCs and marine n3/n6-fatty acids as well as microelements had an impact on the immune status/reactions in sledge dogs when compared to the pork fat. These sledge dog results suggested that possibly polar bears suffer from similar decreased resistance to diseases by a comparable intake of marine mammal blubber due to the immunomodulatory content of both OHCs and the fatty acid n3/n6 profiles, vitamins and microelements (Lie et al., 2004, 2005).

It has been documented that high concentrations of PCBs and/or OC pesticides correlate with reduced specific lymphocyte function and thus may produce impaired resistance against infections in Svalbard polar bears (Lie et al., 2005). Samples of lymph nodes (axillary and inguinal), spleen, thymus and thyroid tissue from a total of 82 polar bears from East Greenland 1999–2002 were examined histologically (Kirkegaard et al., 2005). High secondary follicle count was found in spleen (21%) and lymph nodes (20%), and this was significantly higher in subadults compared to adults of both sexes. Most of the correlations between concentrations of OHCs and the amount of secondary follicles in lymph nodes were insignificant, but ΣPBDE showed a significant and modest positive correlation. In spleen, a significant relationship between low concentrations of OHCs in adipose tissue and few/absent secondary follicles was found with respect to concentrations of ΣCHLs, ΣHCHs, HCB and dieldrin. No histopathological abnormalities (e.g. neoplasia) were found in spleen, lymph nodes, thymus or thyroid. Kirkegaard et al. (2005) suggested that, based on the available sample exposure of polar bears to OHCs, it was unlikely to have resulted in adverse effects on the tissues in question, although moderate relationships were found with ΣCHL, ΣHCH, HCB and dieldrin concentrations.

In a study where polar bears from Svalbard and Canada were recaptured 32–40 days after immunization with inactivated influenza virus, reovirus, and herpes virus and tetanus toxoid, negative associations were found between ΣPCBs and serum immunoglobulin-G levels and between ΣPCB and increased titers against influenza virus and reovirus (Lie et al., 2004). A positive correlation was reported between ΣPCB and increased antibodies against tetanus toxoid. Furthermore, there were correlations between PCB and OC concentrations and lymphocyte proliferation responses (Lie et al., 2005). Thus, as concluded in the previous AMAP assessment (de Wit et al., 2004), high OC levels may impair the polar bears ability to produce antibodies and may thus produce impaired resistance to infections.

Studies in arctic ursids and canids are consistent with cause–effects of PCB exposure on the immune system of captive goats. In a study by Ropstad et al. (2006), goats were assessed during the first 6 weeks of the offspring life of female goats that had been exposed to CB-153 and CB-126 during gestation and lactation. Offspring exposed to PCBs had significantly higher numbers of white blood cells at an age of 2 weeks, and the lymphocyte response to phytohemagglufinin (PHA) and to concanavalin (Con A) was significantly lower at ages of 2, 4, and 8 weeks (Lyche et al., 2004a). CB-153 also suppressed the maternal and neonatal immunity, as demonstrated by reduced transfer of maternal IgG and specific antibodies (Lyche et al., 2006). CB-126 exposure of the mothers resulted in a significantly lower concentration of monocytes in 2, 4 and 8 weeks old offspring. Furthermore, exposure to CB-126 resulted in a significant reduction of IgG levels in the pregnant mothers (Lyche et al., 2004a, 2006).

Since several PFCAs/PFSAs have been shown to be immunotoxic in laboratory animals (Keil et al., 2008; Lau et al., 2007; Peden-Adams et al., 2008), PFCs may be a potential immunodisruptor in polar bears such as those from East Greenland that have been shown to have PFCA and particularly high PFSA (mainly PFOS) concentrations (Table 1). Concentrations of several PFCAs and PFSAs (e.g., PFOS) have been on the rise in recent years (Dietz et al., 2008). PFOS concentratons in Svalbard bears are comparable to East Greenland bears, but lower PFC (and in particular PFOS) concentrations have been reported in Canadian and Alaskan bears (Smithwick et al., 2005; Letcher, 2009) (Table 1).

2.1.5. Internal organs

2.1.5.1. Liver. In rats and mink, several studies have associated acute exposure to PCBs with liver toxicity (Jonsson et al., 1981; Bergman et al., 1992a; Kelly, 1993; Chu et al., 1994; MacLachlan and Cullen, 1995; Parkinson, 1996). In marine wildlife, chronic exposure to OHCs, such as PCBs, DDTs, and PBDEs has been related to toxic effects on several organ systems (Bergman and Olsson, 1985; Schumacher et al., 1993; Bergman, 1999; Bergman et al., 2001). An investigation into liver histology of East Greenland polar bears was initiated during 1999–2002 (Sonne et al., 2005b). Light microscopy changes revealed nuclear displacement from the normal central cytoplasmic location in parenchymal cells, mononuclear cell infiltrations (12–16%), mild bile duct proliferation accompanied by fibrosis (8%), and fat accumulation in hepatocytes and pluripotent Ito cells (75–100%). For adult females, increases in hepatocytic intracellular fat were significantly correlated with concentrations of ΣHCHs, as was the case for lipid granulomas and HCB in adult males. Based on these relationships and the nature of the chronic inflammation, it was suggested that these effects were caused by factors including long-term exposure to various groups of OHCs, i.e. OCs, BFR, PFCs and mercury, and recurring infections with environmental micropathogens (virus bacteria) as well as parasites (Sonne et al., 2005b, 2007e, 2008a). It should also be strongly emphasized that the lesions are a

result of environmental as well as endogenous factors. Of environmental factors known to induce similar lesions are bacteria, virus, fungi and parasites as well as contaminants (Sonne et al. 2005b, 2007e, 2008a). Overall, the most important endogenous individual factors in the development of liver lesions in polar bears is age, which is also the case for other free-ranging mammals (Sonne et al. 2005b, 2007e, 2008a).

The possible links between liver changes and OHC exposure in polar bears was supported by Sonne et al. (2008b) who found similar histopathological liver changes in the OHC exposed group of sledge dogs previously mentioned. Sonne et al. (2008a) also investigated liver histopathology in relation with PFCA and PFSA (essentially all PFOS) concentrations in East Greenland polar bears. Although no statistical relationships were found the authors suggested a potential relationship due to the nature of the chronic lesions.

The results of a contaminant exposure study using domesticated (farmed) Arctic foxes was recently completed (Hallanger, 2006). In addition to a control cohort, an exposure cohort was fed, similarly to recent captive sledge dog studies, i.e., a diet that contained blubber from naturally POP contaminated minke whale blubber. When foxes had been fed for 15 and 22 months, there were higher prevalences of glomerular, tubular and interstitial hepatic lesions than the control group (Sonne et al., 2008c).

2.1.5.2. Kidney. Kidney samples from East Greenland polar bears collected from 75 individuals during 1999 to 2002 showed OHC-related lesions of diffuse glomerular capillary wall thickening (found in 22% of the animals examined), glomerular mesangial deposits (74%), tubular epithelial cell hyperplasia (21%), hyalinization of the tubular basement membrane, tubular dilatation, atrophy and necrosis (36%), tubular medullary hyaline casts (15%), interstitial fibrosis (30%) and mononuclear cell infiltration (51%) (Sonne et al., 2006b). With the exception of mononuclear cell infiltrations, these parameters were all correlated with age, whereas none was associated with the sex of the animals. In an age-controlled statistical analysis of covariance, increases in glomerular mesangial deposits and interstitial fibrosis were significantly correlated with ΣPBDE concentrations in subadults. In adult males, statistically significant positive correlations were found for tubular epithelial cell hyperplasia and dieldrin concentration, diffuse glomerular capillary wall thickening and ΣCHL concentrations, and tubular medullary hyaline casts and ΣCHL, ΣPBDE, ΣPCB and ΣHCH. The lesions were consistent with those reported previously in highly OHC-contaminated Baltic seal populations and exposed laboratory animals (Bergman et al., 2001). In conclusion, age was an important parameter in the development of polar bear renal lesions. However, based on the above findings as well as the nature of the findings, it was suggested that long-term exposure to OHCs may be a cofactor in renal lesion occurrence, although other cofactors, such as exposure to Hg and recurrent infections from viruses, bacteria and parasites, could not be ruled out (Sonne et al., 2006c). In a recent experiment on OHC exposed (via a naturally contaminanted minke whale diet) sledge dogs, likewise significantly higher frequencies of glomerular, tubular and interstitial lesions were found in the exposed group (Sonne et al., 2007c). Furthermore, higher urine protein:creatinine ratio and plasma urea levels were found in the exposed group, which indicated a negative impact on kidney function via tubular and glomerular dysfunctions (Sonne et al., 2008d). Similar histopathological lesions were found in OHC exposed Arctic foxes also fed polluted minke whale blubber (Sonne et al., 2008e).

Sonne et al. (2009a) also investigated thyroid histology in the OC exposed (farmed) Arctic foxes. Four OHC-related histopathological changes were observed: flat-epithelial-cell true thyroid cysts, remnants of simple squamous epithelial cell embryonic ducts and disseminated thyroid C-cell hyperplasia. The results indicated that the consumption of a minke whale blubber diet was a causative factor in the disruption of the HPT-axis, a disturbance of the calcium homeostasis/metabolism or energy metabolism or immune suppression. Because concentrations of OHCs are higher in wild Arctic foxes it is likely that these animals suffer from similar OHC-induced thyroid gland pathological and functional changes.

2.1.6. Skeletal system

2.1.6.1. Bone mineral density. Bone mineral composition in mammals is based on a complex set of interrelated mechanisms and is influenced by various nutritional and environmental factors (e.g. Ganong, 2005; Sarazin et al., 2000; Johansson and Melhus, 2001; Johansson et al., 2002; Promislow et al., 2002; Michaelsson et al., 2003). In marine mammals such as grey seal, ringed seal, harbour seal (*Phoca vitulina*), or in a reptile, the alligator (*Alligator mississippiensis*), osteopenia and macroscopic pathology have been examined in bone during distinct periods of exposure to anthropogenic pollutants (Zakharov and Yablokov, 1990; Bergman et al., 1992b; Mortensen et al., 1992; Schandorff, 1997; Sonne-Hansen, et al., 2002; Lind et al., 2003, 2004). The studies showed relationships between OHCs and exosmosises, periodontitis, loss of alveolar bone structures, osteoporosis, widening of the canine opening, and enlargement of the foramen. In an analysis of BMD in skulls of polar bears from East Greenland sampled during 1892–2002, BMD in skulls sampled in the period of OHC introduction into the Arctic (1966–2002) was significantly lower than in skulls sampled in the pre-OHC period (1892–1932) for subadult females, subadult males, and adult males but not adult females (Sonne et al., 2004). In addition, a negative correlation was found between OHCs and skull BMD for ΣPCBs and ΣCHL in subadults and for dieldrin and ΣDDT in adult males. For ΣPBDE in subadults, an indication of a relationship was detected. It was therefore concluded that bone mineral composition in East Greenland polar bears may have been a function of OHC exposure (Sonne et al., 2004). Furthermore, Sonne et al. (2008f, 2009b) investigated the impact from PCBs on BMD and biomechanical properties in semi-controlled studies of sledge dogs and arctic foxes. In these studies no statistically significant relationships were found between PCBs and BMD (measured as controls vs. exposed). Emaciation (seasonal fasting) seemed to decrease the biomechanical properties of femoral bone tissue in arctic fox (lowered stiffness). For a study on Greenland sledge dog cohorts fed a porcine fat control diet or exposed to a natural cocktail of OHCs via a minke whale blubber diet, sledge dog males were followed for up to six months and bone mineral density was determined (Kirkegaard et al., 2010d). BMD was lower in the exposed group although not significantly.

Using a goat model, a study on bone tissue composition of the female offspring of the goats revealed that the trebecular bone mineral density was higher in kids that had been exposed to CB-153 during gestation and lactation as compared to the control group (Lundberg et al., 2006). No such effects were observed in the group exposed to CB-126, nor did any of the two compounds affect bone strength (Lundberg et al., 2006).

2.1.6.2. Gross skull pathology and asymmetry. Laboratory studies have shown that OHCs can induce periodontitis in mink (Render et al., 2000a,b, 2001), and in humans PCBs seem to interfere with normal tooth development (Rogan, 1979; Miller, 1985; Gladen et al., 1990). In various studies of wildlife including marine mammals, relationships between exposure to OHCs and exostosis, periodontitis, osteoporosis and widening of canine alveoli have been documented (Zakharov and Yablokov, 1990; Bergman et al., 1992b; Mortensen et al., 1992; De Guise et al., 1995; Schandorff, 1997). A time–trend study of skull pathology on East Greenland and Svalbard polar bears sampled during 1892–2002 was reported to investigate the possible negative health impacts in polar bears (Sonne et al., 2007d). Of seven different pathological changes, differences could only be observed for tooth

wear and periodontitis. In East Greenland, the prevalence of tooth wear was significantly higher in polar bears collected in the pre-contamination period than in bears sampled during periods after introduction of and contamination of the environment by OHCs. Considering periodontitis, prevalence was not significantly different between pre-contamination and contamination periods. Polar bears from Svalbard had significantly higher prevalence of tooth wear and periodontitis than polar bears from East Greenland. Hence, a clear geographical difference was found but no evidence for an association between skull pathology and exposure to OHCs in East Greenland and Svalbard polar bears (Sonne et al., 2007d).

Interactions of OHCs with hormone receptors have occasionally been associated with endocrine disruption and stress in vertebrates. With respect to skull pathology, this has been shown to lead to elevated blood corticosteroid levels that may induce fluctuating asymmetry (FA) of the skull (Colborn et al., 1993; Feldman, 1995; Borisov et al., 1997; de March et al., 1998; Bergman, 1999; Damstra et al., 2002). Sonne et al. (2005c) investigated FA in skulls of 283 polar bears sampled in East Greenland from 1892 to 2002. Thirteen metric bilateral traits in skull and lower jaw were measured and compared between polar bears born before 1960 (pre-OHC exposure period) and after 1961 (OHC exposure period). The degree of fluctuating asymmetry did not differ statistically between the two periods in 10 of the 13 traits. In fact, when significant differences were found in four of the traits, the fluctuating asymmetry was lower in skulls sampled after 1960. A time trend analysis did find fluctuations over time for five traits, but the relationship was weak as the trend appeared to occur by chance due to the high number of regressions analysed. A correlation analysis of FA versus the sum concentrations of various classes of OHCs in adipose tissue from a subsample of 94 recently collected polar bears (1999–2002) did not show a trend either. Hence, this study could not document any relationship between skull asymmetry in polar bears and periods with different exposure to OHCs (Sonne et al., 2005c). It was therefore concluded that the differences were likely to be influenced by nutritional status, genetic factors, a sub-effect exposure to OHCs or other confounding environmental factors such as temperature differences within the two investigated periods. In a recent paper, Bechshøft et al. (2008) investigated eight bilateral metric traits from East Greenland and Svalbard with respect to temporal trends from 1950 to 2004. Three of 24 trait vs. group combinations (subadults, adult female and adult males) showed a significant negative slope with OHC concentrations. The general decrease in FA during 1950–2000 may be explained by the declining OHC concentrations found within the same period (Derocher et al., 2003; Dietz et al., 2004). Thus, no indications were found for a linkage between FA and OHCs that were measured.

2.1.7. Neurological and behaviour effects

Relationships between spatial behaviour (e.g., habitat use) and levels of PCBs have been reported in female polar bears in the Svalbard and Barents Sea region (Olsen et al., 2003). However, it is not likely that these relationships reflect that the contaminants affect the spatial behaviour of the polar bears. Rather, the relationships between spatial behaviour and their PCB levels are due to that animals that have home range areas in the eastern parts of the Svalbard–Barents Sea regions consume seals that have higher concentrations of OHCs as compared to bears which have habitats further west. In addition, the finding that levels of PCBs were positively associated with the annual home range size of the animals is most likely due to the expenditure of more energy and therefore also greater food consumption. Thus, animals with large home range sizes will be exposed to larger amounts of OHCs than animals with low home range sizes.

Disruption of the TH homeostasis caused by OHCs has been linked to neurodevelopmental and behavioural disorders in humans and laboratory animals (Lilienthal et al., 2006; Meerts et al., 2004). Since there are several reports that polar bears with the highest levels of PCBs also have low plasma concentrations of THs (Braathen et al., 2004; Skaare et al., 2001) (Table 5), there are reasons to be concerned that thyroid disruption may result in neurodevelopmental and behavioural disorders in polar bears. However, no studies have been designed to focus on this issue, probably because it is difficult to assess such effects in free-living apex predators. There are no reports of effects related to neurotoxic effects of OHCs in neither polar bears nor other ursids or canids. However, in a recent study by Basu et al. (2009), several neurochemical biomarkers were measured in the brain stem (*medulla oblongata*) from 82 polar bears hunted in East Greenland, and the relationships to various OHC levels were assessed in the same tissue. There were no significant correlations between dopamine-2, GABA-A, muscarinic cholinergic, nicotinic cholinergic receptors, cholinesterase, monoamine oxidase enzyme, neurochemical biomarkers and the concentrations of numerous classes of OHCs and metabolites or degradation products (e.g., ΣPCBs, ΣCHLs, ΣOH- and Σ$MeSO_2$-PCB metabolites, ΣDDT and ΣPBDEs).

2.1.8. Toxicokinetics and biotransformation and enzyme systems

Metabolism (or biotransformation) is an important factor in the fate of the OHCs via processes that render the OHC more or less toxic, is target tissue specific (occurring mainly in the liver) and is expected (but not necessarily) to result in the excretion and depuration of the formed metabolite(s). Lipid cycling, bioenergetics, seasonal physiological changes can all have an influence on OHC/POP fate and toxicokinetics (e.g., metabolism). Although not a measure of an outright adverse effect, i.e., it is an expected or normal response, OHC oxidative metabolism can be mediated via cytochrome P450 (CYP) monooxygenases (constituent and induced), and result in the formation of oxygenated or hydroxylated metabolites that are themselves persistent and/or bioaccumulative OHCs such as hepachlor epoxide and oxychlordane (from heptachlor and *cis*- and *trans*-chlordane, respectively) and OH- and $MeSO_2$-PCBs derived from PCB metabolism (Letcher et al., 2000a) (Table 2). Other enzymes may also be involved in OHC degradation and metabolism such as those mediating the debromination of BFRs including PBDEs and HBCDs as has been indicated *in vitro* as being a possible metabolic process occurring in the liver of polar bears (Letcher et al., 2009). One could also speculate that it is possible that enzymes that are regulated and metabolized by e.g., hormones such as THs could be involved in the mediation of the degradation and interconversion of POPs. For example, TH deiodinases, sulfatases and glucocorticoidases that mediate the half-life or interconversion of THs, could also be mediating the metabolism of POP and/or there (e.g., OH-containing) metabolites. There is evidence, although not confirmed, that TH deiodinases in liver and intestinal microsomes of common carp (*Cyprinus carpio*) mediate the debromination in vitro of brominated diphenyl ether BDE-99 to BDE-47 (Benedict et al., 2007).

The potential chemically-induced effects reported in captive sledge dogs, and wild top predator mammals such as polar bears, may be elicited, in part, through enzyme (e.g., CYP)-mediated biotransformation of major POP classes (e.g., PCBs and PBDEs), and subsequent formation and retention of OH-substituted metabolites (i.e., OH-PCBs and OH-PBDEs). Recently, major OH-PCB, $MeSO_2$-PCB and OH-PBDE congeners have been reported as residues in liver, brain, fat and/or blood of polar bears mainly from the Canadian high Arctic and/or East Greenland populations (Gebbink et al., 2008a,b; Sandala et al., 2004; Verreault et al., 2005a) (Table 2). For East Greenland bears, bioaccumulation and/or biomagnification from a ringed seal blubber diet has also been reported for various OHCs (Letcher et al., 2009). In the case of apparent $MeSO_2$-PCB and OH-PBDE metabolites, PCP and 4-OH-HpCS, it was concluded that $MeSO_2$-PCBs were metabolites formed in both the bears and ringed seals, and OH-PBDEs, PCP and 4-OH-HpCS were not necessarily metabolites but also accumulated from, e.g. natural sources and accumulated in the ringed seal and polar bear food web. In the case of OH-PCBs, these were

metabolites of PCBs formed entirely in the bears. In the captive sledge dog studies with exposure and control cohorts, the comparative concentrations and compositional patterns of OH-PCBs, OH-PBDEs, $MeSO_2$-PCBs, PCP and 4-OH-HpCS demonstrated a similar finding as in the free-ranging East Greenland polar bear studies (Verreault et al., 2008a). In addition, the catalytic activity of major xenobiotic-metabolizing phase I and II hepatic microsomal enzymes in captive sledge dog cohorts, were shown to be induced by increased exposure to a POP-contaminant, minke whale blubber diet (Verreault et al., 2009a). It may be concluded that for some POPs (such as PCBs) and for some (especially top predator) Arctic wildlife species and populations, biotransformation to more biologically active metabolites (e.g., OH-PCBs) may be more important with respect to biological effects. OH-PCBs and OH-PBDE formation from PCBs and PBDEs, respectively, represent examples of biotransformation mechanisms "activating" organohalogen, depending on the OHC class and congener, to potential EDCs. However, one must consider the reproductive status and other components of the diet that may affect CYP enzymes and the level of induction and role in biotransformation that can enhance excretion and/or bioactivation of toxicants in a chemical specific manner. Regardless, the CYP1A induction and enzyme activity are well established as sensitive biomarkers for exposure to dioxin-like pollutants in vertebrates (Goksøyr, 1995; Bucheli and Fent, 1995). Further, the occurrence of organ dioxin-like toxicity in some cases has been shown to be correlated with CYP1A expression in vertebrates. Andreasen et al. (2002) for example concluded that the cardiovascular system is a primary target of 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin (TCDD) mediated developmental toxicity in zebrafish.

2.2. Marine mammals

In the last decade, there has been numerous reviews of OHCs and potential effects in cetaceans and pinnipeds (e.g., O'Hara and Rice, 1996; MacDonald, 2000; O'Hara and O'Shea, 2001, 2005; Pfeiffer, 2002; O'Hara and Becker, 2003; O'Shea and Tanabe, 2003; Vos et al., 2003; de Wit et al., 2004; Houde et al., 2005). The present review focuses and/or highlights several effects-related studies on key Arctic marine mammals.

2.2.1. Cetaceans

2.2.1.1. Bowhead whale. Hoekstra et al. (2002a) studied the Bering–Chukchi–Beaufort Sea population of bowhead whale, and seasonal fluctuation in $\delta^{13}C$ values was consistent for all age classes, suggesting that the Bering and Beaufort seas are both important regions for feeding. This implied that POPs exposure varied seasonally and any assessment must consider the time of year, which certainly applies to all other Arctic wildlife and fish. Despite the chemical evidence for no adverse effects, the bowhead whale continues to be studied since it is an endangered species, important for subsistence users, relatively easily accessible to hunters and scientists for study as a fresh, well characterized animal and numerous other reasons. As part of an ongoing health assessment, Rosa et al. (2007a) evaluated vitamin A and E concentrations in liver, blubber and serum. Serum, liver and blubber retinol and OC concentrations in serum and blubber were examined with no significant correlations noted. In a related study, Rosa et al. (2007b) evaluated serum TH and histomorphology of thyroid tissue (e.g., epithelial–follicular index or EFI). Some biological variation was noted as TH concentrations in pregnant/lactating whales were significantly lower than other cohorts and differences in the EFI between subadult and adults in spring and fall. No association was noted for serum TH concentrations and select OHC concentrations in serum, blubber or liver. Cell culture techniques have succeeded in cell culture lines being established for toxicity testing of bowhead whales and North Atlantic right whales (*Eubalaena glacialis*) (Godard et al., 2006).

Chiral OHCs such as atropisomeric PCBs are subject to process (e.g., biotransformation) that can give rise to changes in enantiomer ratios in Arctic biota (Warner et al., 2005). Hoekstra et al. (2002c) evaluated blubber and liver from bowhead whale and zooplankton for PCB concentrations and determined the enantiomeric fractions of eight chiral PCB congeners (CB-91, -95, -135, -136, -149, -174, -176, and -183) to quantify enantiomer-specific accumulation. Accumulation of several chiral PCBs (CB-91, -135, -149, -174, -176, and -183) in blubber was enantiomer-specific relative to bowhead liver and zooplankton, suggesting that biotransformation processes within the bowhead whale are enantioselective. The enantiomeric fractions for CB-95 and CB-149 were significantly correlated with body length in male and female whales, while enantiomeric fractions for CB-91 correlated with length in males only. Results suggest that enantioselective accumulation of CB-91, -95, and -149 is influenced by PCB concentrations, age, and/or the modification of an uncharacterized stereoselective process (or processes) during sexual maturity. Hoekstra et al. (2003b) applied these enantiomer specific processes to biomagnification in the Arctic food web as well. These findings then led to assessment of actual metabolites and indicate that despite low concentrations in tissues the bowhead whale is responding (unlikely an adverse effect *per se*) to the presence of the POPs. Hoekstra et al. (2003a) further assessed blubber and plasma to quantify the concentrations of $MeSO_2$- and OH-PCB metabolites (Table 2). The $MeSO_2$-PCBs in blubber was dominated by 4-$MeSO_2$-substituted congeners, the most abundant being 4-$MeSO_2$-CB70, 3- $MeSO_2$-CB132, and 4- $MeSO_2$-CB64. $MeSO_2$-PCB concentrations in blubber were low compared to concentrations previously reported in other marine mammals (Table 2). Similar ratios of $MeSO_2$-PCB metabolites to parent PCB congeners among marine mammals suggest that CYP2B-like biotransformation influences the formation and clearance of $MeSO_2$-PCBs. ΣOH-PCB concentrations in bowhead plasma were low compared to humans and many marine mammals (only two detected; 4-OH-CB130 and 4-OH-CB187) (Table 2). These detailed studies suggested that the bowhead whale is very likely not suffering from adverse health effects of OHC exposure, but did indicate selective biotransformation and accumulation processes.

2.2.1.2. Killer whales. To our knowledge, there have been no effects linked or related to POP or OHC exposure for killer whales in Arctic waters, or in animals that migrate in or out of Arctic waters. However, Wolkers et al. (2007) reported that in the blubber of one subadult and eight male adults sampled in northern Norway mean ΣPCB and pesticide levels were similar, approximately 25 μg/g lipid, and ΣPBDEs were approximately 0.5 μg/g lipid, and stated that killer whale from these waters are among the most OHC contaminanted arctic animals, with levels exceeding those in (Svalbard) polar bears (Table 1). Ylitalo et al. (2001) reported on organochlorines (including dioxin-like PCB congeners and DDTs) and PCBs in biopsy blubber samples of free-ranging resident and transient killer whales from the Kenai Fjords/Prince William Sound (Alaska), and acquired during the 1994–1999 field seasons. Concentrations of organochlorines in transient killer whales (marine mammal-eating) were extremely high (ΣPCB = 230 μg/g lw) and much higher than those found in resident animals (fish-eating) apparently due to differences in diets of these two killer whale eco-types. Certain life-history parameters such as sex, age and reproductive status also influenced the concentrations of OCs in the Alaskan killer whales. Reproductive female whales contained much lower levels of organochlorines than sexually immature whales or mature male animals in the same age class. Finally, very recently, various OC pesticides, PCBs, PBDEs, OH-PCBs, OH-PBDEs, MeO-PBDEs and other OHCs were reported in the blood of a single captive (female) killer whale fed a natural diet of Pacific herring (*Clupea pallasii)* (Bennett et al., 2009). ΣPCBs, ΣDDTs, the antimicrobial compound triclosan and ΣOH-PCB were at the highest concentrations of 32, 45, 9 and 6.5 ng/g ww, respectively. It was concluded that this

captive whale provided a rare glimpse at the accumulation, retention and metabolism of several classes of persistent contaminants in a killer whale, and because of the Pacific Ocean origins of this whale's diet of herring, these results also provided an indication of what metabolites might be expected in the coastal marine mammals of British Columbia and Alaska (including the Bering Sea). Given the OHC-effects associated reported for East Greenland and Svalbard polar bears, further effects studies are warranted in killer whales given that several OHC class (i.e., ΣPCB, ΣCHL and ΣCBz) exceed 100 ppm (lw) and are around 10 ppm (lw) in blubber from Alaskan and Northern Norway populations, respectively (Table 1).

2.2.1.3. Beluga whale. The beluga whale is a toothed whale (odontocete) known to feed in the upper trophic levels and inhabits Arctic waters as well as marine areas of well known industrial contamination (St. Lawrence River Estuary (SLE) in Québec, Canada) and may be impacted at the individual animal and population levels as described in Martineau et al. (2003), Gauthier et al. (2003), and Brousseau et al. (2003). In the Arctic some populations of beluga whales are low and of concern including those in Cook Inlet (near Anchorage, Alaska USA) and Hudson Bay (Canada) as well as in the SLE. With respect to OHCs, levels are relatively high (Tab. 1), and appear to be similar in beluga whales at Svalbard and eastern Canada (Andersen et al., 2001, 2006). Hoevever, levels of toxaphenes appear to be somewhat lower in Alaska as compared to in eastern Canada and Svalbard (Andersen et al., 2006).

Numerous investigations assessing the health of this species have utilized *in vitro* (e.g., DeGuise et al., 1995a, 1998; Gauthier et al., 1999a,b, 2003; Brousseau et al., 2003) and *in vivo* (e.g., Martineau et al., 1988, 1994, 2003; Lair et al., 1997; Mikaelian et al., 2000) tools, including bioassays (Lapierre et al., 1999; Fournier et al., 2000). It is not possible to review all of these efforts in the present review, but rather use examples to better present some of the current knowledge concerning POPs/OHCs in beluga whales with an emphasis on the immune system and prevalence of neoplasia as shown for SLE animals. Readers are encouraged to seek more details in the published studies (Andersen et al., 2001; O'Hara and O'Shea, 2001; Vos et al., 2003).

Belugas from the SLE have been studied for approximately twenty years and are contaminated by high concentrations of POPs including OHCs, where for instance levels of PCBs have been reported in the range of 80 ug/g (lw) (e.g., Martineau et al., 1987; Letcher et al., 2000b). Thus, in this population of belugas, levels of OHCs in general are about 10-fold higher than in Arctic populations of belugas in eastern Canada and Svalbard (Andersen et al., 2001).

Many studies have attempted to determine if POP exposures are resulting in harmful biological effects in arctic belugas by comparing the contaminants and biological data with the heavily polluted and more intensively examined SLE beluga population (more easily accessed and examined stranded animals). Some reports have associated high levels of POPs with apparently severe lesions (likely lethal), widespread infections and a high rate of neoplasia (an abnormal proliferation of cells) for the SLE beluga population (e.g., Martineau et al., 1987, 1994, De Guise et al., 1995a, 1998). This rate of neoplasia is alarming as compared to other wildlife populations (Martineau et al., 2002). Comparisons to more northerly populations are complicated by logistical constraints and variations in bias of sampling. For example, hunter-killed animals will be selected differently as compared to live or found dead stranded animals as is the case for the SLE or Cook Inlet (Alaska) whales. Thus, a basic comparison of prevalence rates of neoplasia or other pathologies are confounded by the selection bias as well as age and sex of animals evaluated; along with other variable environmental factors (e.g., proximity to specific industries and municipalities). A case of a lethal neoplasia outside the SLE has been documented as a poorly differentiated carcinoma within the brainstem of a captive beluga whale (Ridgway et al., 2002). Stranded SLE belugas are affected by relatively high rates of cancer of the digestive tract and could be associated with exposure to the POP class of polycyclic aromatic hydrocarbons (PAHs) (some PAHs are well known mutagens and carcinogens such as benzo[a]pyrene) from local aluminum smelters (Martineau et al., 2002). This type of exposure in the high Arctic is currently unlikely for the many stocks of whales. However, with expansion of certain industries into the arctic region (e.g., hydroelectric and/or hydrothermal power; petroleum processing and mining) this situation could change in the future. Still, one should use great caution in linking the neoplasia that is well documented for the SLE and chemical contamination with the chemical contamination of arctic beluga whales and potential adverse health effects.

It is known that PCBs exhibit tumor-promoting effects in experimental animals. However, not all congeners are involved as shown by Vondracek et al. (2005) who demonstrated *in vitro* using rat liver epithelial WB-F344 cells that the dioxin-like PCB congeners (CB-126, CB-105), and 4-OH-CB79, a metabolite of the planar CB-77 congener, induced cell proliferation in a concentration-dependent manner; while the 'non-dioxin-like' compounds that are not aryl hydrocarbon receptor agonists (CB-47, 153, and 4-OH-CB187) had no effect on cell proliferation at concentrations up to 10 mM. This indicates the need to consider dioxin-like congeners and metabolites such as OH-PCBs in these marine mammals when discussing neoplastic responses and/or risks, as well as when considering the immune system. Thus, reporting ΣPCB concentrations and comparing among stocks and other cohorts can overlook a large toxicological consideration, e.g. congener-specific profiles and concentrations.

Some investigators claim that comparing the SLE population (more contaminated) to Arctic populations (less contaminated) provides a contrasting "dose–response" opportunity. This simplistic view should be considered with caution regarding contaminant exposure and response comparisons for two very distinct populations (geographically isolated). Severity and prevalence of lesions comparisons by populations and their correlation with POP concentrations within specific cohorts (e.g., age categories) may help characterize the effects of these compounds on beluga, but this approach should be used with caution. One limitation is the lack of health (clinical or adverse health effects measures) or biomedical data even though tissue contaminant concentrations in arctic belugas have been monitored for approximately two decades (e.g., Muir et al., 1990, 1996a,b; Béland et al., 1991, 1993; Wade et al., 1997; Krahn et al., 1999; MacDonald, 2000).

Research reports strongly suggest that OHCs adversely affect the immune system of animals at many levels (e.g., Davis and Safe, 1989; Kerkvliet et al., 1990; Andersson et al., 1991; Tryphonas et al., 2000). Enhanced vulnerability to infectious agents is a concern with immune suppression (e.g., Imanishi et al., 1980) and thus could be an underlying factor to marine mammal mortality events (even though the diagnosis is "viral"). Considering immunotoxic effects of OHCs are well characterized in laboratory animals, it should be noted that some similar correlations have been demonstrated in wild and captive marine mammals (Lahvis et al., 1995; De Swart et al., 1996; De Guise et al., 1995b, 1998; Ross et al., 2000; van Loveren et al., 2000). However, the correlative nature of these findings needs to be emphasized and more direct evidence is needed that establishes a cause-effect relationship with a recognized mechanism. As emphasized for evidence of effects for East Greenland polar bears, this provides stronger, direct evidence as opposed to a "weight of evidence" from multiple associative effects indicators.

A daunting enterprise is to consider the very realistic exposure scenarios that involve chemical mixtures. Consideration of single chemical toxicity is easier for study (actual toxicity) and assessing risk (potential toxicity). Levin et al. (2005) and Mori et al. (2006) indicated there is increasing evidence to support that OHCs can produce immunotoxic effects in marine mammals as mixtures of

OHCs on phagocytosis and lymphocyte proliferation, respectively. All species (marine mammals and mice) were not equally sensitive to the adverse effects of OHCs on either neutrophils or monocytes phagocytosis. Except for harbour seals, all mixtures that significantly modulated neutrophil or monocyte phagocytosis contained at least one non-coplanar PCB. The authors indicated non-coplanar congeners explain variability in phagocytosis responses. Mori et al. (2006) determined OHCs significantly altered lymphocyte proliferation in the species tested (mostly non-coplanar PCBs). Synergistic (non-additive) and antagonistic interactions between OHCs were detected in most of the species tested and this highlights the complexity of considering chemical mixtures. The dioxin TEQ approach and the traditional mouse model both failed to predict experimentally induced effects on both phagocytosis and lymphocyte proliferation in the marine mammals tested in this *in vitro* system, thus reducing confidence in TEQs and mouse models in risk assessment of OHC mixtures for marine mammal immune systems (Levin et al., 2005; Mori et al., 2006). Testing the relative sensitivity to immunomodulatory effects of contaminants (including contaminant mixtures) for varying marine mammals likely have important implications for risk assessment, conservation and management. However, dependence on *in vitro* models still allows for a great deal of uncertainty. Although there are larger ethical issues, consideration is warranted of limited *in vivo* studies with captive odontocetes (especially beluga whales) to improve basic understanding of the immune system in concert with *in vitro* methods. We need to know what stressor(s) can affect immunity, and what may result with respect to adverse health outcomes (e.g., opportunistic cases presented). Levin et al. (2005) and Mori et al. (2006) indicated phylogeny does not predict immune system toxicity of OHCs. To highlight the complexity of this issue the authors indicated; "Overall, our data suggest the presence of species-specific sensitivities to different mixtures, in which OCs interactions may be complex and that may exert their effects through dioxin-like or dioxin-independent pathways.". These types of effects may be involved with recent epizootics, especially harbour seals (Ross et al., 1995, 2000; van Loveren et al., 2000). These negative effects are also consistent with the infections caused by opportunistic agents as observed in SLE beluga (Martineau et al., 1994).

Cook Inlet (Alaska) belugas have not been as intensively assessed as for the SLE. POP/OHC data are available (Krahn et al., 1999; Becker, 2000) but there is very limited live capture or necropsy based information on health and disease status. The Cook Inlet belugas are know to have much lower concentrations of OHCs than those which have been reported for belugas throughout Alaska, as well as for western Hudson Bay beluga (Letcher et al., 2000b) (Table 1), and much lower than SLE whales. In the case of Cook Inlet belugas, it was suggested that a different source (geographic or food web) of these compounds may exist. Again, this indicates the need to take great caution when comparing possible effects among regions or stocks.

As was described for polar bears and sled dogs, CYP enzyme induction and catalytic activity has commonly been assessed in marine mammals as a biomarker for OHC exposure (e.g., White et al., 1994; Letcher et al., 1996; McKinney et al., 2004, 2006a; Wilson et al., 2005). For example, Wilson et al. (2005) and McKinney et al. (2004) examined CYP1A1 protein expression immunohistochemically in numerous organs of beluga whales from the Arctic (western Hudson Bay) and SLE. They concluded that the pattern and extent of CYP1A1 staining in whales from all three locations were similar to those seen in animal models in which CYP1A has been highly induced, indicating a relatively high-level expression in these whales. CYP1A1 induction has been related to toxic effects of planar, aromatic and dioxin-like compounds including PAHs in some species by activation via biotransformation of parent compounds to carcinogens (or other actions). In SLE beluga whales, the apparently induced CYP1A1 expression in combination with relatively high concentrations of OHC and PAH contaminants (and metabolites) indicated that CYP1A1 could be involved in the development of neoplastic lesions in SLE whales. The induction of enzyme in itself is not a toxic response but is important in understanding bioactivation and the response of the whales (e.g., McKinney et al., 2006a). McKinney et al. (2006a,b) reported on PBDEs and PCBs and OH- and/or $MeSO_2$-containging metabolites in the liver of beluga whales from SLE in comparsion to Western Hudson Bay (Tables 1 and 2), as well as looking at the PCB and PBDE congener-specific *in vitro* metabolism using liver microsomes from Western Hudson Bay individuals.

2.2.2. Pinnipeds

Some pinniped species have demonstrated associations with adverse health effects, as well as apparent induction of xenobiotic-metabolizing enzyme systems (e.g., CYPs) and OHC metabolite formation, and concentrations of some OHCs. The present pinniped section focuses on ringed seal and grey seal studies. Other species studied are worthy of brief mention as well, especially harbour seals and northern fur seals (*Callorhinus ursinus*). Beckmen et al. (1999, 2003) indicated that pups of primiparous northern fur seal dams were exposed to higher concentrations via milk than other pups, and these pups were immunologically suppressed in comparison to pups of multiparous (older) dams. Harbour seals represent a relatively well studied species and reports have associated POPs concentrations with enhanced susceptibility to infectious agents (e.g., Reijnders et al., 1997; van Loveren et al., 2000), immune suppression (Ross et al., 1995, 2000; DeSwart et al., 1996; Levin et al., 2005; Neale et al., 2005; Mori et al., 2006), and reproductive or endocrine disruption (Reijnders, 1980, 1986, 1994; Reijnders et al., 1999). Immunotoxicological effects have also been reported in grey seals (Sørmo et al., 2009). We encourage interested readers to consider the harbour seal, ringed seal and/or grey seal as a model(s) for effects of contaminants on pinnipeds, especially pups (Debier et al., 2003a,b; Jenssen et al., 2003; Sørmo et al., 2005).

By far, the majority of OHC effects-related reports have been on Arctic and non-Arctic populations of ringed seals, although it is also important to point out the apparent adverse health effects of OHCs reported for ringed seals primarily from the Baltic Sea region (e.g., Helle et al., 1976a,b, 1983; Olsson et al., 1992, 1994; O'Hara and Becker, 2003; Nyman et al., 2003; Routti et al., 2008a) and the Dutch Wadden Sea (Reijnders, 1980, 1986). As described in O'Hara and Becker (2003), linking contaminants to health effects and/or population declines in pinnipeds occurred in earlier studies of ringed seals as well as for grey and harbour seals in the Baltic Sea during the 1980 s (e.g., Olsson et al., 1992, 1994). Other studies have shown the utility of the harbour seal to assess OHCs with respect to the immune system, thyroid, and vitamin A status (e.g., Mos et al., 2002, 2006, 2007a,b; Tabuchi et al., 2006). An apparent decline in some populations of seals occurred in the Baltic during the 1950 s and a hypothesis that OHCs may be involved was formulated (Olsson et al., 1992). Critical to this evaluation was the observation of reproductive impairment and symptoms suggesting immune dysfunction, pathology of bone tissue, proliferation of gastrointestinal parasites and lesions. Studies of free-ranging grey seals and ringed seals from the Baltic Sea (Bergman et al., 2001) have shown an association between OHCs and renal lesions. In dose–response and case-control experiments with OHCs, toxic effects on renal tissue have been found in rats (Bruckner et al., 1974; McCormack et al., 1978; Wade et al., 2002). Impacts on recruitment were documented as decreases in fecundity concurrent with lesions (abnormalities) of the female reproductive organs (i.e., uterine stenosis or occlusions) (Olsson, 1978' Olsson et al., 1994; Helle et al., 1976a, 1983). A 60% decrease in the number of females becoming pregnant occurred in ringed seals from PCB-contaminated Bothnian Bay (Helle et al., 1976a). O'Hara and Becker (2003) elaborated on the above with a focus on grey seals, and the strength of this study was the intensive assessment of animals for multidisciplinary evaluation with a pre-planned approach to

processing (post mortem examination and sampling with follow up analyses) of stranded animals. This well designed approach could be a model for assessing the health and potential impacts of contaminants on arctic pinnipeds (ringed seal) by region either via hunter kill, bycatch or stranded opportunities. This above approach used qualitative, semi-quantitative and quantitative measures to get an overall "picture" of the seal epidemiology. Numerous organ systems appear to be involved with the clinical presentation but adrenal changes (adrenocortical hyperplasia and adenomas) may be driving the other observed changes as the complex of lesions and tissue changes are consistent with hyperadrenocorticism (e.g., Cushing's syndrome). Temporal relationships with decreasing OHCs in seals and the reduction of uterine obstructions with a concurrent increase in pregnancies offer additional evidence of a correlative link. However, O'Hara and Becker (2003) noted that Finnish scientists still report relatively high prevalence of uterine occlusions in ringed seals of the Baltic Sea. Debier et al. (2003a,b) emphasized the importance of lactation and pup (grey seal) exposure to PCBs and that exposures for this cohort may remain high. For seals it should be emphasized that not only the adrenal gland should be considered as a target, but some vitamins (e.g., vitamin A) and THs could be linked with the adrenal gland and the noted lesions and clinical effects via EDCs and possibly other OHCs (Hall et al., 2003; Jessen et al., 2003; Sørmo et al., 2005; Routti et al., 2008a). It is critical to consider the numerous direct and indirect positive and negative endocrine feedback mechanisms involved and that identifying the "primary" target (e.g., receptor) and lesion (e.g., histological change or altered enzyme function) is daunting without controlled studies.

In vivo studies of harbour seals fed contaminated Baltic fish showed a cause-effect relationship between OHC exposure and effects on humoral (antibody response) and cell-mediated (lymphocyte proliferation) immunity (De Swart et al., 1994, 1995; Ross et al., 1995, 1996a,b,c). In a study on free-living Baltic and Atlantic grey seal pups, it was shown that T-cell and T/B-cell mitogen responses were significantly lower in the more PCB-contaminated pups from the Baltic Sea as compared to the reference pups from the much less contaminated coast of Norway (Sørmo et al., 2009). It was shown that dioxin-like mono-*ortho* PCBs explained the variation of immunosuppressive responses.

Considering these relatively low concentrations in the western Arctic this review of apparent adverse health effects focuses on the eastern Arctic. However, reference material is critical for any study and matched samples and analyses (chemical and health) from populations with varying exposures to OHCs would be more powerful then isolated assessments of single populations. The OHCs may be decreasing but other OHCs may not be and some may be increasing, thus adverse effects may be maintained or arise due to chemicals other than OHCs that have been identified and are routinely measured in wildlife.

Similar to the Arctic species discussed thus far, there is no evidence or study that exposure of pinnipeds to PFC such as the highly bioaccumulative PFOS is associated with effects. Bossi et al. (2005a,b) report that perfluorinated acids were detected in livers of fish, birds and marine mammals from Greenland and the Faroe Islands (Table 1) indicating another OHC class of consideration with respect to potential adverse health effects. As has been shown for East Greenland polar bears, over the last few decades PFOS continues to increase and biomagnification of PFOS has been shown for its marine food chain (Bossi et al., 2005b; Dietz et al., 2008).

2.2.3. Other marine mammals

In free-ranging cetaceans, OHC immunotoxic effects, through mitogen-induced lymphocyte response and IgG concentration, have been suggested in bottlenose dolphins (*Tursiops truncatus*) (Lahvis et al., 1995), striped dolphins (*Stenella coeruleoalba*), and harbour seal (Troisi et al., 2001), as well in SLE beluga whale as was described in the previous sub-section (Martineau et al., 1994, De Guise et al., 1995, 1998). In harbour porpoise the concentrations of some OHCs have shown strong correlative relationships with thymus atrophy likely by increasing lymphocyte depletion from lymphatic organs (Siebert et al., 2002). Exposure of mice to BDE-47, the dominant PBDE congener found in Arctic wildlife tissues, suppressed the proliferation of lymphocytes and the production of antibodies (Darnerud and Thuvander, 1998). Likewise thymotoxic effects occurred in mice exposed to BDE-71 (Fowles et al., 1994). Siebert et al. (2002) also found a correlation between elevated concentrations of *p,p′*-DDE and spleen depletion in harbour porpoise. In wildlife, histopathological changes in lymphoid organs have been correlated to concentrations of OHCs in harbour seal, grey seal, ringed seal and harbour porpoise (Bergman and Olsson, 1985; Schumacher et al., 1993; Bergman et al., 2001; Siebert et al., 2002).

Some non-arctic marine mammal species or stocks studies offer insights to potential adverse effects of OHCs (and/or associations with other stress factors). PCBs are a factor found to be strongly associated with harbor porpoise mortality as potential immunosuppressants (e.g., Jepson et al., 1999, 2005). Jepson et al. (2005) described a significant, positive relationship between PCB concentrations and nematode burdens in harbour porpoise from the UK. The observed association was confounded by sex, age and cause of death and the PCBs were clearly not the sole determinants of nematode burdens; but a role was suspected. These parasite infestations may also be associated with infectious agents that contribute to mortality (e.g., Jepson et al., 2000; Jepson, 2003), most of which were pneumonias associated with various combinations of parasitic, bacterial and mycotic agents. The risk of infection from PCB exposure in the harbour porpoise in a controlled situation was recently reported by Hall et al. (2006).

2.2.4. Toxicokinetics and biotransformation and enzyme systems

As already described for ursids, canids and cetaceans, a lot can be learned about how animals respond to OHC exposure via assessments of e.g., OHC enantiomer selective processes and the generation and retention and/or accumulation of specific metabolites. For example, Warner et al. (2005) evaluated chiral PCBs in biota from the Northwater Polynya (NOW) in the Canadian Arctic to examine potential biotransformation of chiral PCB atropisomers, including ringed seals. Highly non-racemic enantiomeric fractions were observed in ringed seals and racemic enantiomeric fractions were found in prey (zooplankton and fish). These findings demonstrated a stereoselective accumulation and/or biotransformation of individual PCB stereoisomers. As for the legacy OHCs, congener-specific accumulation and food chain transfer of PBDEs has been documented for ringed seals and its food web. Wolkers et al. (2004) recently evaluated the congener-specific accumulation of PBDEs in polar cod to ringed seal from Svalbard (Table 1). The concentrations were relatively low with congeners 47, 99, and 100 as most dominant. In ringed seal the pattern was simple as compared to polar cod, with BDE-47 representing 90% of total PBDEs. Wolkers et al. (2004) considered differences in concentrations and patterns to be a result of differences in PBDE metabolism and accumulation, although consideration of variations in prey was not adequately considered. Regardless, these profiles are important to consider with respect to the response of the host. In studies on CYP enzyme activity, OHC levels and patterns and OHC metabolism in ringed seals, there are three very recent reports contrasting individuals from the exposure contrasted Baltic Sea and Svalbard populations (Tables 1 and 2). Routti et al. (2008b) reported that animals from the two populations were contrasted by the activity of CYP enzymes (as measured by EROD, benzyloxyresorufin-*O*-dealkylation, methoxyresorufin-*O*-demethylation and pentoxyresorufin-*O*-dealkylation activities) and Phase II activities (as measured by uridine diphosphophate glucuronosyl transferase and glutathione-*S*-transferase (GST) activities). The level of ΣPCBs had

a positive impact on CYP and GST enzyme activities leading to biotransformation of several PCB congeners, which were precursors for the major OH-PCBs (plasma) and $MeSO_2$-PCBs (liver) detected in seals from both populations. For the same wild seal cohorts, Routti et al. (2009a) reported that among organochlorine pesticides, *p,p′*-DDE and ΣCHLs were the highest in concentration, and with increasing hepatic contaminant concentrations and activities of CYP enzymes, the concentration ratios of 3-methylsulfonyl-*p,p′*-DDE/*p′p*-DDE and pentachlorophenol/hexachlorobenzene increased. Relative concentrations of the CHL metabolites, oxychlordane and heptachlor epoxide, to ΣCHLs were higher in the seals from Svalbard compared to the seals from the Baltic, while the trend was opposite for *cis*- and *trans*-nonachlor. It was concluded that the observed differences in the OHC patterns in the seals from the two populations are probably related to the catalytic activity of xenobiotic-metabolizing enzymes, and also to differences in dietary exposure. Finally, and again for the same ringed seal cohorts, Routti et al. (2009b) reported that ΣPBDE concentrations in liver were six times higher in the ringed seals from the Baltic Sea compared to the seals from Svalbard. BDE-47 was the dominant congener, and the BDE-47/ΣPBDE ratio was higher in the seals from Svalbard compared to that for Baltic seals, while the trend was opposite for BDE-153 and -154. In plasma samples, OH-PBDEs were detectable in 74 % and 93 % of samples from Svalbard and Baltic Sea, respectively and the congeners dominated by bioaccumulation of naturally occurring congeners. However, low levels of 3-OH-BDE47 and 4′-OH-BDE49 were detected in the higher contaminant exposed Baltic ringed seals, which suggested minor oxidative biotransformation of BDE-47. In the Baltic seals, relative concentrations of BDE-153 and -154 to ΣPBDEs increased and BDE-28/ΣPBDE decreased with increasing ΣOHC concentration, which suggested BDE-153 and -154 are more persistent than BDE-28. In the case of OH-PCBs and OH-PBDE formation, and as suggested for e.g. polar bears, this represents a biotransformation mechanism by which organohalogens are "activated" to potential EDCs in ringed seals.

2.3. Birds

In the present assessment, the review of OHC exposure and association to effects in birds includes species that spend at least some portion of the year (e.g., breeding season) in the Arctic. With respect to these species (e.g., American kestrel) there are recent captive dosing studies with PBDEs have shown effects in exposed birds versus controls, and thus these studies are highlighted in the present review.

2.3.1. Terrestrial — American kestrel and peregrine falcon

2.3.1.1. Endocrine system and vitamins. Experiments with PCB-exposed American kestrels showed that both baseline and stress-induced corticosterone levels were lower compared to control birds of the same age (Love et al., 2003). This suggests that PCB exposure can impair the corticosterone stress response and increase the birds' susceptibility to environmental stressors. It has also been reported that kestrels exposed to PCBs had significantly depressed TH levels compared to unexposed individuals (Smits et al., 2002). Moreover, in another study, eggs of American kestrels were injected with environmentally relevant concentrations of penta-BDE congeners (DE-71 technical mixture), and the nestlings were fed doses of this mixture for 29 days post-hatching. The exposed kestrel chicks had lower plasma T_4, plasma retinol, hepatic retinol and retinyl palmitate levels compared to control birds (Fernie et al., 2005a,b). In this same investigation, PBDE exposure also induced hepatic oxidative stress (i.e. increased GSSG:glutathione ratio, increase in lipid oxidation and increased oxidized glutathione), with more pronounced effects observed in females.

2.3.1.2. Carotenoids and iris color. Carotenoids are disproportionately components of animal colour signals such as those used in sexual communication and signalling between offspring and their parents, and in warning colours (Møller et al., 2000). They are a large group of more than 600 different biochemicals, with similar properties, synthesised by bacteria, fungi, algae and plants. The signalling functions of carotenoids are reflecting other physiological properties of these biochemicals. They play important roles in immunoregulation in vertebrates by stimulating the production, capacities and functions of different immunological components (Bendich, 1989; Chew, 1993; Olson and Owens, 1998). Bortolotti et al. (2003a) showed experimentally that PCB dosing in American kestrels disrupted both color expressions and plasma carotenoid levels; that is, the breeding PCB-exposed birds became duller in plumage relative to the controls. In winter, adult males exposed to PCBs were duller, while juveniles were brighter than control birds. It was suggested that PCB confounded carotenoids through endocrine disruption (Bortolotti et al., 2003a). Also, it has been reported that PCB exposure altered the iris color of American kestrels, which may indicate that PCB has the potential to alter important social signals in birds (Bortolotti et al., 2003b).

2.3.1.3. Reproduction. A recent study by Fernie et al. (2009) was reported on captive American kestrel females dietarily exposed to environmentally relevant concentrations of DE-71 mixture and unintentionally to HBCD. Relative to control birds there was delayed egg laying and smaller eggs being laid, thinner eggshells and differential weight loss during embryonic development, and reduced fertility and reproductive success (Fernie et al., 2009). The degree of egg shell thinning in the ΣPBDE and HBCD exposed group was comparable to previous studies with captive kestrels exposed to 15000 ng/g of DDT (Porter et al., 1969). In the exposed kestrels the ΣPBDE and HBCD concentrations in eggs were 1130 ng/g ww and 16 ng/g ww, respectively. In the control bird eggs the ΣPBDE and HBCD concentrations were 288 ng/g ww and 3 ng/g ww, respectively. A study of peregrine falcon diets in British Columbia showed that a 10% inclusion of prey species such as starlings, robins, gulls and magpies result in *p,p'*-DDE concentrations in falcon eggs greater than 15000 ng/g, and negative reproductive effects would be expected based on these levels. In fact, only pigeons were considered a safe diet for peregrine falcons. These assessments give a plausible explanation as to why peregrine falcons still cannot overcome the difficulties related to their establishment in certain areas (Elliott et al., 2005). Moreover, a recent study on peregrines from Sweden showed that the average brood size for individual females decreased with increasing concentrations of ΣPBDE in eggs, suggesting that PBDEs might influence reproduction in this species (Johansson et al., 2009). In reference to Table 3, thus far and recently in whole eggs for any Arctic bird, no ΣPBDE concentration has been reported higher than ~9 ng/g ww as shown for black guillemot eggs from East Greenland (Vorkamp et al., 2004), and for HBCD < 1 ng/g ww in eggs of Arctic tern from Svalbard (Jenssen et al., 2007) and ivory gulls from the central Canadian high Arctic (Braune et al., 2007). It would appear that there is currently a low risk from ΣPBDE and HBCD exposure in the eggs of Arctic birds with respect to the reproductive and developmental effects reported for captive kestrels in Fernie et al. (2009).

2.3.1.4. Development. Experiments with American kestrels have demonstrated developmental effects associated with exposure to both PCBs and PBDEs (Fernie et al., 2003a,b, 2006). In these studies, it was found that the development of second generation birds was altered by *in ovo* exposure of the parents to PCBs; i.e., the growth patterns levels were altered in the first generation and the TH levels were altered in second generation offspring as a result of PCB exposure. It was suggested that these changes may be caused via different mechanisms including maternal deposition of PCBs, paternal behavior or

neurobehavioral and endocrine-thyroid functions in the nestlings (Fernie et al., 2003a). Reported developmental effects related to PCB exposure also included embryonic underdevelopment and edema, and increased incidences of multiple deformities within the kestrel clutches (Fernie et al., 2003b). In American kestrel eggs that were injected with environmentally relevant concentrations of penta-BDE congeners, and chicks that were also fed doses of this mixture for 29 days, PBDEs did not affect hatching and fledging success (Fernie et al., 2006). However, the PBDE-exposed nestlings ate more food, grew faster and reached a larger body size. It was suggested by the authors that larger nestling size may be detrimental to their bone structure and may carry excessive energy costs. It has also been shown that PCB-exposure in American kestrels alters brood patch size in both breeding and non-breeding birds (Fisher et al., 2006a).

2.3.1.5. Immune system. Immunological effects have been documented in American kestrel males exposed to PCBs relative to controls; for example, an increase in total white blood cell counts associated with a decrease in heterophile-to-lymphocyte ratio (Smits et al., 2002). In addition, PCB-exposed birds had a significantly greater skin response to PHA (T-cell mediated immunity) than did the controls. In another study in which American kestrel eggs were injected with an environmentally relevant penta-BDE mixture, and the chicks fed doses of this mixture for 29 days after hatching, the PBDE-exposed nestlings had increased PHA responses and a reduced antibody-mediated response (Fernie et al., 2005a). In addition, in kestrels exposed to PBDEs were found alterations in the spleen (fewer germinal centers), bursa (reduce apoptosis) and thymus (increased macrophages).

2.3.1.6. Behaviour. Captive American kestrels were exposed to a PCB mixture prior to pairing and throughout the entire incubation period (Fisher et al., 2006b). The exposure resulted in longer incubation periods and altered incubation behavior; i.e., seven of the 14 behavior variables were related to the PCB treatment, but the effects were largely biased toward disrupted male behavior. Moreover, Fernie et al. (2003a) found that dietary exposure to PCBs resulted in particularly aggressive courtship interactions, clutch abandonment and the occurrence of cracked eggs. Fernie et al. (2008) also reported that American kestrels exposed to a relevant PBDE-containing DE-71 mixture over a short period showed alteration in the quality of the pair bonds, and both males and females showed an altered reproductive behavior pattern.

2.3.2. Marine — Glaucous gulls

2.3.2.1. Endocrine system. A number of glaucous gull field studies carried out on Bjørnøya (Bear Is., Svalbard) during the incubation period have reported significant relationships between circulating levels of endogenous hormones and blood (or plasma) concentrations of major OHC classes, including OCs, BFRs and OH-containing analogues. Overall, these studies strongly suggest that the high exposure to OHCs may contribute at disrupting endocrine functions and homeostasis in nesting glaucous gulls from Bjørnøya.

Using a low and a high POP/OHC-exposed nesting colony selected based on previously documented differences in feeding ecology (Bustnes et al., 2000), Verreault et al. (2004) reported that incubating male glaucous gulls from the most contaminated colony exhibited significantly lower plasma levels of T_4 compared to the less exposed colony. As summarized in Table 5, with respect to effects of OHCs on THs, for Svalbard glaucous gulls significant negative relationships were reported between blood ΣPCB, ΣDDT, HCB and oxychlordane concentrations, and plasma T_4 levels. The lower levels of T_4 in males were associated with a slight, although non-significant level increase of the metabolically active T_3. No significant result was found for females. However, in a subsequent study, Verreault et al. (2007a) reported for Bjørnøya glaucous gulls, that for both males and females, levels of free and total T_4 and T_3 were not associated significantly with the variation of concentrations of any of the OHCs determined. In another study using the same glaucous gull nesting sites on Bjørnøya, circulating levels of progesterone (P_4) in incubating males were found to be significantly and positively correlated with plasma concentrations of PCBs, DDTs, chlordanes and PBDEs (Verreault et al., 2006). No such correlation was found for females as well as between concentrations of any of the selected OHCs and plasma levels of testosterone (T) in either sex. The 17β-estradiol (E_2) was below the radioimmunoassay detection limit in both male and female plasma. In a follow up study, Verboven et al. (2008) reported positive correlations between concentrations of selected OCs and BFRs, and T and E_2 levels in the yolk of unincubated, third-laid eggs of glaucous gulls. In this study, eggs from nests in which two sibling eggs hatched or failed to hatch differed in POP profiles (i.e., contribution of different POP classes) and in the relative levels of T and E_2.

A study was undertaken to examine the variation of plasma prolactin (PRL) levels in relation to POP exposure in incubating glaucous gulls from Bjørnøya (Verreault et al., 2008b). PRL is an anterior pituitary hormone that is closely associated with the reproduction, and particularly in parental behaviors. Levels of PRL were determined in plasma collected from males and females 3 min following capture (i.e., baseline PRL) and after a 30 min standardized capture and restraint protocol (i.e., handling PRL). The baseline PRL levels and the rate of decrease in PRL levels during this 30-min capture/restraint period tended to vary negatively with plasma POP concentrations (OC, BFR and OH-metabolite concentrations were extracted using principal component analysis) in males, but not in females. No significant relationship was found between plasma handling PRL levels and POP concentrations in either sex.

A major concern is that TH-dependent processes, such as thyroid hormone transport, are susceptible to chemical stress and can be disrupted by thyroidogenic, xenobiotic compounds accumulated in an organism. TTR, thyroid hormone binding albumin (ALB), and thyroid binding globulin (TBG) are the major hormone transport proteins of THs in all vertebrates including birds (McKinnon et al., 2005). As reported recently by Ucán-Marin et al. (2009a,b), for the first time for a bird species TTR and ALB cDNA were isolated, cloned and sequenced from the brain and/or liver of Svalbard glaucous gull. Identical TTR nucleotide and amino acid sequences were obtained for liver and brain (Ucán-Marin et al. (2010). Recombinant TTR (rTTR) was expressed and purified, and used to generate concentration dependent, competitive TTR binding curves with each of T_3 or T_4 by treatment with CB-187, BDE47, 4-OH-CB187, 6-OH-BDE47, 4′-OH-BDE49, 4-MeO-CB187, and 6-MeO-BDE47. Relative to the nonsubstituted BDE-47 and CB-187 and their MeO-substituted analogs, the OH-substituted analogs all had greater affinity and more potent competitive binding than both T_3 and T_4. Similar results were found using the same ligands and concentrations in competitive binding studies with gull rALB protein (Ucán-Marin et al., 2009; 2010). Furthermore, known circulating levels of 4-OH-CB187, and to a lesser extent for 6-OH-BDE47, and 4′-OH-BDE49, in the plasma of free-ranging Svalbard glaucous gulls (Verreault et al., 2005b, 2006) (Table 2) were comparable to the concentration of *in vitro* competitive potency of T_3 and T_4 with gull rTTR and rALB. It was suggested that environmentally relevant and selected OH-containing PCBs, and to a lesser extent OH-PBDE congeners have the potential to be physiologically effective in these gull species via perturbation of T_3 and T_4 transport. In the context of overall thyroid hormone binding in birds, OHC binding interactions with TTR may be of lesser importance than ALB since in birds the proportion of circulating TH-binding transport proteins is low for TTR. According to McNabb et al. (2003) in chicken the circulating T_4 is bound 75% to ALB, 17% to TTR, and 7.5% to an α-TBG.

2.3.2.2. Reproduction. In glaucous gull females on Bjørnøya, there was increasing frequencies of non-viable eggs with increasing OHC levels

in the blood. Moreover, chicks from females with high OC residues were in relatively poor body condition (Bustnes et al., 2003), and the growth rate was relatively poor in these chicks. The latter effect was only found in females having long feeding trips, suggesting a combined effect of OHCs and potential natural stressors (Bustnes et al., 2005). In a study by Verboven et al. (2009a), Bjørnøya glaucous gulls exhibiting relatively high plasma concentrations of ΣCHL and HBCD were found to lay smaller third-laid eggs in a clutch of three. Eggs into which females had deposited relatively low concentrations of ΣPCB and relatively high concentrations of ΣDDT also were smaller. Moreover, positive correlations were reported between plasma POP patterns (i.e., relative contribution of compounds to ΣOHC) in glaucous gull females and changes in total water and lipid content in yolk of their eggs. These results suggest that egg quality may not only be affected by the direct transfer of OHCs from the mother to the egg, but also through associated changes in egg size and composition.

2.3.2.3. Development and survival. In glaucous gulls from Bjørnøya, there was a significant drop in adult survival rate with increasing blood residues of OHCs. For example, a 10-fold increase in the levels of oxychlordane in the blood (from 5 to 50 ng/g wet weight) was associated with a 29% reduction of the survival rate of females and 16% in males (Bustnes et al., 2003). Bustnes et al. (2002) found that glaucous gulls with high blood concentrations of OHCs, especially HCB, were more likely to have asymmetric primary wing feathers; i.e., differences in the length of the feathers between the right and the left wing.

2.3.2.4. Immune system. In glaucous gulls from Bjørnøya, the levels of white blood cells were positively related to blood concentrations of several major OHCs, and the immune response to novel antigens was significantly lower in females with high OHC concentrations, especially HCB (Bustnes et al., 2004). Furthermore, Sagerup et al. (2000) found that individuals with high OHC levels had higher parasite (nematodes) burdens than birds with low levels, and a parasite removal experiment found some evidence of a trade-off between immune function and defense against OHCs (Bustnes et al., 2006a). This study showed that in untreated male glaucous gulls there was a negative relationship between nesting success and OHC concentrations, while in males receiving an anti-parasite drug there were no such effects. In a laboratory design by Sagerup et al. (2009), chicks of glaucous gulls were given a naturally contaminated marine diet (seabird eggs) or a control diet (hen eggs). All chicks were immunized with herpes virus (EHV), reovirus (REO), influenza virus (EIV) and tetanus toxoid (TET). After eight weeks of feeding, the experimental group fed seabird eggs had 3- to 13-fold higher concentrations of HCB, oxychlordane, *p,p′*-DDE and PCBs relative to the control group fed hen eggs. The experimental group had significantly lower antibody titre against the EIV and lower concentration of IgG and immunoglobulin-M (IgM) in the blood. The experimental group also had a significantly higher peripheral blood lymphocyte response to PHA and to spleen lymphocytes stimulated with Con A and PCB. This indicates that the occurring OHC exposure in the Arctic affects the immune system and reduces the infection resistance of glaucous gull chicks.

2.3.2.5. Bioenergetics. Based on previous findings suggesting that circulating thyroid hormone homeostasis may be perturbed in highly POP/OHC-exposed glaucous gulls (males) breeding on Bjørnøya (Verreault et al., 2004), a follow up study was conducted to investigate the associations between plasma T_4 and T_3 levels, plasma POP concentrations and basal metabolic rate (BMR) (i.e., minimal oxygen consumption) (Verreault et al., 2007a). In both males and females combined, negative associations were found between BMR and plasma concentrations of ΣPCBs, ΣDDTs and particularly ΣCHLs, thus suggesting potentially altered functions of the basal metabolism. However, levels of free and total T_4 and T_3 were not associated significantly with the variation of BMR or concentrations of any of the OHCs determined. A companion study by Verboven et al. (2009b) using the same colonies on Bjørnøya showed the nest temperature of glaucous gull males and females was negatively correlated with the concentrations of certain OHCs, BFRs (PBDEs and HBCD) and OH-PCB metabolites in plasma of the incubating parent. To test the parental control of incubation conditions in relation to OHC exposure, the energetic cost of incubation was augmented by artificially increasing clutch size from two to four eggs using dummy eggs. Clutch enlargement in glaucous gulls was followed by a decrease in nest temperature, although this decrease was not associated with plasma OHC concentrations.

2.3.2.6. Genotoxicity. The formation of DNA adducts was investigated in liver of captive glaucous gulls in Ny-Ålesund (Svalbard) fed hen eggs (control group) or naturally POP/OHC-contaminated seabird eggs (exposed group) (Østby et al., 2005). DNA adducts were detected in liver samples of all birds with the exception of one individual, and the exposed group had significantly higher levels of DNA adducts relative to the control group. However, there was no correlation between DNA adduct levels and blood concentrations of the selected OCs. Using the same dietary-exposed glaucous gull cohorts in Ny-Ålesund, Krøkje et al. (2006) demonstrated that for males and females, the fraction of damaged metaphases (i.e., chromosomal aberrations) and DNA strand breaks in liver were quantitatively higher in the exposed group relative to the control.

2.3.2.7. Toxicokinetics and biotransformation enzyme systems. Hepatic homologues to mammalian CYP1A proteins were quantified in captive glaucous gulls in Ny-Ålesund (Svalbard) fed hen eggs (control group) or naturally POP/OHC-contaminated seabird eggs (exposed group) (Østby et al., 2005). The levels of CYP1A protein in liver were significantly higher in males of the exposed group relative to those of the control group, and were positively correlated to the blood concentrations of most OHCs. The metabolism of OHCs such as PCBs and PBDE are not well understood in wildlife and particularly in birds (Hakk and Letcher, 2003; Letcher et al., 2000a). However, putative OH-PCB and OH-PBDE metabolites have been reported in the tissues of certain avian species (Table 2). Several OH-PCB and OH-PBDE congeners were recently quantified in the plasma of adult glaucous gulls from the Norwegian Arctic. i.e., 6-OH-BDE47, 4′-OH-BDE49, 4-OH-CB187, tended to dominate (Verreault et al., 2005a,b). As was described for ursids, canids and marine mammals, OH-PCBs in the plasma of birds is to CYP-mediated PCB biotransformation. However, some OH-PBDE congeners can also bioaccumulate in aquatic food webs as natural products produced by marine organisms such as sponges and algae. As was reported by Ucán-Marin et al. (2010), several OH-PCB and OH-PBDE congeners can competitively and potently displace T_4 and T_3 from gull rTTR and rALB. As a consequence, this could result in the release of FT_4 and FT_3, which can enhance T_4 and T_3 metabolism and excretion.

2.3.2.8. Behaviour. In glaucous gulls on Bjørnøya, the time away from the nest site during incubation pauses was positively related to blood concentrations of OHCs, especially PCBs, suggesting endocrine or neurotoxic effects on the feeding behavior (Bustnes et al., 2001, 2005). A study by Verboven et al. (2008b) confirmed previous findings by Bustnes et al. (2001, 2005) suggesting that nest-site attendance (i.e., presence of the non-incubating parent) in Bjørnøya glaucous gulls was negatively correlated with plasma concentrations of major OHCs (e.g., organochlorines and BFRs). However, in this study the amount of time the eggs were being incubated was not associated with any of the organochlorine and BFR concentrations.

2.3.3. Marine — Great black-backed gulls

2.3.3.1. Reproduction. In a large scale study of great black-backed gulls breeding along the coast of northern Norway, several different

ecological variables suggested adverse relationships with OHCs (Helberg et al., 2005; Bustnes et al., 2008a). Reproductive variables such as laying date, egg size, nesting success, hatching condition of chicks and early chick survival were adversely correlated to blood concentrations of OHCs (PCBs, *p,p′*-DDE, HCB and oxychlordane) in both males and females. In general, these studies suggested that the concentrations and reproductive effects of OHCs were greater when the environmental conditions were poorer. More specifically, when there was little food available for the gulls, the levels of OHCs increased in their blood and the effects of OHCs became more pronounced.

2.3.3.2. Development and survival. Among great black-backed gulls at three colonies along the northern Norwegian Coast there was increasing wing feather asymmetry (i.e., differences in the length of the feathers between the right and the left wing) with increasing blood residues of OHCs at the site where birds exhibited the highest blood concentrations of OHCs (Bustnes et al., 2007). In great black-backed gulls breeding along the coast of northern Norway, there was a significant drop in adult return rate between the breeding seasons for birds that had more elevated blood residues of *p,p′*-DDE at one of the three study locations investigated (Bustnes et al., 2008a). In that particular colony the levels of OHCs were in general higher compared to the other two colonies.

2.3.3.3. Immune system. In breeding great black-backed gulls from coastal northern Norway, it was examined whether white blood cells and carotenoid color, both measurements related to immune status and function, were related to blood concentrations of OHCs (Bustnes et al., 2007). However, no correlation was found. This suggests that concentrations of OHCs were likely too low to result in measurable effects on these immune parameters.

2.3.4. Marine — Lesser black-backed gulls

In lesser black-backed gulls from the coast of northern Norway, the blood levels of most OCs quantified were lower compared to larger gull species such as the glaucous gull and the great black-backed gull (Bustnes et al., 2006b). However, the levels of *p,p′*-DDE were relatively high, which also was reported in a study of Finnish lesser black-backed gulls (Hario et al., 2000, 2004). This distinction was postulated to be the result of the bird's migration route as the majority of these lesser black-backed gulls winter in eastern Africa where *p,p′*-DDE is still used today in many areas (Hario et al., 2004; Bustnes et al., 2006b). No effects of *p,p′*-DDE were found on eggshell thickness in the Norwegian study (Bustnes et al., 2006b), but in Finnish gulls frequent chick deaths have been attributed to high loadings of *p,p′*-DDE as well as other OC compounds (Hario et al., 2000, 2004). In one Norwegian lesser black-backed gull colony, the probability of chick loss was higher in males with high blood levels of OCs, and the return rate of these individuals between the breeding seasons was negatively related to increasing OC levels (Bustnes et al., 2008b). Moreover, Bustnes et al. (2008c) reported that the blood levels of perfluorinated compounds (PFCs) were as high as those of OCs in lesser black-backed gulls, although PFSAs and PFCAs were not found to negatively affect any ecological parameters (Bustnes et al., 2008b).

2.3.5. Marine — Ivory gulls

One species that may be particularly vulnerable to lipid-soluble OCs is the ivory gull since it has a largely lipid-based diet from scavenging (e.g., seal and whale carcasses). The populations has also declined substantially over the last few years, e.g. in the Canadian Arctic (Braune et al., 2007). Eggs from ivory gulls were collected from the Canadian Arctic in 1976, 1987 and 2004 and analyzed for a wide range of OHCs (OC pesticides, PCBs, PCDDs and PCDFs, PBDEs and HBCD) (Braune et al., 2007). One objective in this study was to determine if the contaminant burdens in ivory gulls may have played a role in the population decline of the species. Concentrations of most OCs decreased or were stable over the time period, while those of BFRs generally increased, particularly for BDE47. The egg OC levels found in this study were in general lower compared to published toxicological threshold values for eggs of wild birds, but synergistic/additive sublethal effects could not be ruled out.

In a study of Svalbard and Russia Arctic ivory gull eggs, Miljeteig et al. (2007) found negative associations between eggshell thickness and concentrations of a wide range of contaminants including OCs, BFRs and selected PFCs (e.g., PFOS and several PFCAs). Comparisons of eggshell thickness between museum archived samples from 1930 and the eggs collected in Russia in 2006 showed a 13% reduction in eggshell thickness. The authors concluded that the ivory gull presently suffers from reproductive effects, potentially mediated by elevated OC levels. It was also concluded in this study that these findings may warrant further investigation as the levels of *p,p′*-DDE measured in ivory gull eggs were nearly as high as those reported in peregrine falcon and sparrowhawk eggs from Britain in the 1960 s.

Thirty-five eggs of ivory gulls were collected in the Norwegian (Svalbard) and Russian Arctic in 2006 (Miljeteig et al., 2007). Higher levels of organochlorine pesticides and PCBs were determined in these eggs compared to other Arctic seabirds (e.g., glaucous gulls and black-legged kittiwakes), with particularly high concentrations for *p,p′*-DDE. Positive correlations were reported between retinol and contaminant levels in the eggs, while concentrations of the antioxidant vitamin E were decreasing with increasing contaminant levels. The authors of this study suggest that the ivory gull may be affected by contaminant-induced oxidative stress.

2.3.6. Marine — Black-legged kittiwakes

Levels of vitamin A, retinyl palmitate and vitamin E were measured in plasma and liver of black-legged kittiwake hatchlings from Kongsfjorden (Svalbard) and Runde (an island along the coast of Northern Norway) (Murvoll et al., 2006a). No significant association was found between concentrations of OHCs (OCs and BFRs) in egg yolk sacs and vitamin levels or morphological variables (e.g., hatching, yolk sac and liver mass, hematocrit, and head and tarsus length). However, multivariate regressions showed a non-significant tendency for association between liver vitamin E levels and yolk sac OHC concentrations.

2.3.7. Marine — Northern fulmars

In a study of breeding northern fulmars from Bjørnøya, levels of total and unbound T_4 and T_3 were determined in plasma as well as retinol and retinyl palmitate levels in liver (Knudsen et al., 2007). Among the OHCs determined (OCs and polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs)) in blood and liver samples, only the di-*ortho*-CB-146 concentrations significantly and positively explained some of the level variation in total and unbound T_4 and T_3, retinol and retinyl palmitate. In another study by Mallory et al. (2007), liver levels of retinol and retinyl palmitate and plasma levels of retinol and total T_4 and T_3 also were determined in northern fulmars from two colonies in the Canadian Arctic: Cape Vera on northern Devon Island and Migratory Bird Sanctuary on Prince Leopold Island. None of these biomarkers significantly differed between male and female northern fulmars, or between the two breeding colonies investigated. No correlation was found between liver OC concentrations and total T_4 levels and retinol in plasma. However, this study reported significant negative relationships between circulating total T_3 levels and liver *p,p′*-DDD concentrations in both males and females; negative correlations between liver retinyl palmitate and pentachlorobenzene in females; and positive correlations between liver retinol and retinyl palmitate and heptachlor epoxide in males.

Relationships between liver OC concentrations, parasite (gastro-intestinal helminths) prevalence and physiological indices of chronic

stress (spleen size and heterophil:lymphocyte ratios) were examined in northern fulmars collected during the breeding season in Cape Vera, Nunavut (Canadian Arctic) (Mallory et al., 2007). Spleen size was not significantly related to either OC concentrations or presence of parasites (mainly cestodes). Liver OC concentrations and heterophil:lymphocyte ratios in northern fulmars having burdens of cestodes did not differ significantly from those in individuals with no or little cestodes at this breeding colony.

Hepatic EROD activity determined in breeding northern fulmars from Bjørnøya correlated positively with liver concentrations of TEQs based on concentrations of PCDDs/Fs and non-*ortho* and mono-*ortho* PCBs (G.W. Gabrielsen, personal communication). Moreover, in northern fulmars from Devon Island and Prince Leopold Island in the Canadian Arctic, significant positive relationships were found between hepatic EROD activity and liver concentrations of most of the OC classes monitored for (B.M. Braune, personal communication).

2.3.8. Marine — Eiders and other ducks

In a study of newly hatched common eider chicks from Kongsfjorden (Svalbard), Murvoll et al. (2007) investigated the retinol, retinyl palmitate and α-tocopherol status in plasma and liver as well as various morphological variables (e.g., hatching, yolk sac and liver mass, hematocrit, and head and tarsus length). Significant positive relationships were reported in this study between egg yolk sac concentrations of PCBs, HCH and oxychlordane, and liver vitamin E levels. However, none of the morphological traits were related to OHC concentrations in these common eider chicks.

Common eiders nesting in the Baltic Sea (eight colonies), which are exposed to high concentrations of potentially genotoxic PAHs and OHCs, and a less polluted area, the Beaufort Sea (two colonies), were investigated for genetic damage via analysis of DNA content variation in blood samples (Matson et al., 2004). No significant difference in genetic damage was observed in this study among the common eider colonies within either the Baltic Sea or the Beaufort Sea. However, common eider colonies from the Baltic Sea had significantly elevated estimates of genetic damage compared to those from the Beaufort Sea.

EROD activity was measured in liver of Steller's eiders (*Polysticta stelleri*) and Harlequin ducks (*Histronicus histronicus*) from Unalaska (high contamination) and Popof/Unga Islands (low contamination) in the eastern Aleutian Islands, Alaska (Miles et al., 2007). Hepatic EROD activity was significantly higher in Harlequin ducks compared to Steller's eiders, and significantly higher in individuals from industrial sites compared to those from nonindustrial sites. No relationship was found between blood PCB concentrations and EROD activity in any of these species. Dosing of captive Steller's eiders with known CYP1A inducers also yielded higher EROD activity, although the results indicated that wild Steller's eiders are exposed to CYP1A inducing OHCs at concentrations greater than those used in this laboratory design.

2.3.9. Guillemots

The plasma and liver status of vitamin A, retinyl palmitate and vitamin E as well as selected morphological variables (e.g., hatching, yolk sac and liver mass, hematocrit, and head and tarsus length) were investigated in newly hatched Brünnich's guillemot (thick-billed murre) chicks from Kongsfjorden (Svalbard) (Murvoll et al., 2007). Negative and significant relationships were found between yolk sac HCB, oxychlordane and *p,p′*-DDE concentrations, and liver α-tocopherol levels, although these relationships became weaker when liver mass was included as covariable. Moreover, morphological traits tended to be negatively, but non-significantly, related to egg yolk sac OC and BFR concentrations in Brünnich's guillemot hatchlings. In another investigation, levels of retinol and retinyl palmitate were quantified in liver of black guillemot nestlings from Saglek Bay (Labrador, Canada), which accumulate high PCB concentrations from contaminated marine sediments in the proximity of a former military site (Kuzyk et al., 2003; Environmental Sciences Group, 2002). Black guillemot nestlings from the highly and moderately PCB-exposed groups (Beach and Islands, respectively) generally exhibited lower liver levels of retinol and retinyl palmitate relative to the low PCB-exposed (reference) group, although some differences existed between males and females. Levels of total T_4 and T_3 were measured in thyroid glands and plasma samples of these nestlings, although no significant difference was found among the three PCB exposure groups. In contrast, tendencies in the dataset suggested that both plasma T and E_2 levels were elevated in black guillemot nestlings from both the Beach and Island groups, relative to the reference group. However, the important number of samples with non-detectable levels of these hormones (mainly T) hampered a more in depth statistical comparison. Furthermore, levels of plasma corticosterone did not vary as a function of the PCB exposure groups.

Cell-mediated immunity was examined in locally PCB-contaminated black guillemot nestlings from Saglek Bay (Labrador, Canada) via field measurement of the skin-swelling response to an intradermal injection of PHA (Environmental Sciences Group, 2002). Significant immune suppression, measured as a lower age-adjusted stimulation index, was found in the highly PCB-exposed nestlings (Beach group).

EROD and malic enzyme activities as well as porphyrin concentrations were determined in liver of black guillemot nestlings from Saglek Bay (Labrador, Canada) (Kuzyk et al., 2003; Environmental Sciences Group, 2002). Livers of nestlings collected from the high PCB-exposed group (Beach) were enlarged relative to the low PCB exposure group (reference) (significant for females only), and had higher EROD activity. Hepatic EROD activity also was elevated in nestlings from the moderately PCB-exposed group (Islands) compared to the reference group birds. Liver malic enzyme activity and porphyrin concentrations did not vary as a function of these PCB exposure groups.

Hatching success was estimated in black guillemot nestlings from Saglek Bay (Labrador, Canada) based on the ratio of the number of eggs that hatched to the number of eggs that were laid during the period July–September (Environmental Sciences Group, 2002). Hatching success rates were not different among the low (reference), moderate (Islands) and high (Beach) PCB-exposed groups, and were consistent with those reported elsewhere for black guillemot populations (Cairns, 1980).

Histological examination of reproductive systems was conducted in black guillemot nestlings from Saglek Bay (Labrador, Canada) (Environmental Sciences Group, 2002). Reproductive systems were examined qualitatively for any gross morphological differences in ovaries, oviducts, testes or Wolffian ducts, and compared among the three PCB exposure groups. In males, sections were analyzed for total area, medullary area, capsule area, number of Sertoli cells and number of primordial germ cells. Testes weights were also determined. Females were analyzed for number of oocytes, number of oocytes with deposits, oocyte stage, oocyte area, number of primordial germ cells and total ovary weight. Results of histology of black guillemot nestling's reproductive systems found evidence of altered reproductive development for males and, to a limited extent, females. In the case of males, structural abnormalities appeared to be present at higher frequencies among the high PCB-exposed group (Beach) and moderately PCB-exposed group (Islands) nestlings than among the low PCB exposure group (reference) nestlings. However, given the small sample size, no statistical justification was found for relating this apparent trend to PCB exposure. For females, statistical analysis of relative ovary weights and PCB exposure was suggestive of a possible relationship, but overall inconclusive.

2.3.10. Herons and shags

In great blue herons (*Ardea heridias*) and black-crowned night herons (*Nycticorax nycticorax*) on the St-Lawrence River in North America, there were differences in plasma and liver retinoid and

thyroid hormone levels between the colonies investigated, which was consistent with differences in levels of PCBs between these colonies (Champoux et al., 2002). In a companion investigation, plasma retinols were negatively correlated with several OCs in these birds (Champoux et al., 2006). It was also reported in this study that in great blue heron eggs, the molar ratio retinol:retinyl palmitate was strongly correlated with PCB and mirex concentrations. Moreover, in a study of European shag (*Phalacrocorax aristotelis*) nestlings, plasma retinol levels were negatively correlated with concentrations of PCBs and some OC pesticides (Murvoll et al., 2006b).

In black-crowned night heron, measures of genotoxic effects in bird embryos from more OC-contaminated colonies in Illinois, Minnesota and Virginia were the same as from the less contaminated colonies (Levengood et al., 2007).

In great blue herons and black-crowned night herons, differences in EROD activity and porphyrins were observed between colonies from the St-Lawrence River in North America, being consistent with differences in levels of PCBs between those colonies (Champoux et al., 2002, 2006). In another study, increased enzyme induction with increasing PCB levels also was found in black-crowned night heron embryos (Levengood et al., 2007). In great blue herons from the western USA, birds from breeding colonies with high concentrations of PCBs and *p,p′*-DDE had significantly lower nest attendance relative to reference colonies with lower levels of these contaminants (Thomas and Anthony, 2003).

Harris et al. (2003) reported that the predominant factors influencing reproductive success in great blue herons in 23 colonies along the southern coast of British Columbia was disturbance by humans and bald eagles combined with the loss and degradation of nesting habitats, but not the sublethal toxicity mediated by organochlorine concentrations measured in these birds.

In grey heron colonies from the UK, there has been high mortality of nestlings, many of these suffering from skeletal deformities. Dead chicks and eggs from these same colonies had levels of PCBs, PCDDs and PCDFs within the range sufficiently high to cause deformities (Thompson et al., 2006).

A recent field study on European shag in Northern Norway reported significant positive associations between FA of wing bone length of 21 days old chicks and hepatic concentrations CB-105, -118, -138, -153, and -180. There were no effects of other OHCs, such as PBDEs, DDTs, HCHs, chlordans and toxaphens on the FA. It was suggest that the effects of the PCBs on FA may be due to effects of these compounds on wing bone growth and structure (Jenssen et al., 2010).

Japanese studies have suggested that common cormorants (*Phalacrocorax carbo*) may suffer from oxidative stress due to chemically induced (OCs and other contaminants) formation of reactive oxygen and subsequent formation of antioxidant species and subsequent reduction of antioxidant resistance (Nakayama et al., 2006).

2.3.11. Eagles and ospreys

A long term study (1964–1999) of white-tailed sea eagles (*Haliaeetus albicilla*) from three different regions in Sweden (Baltic Sea Coast, inland central Sweden and Lapland) found highly significant correlations between nest productivity and *p,p′*-DDE levels in eggs (249 eggs from 205 clutches), and somewhat weaker effects of PCBs (Helander et al., 2002). In this study, the estimated lowest observed effect level (LOEL) in eggs for depressed productivity was 120 ug/g for *p,p′*-DDE and 500 ug/g for PCBs. Also, *p,p′*-DDE was related to eggshell thickness, but it was concluded that eggshell thinning may be a parallel syndrome of *p,p′*-DDE poisoning rather than the mechanism of reproductive failure. Moreover, at the Baltic Sea Coast colony there was a great improvement in the productivity of white-tailed sea eagles with reductions of *p,p′*-DDE and PCBs in the environment, and presently the production is almost the same as in lowest polluted areas such as the Lapland, and the Baltic population is increasing. This study is a strong demonstration of the time needed from the banning of a detrimental agent such as *p,p′*-DDT to recovery of the population (~25 years), and the mean brood size had not reached normal background level yet. A another study from southern Finland where OCs were measured in 11 dead white-tailed sea eagles, the organ levels of OC pesticides and PCBs were moderate, and not expected to cause adverse effects (Krone et al., 2006). In Greenland, levels of OC pesticides and PCBs in white-tailed sea eagles also were moderate and indicative of no health effect (Krone et al., 2004). In a large scale study of bald eagles (*Haliaeetus leucocephalus*) from different colonies in the Great Lakes area (North America), levels of *p,p′*-DDE and PCBs were measured in 309 nestlings from 10 subpopulations (Bowerman et al., 2003). Geometric mean concentrations of *p,p′*-DDE and PCBs were inversely related to productivity and success rates of eagles in nine of the 10 subpopulations. In Lake Superior in Wisconsin (USA), however, a temporal study (1989-2001) of bald eagles measuring *p,p′*-DDE and PCBs in nestling plasma failed to find any correlation between reproductive rate and contaminant concentrations (Dykstra et al., 2005). In this study, the *p,p′*-DDE and PCB levels were also below the estimated thresholds for impairment of reproduction, and it was concluded that *p,p′*-DDE and PCBs no longer limit the reproductive rate of this particular bald eagle population. In the Aleutian Islands, OCs and mercury were measured in 136 unhatched bald eagle eggs between 2000 and 2002 (Anthony et al., 2007). Eggshell thickness and productivity were normal and indicative of healthy populations as the concentrations of most contaminants were below threshold levels for effects on reproduction. A study of osprey (*Pandion haliaetus*) eggs from regions of the Chesapeake Bay (USA) of particular contaminant concern reported higher levels of PCBs, *p,p′*-DDE and several other OC pesticides, in addition to PBDEs and PFCs (e.g., PFOS), relative to adjacent, less contaminated regions (Rattner et al., 2004). Although the productivity was marginal for sustaining the local populations in these regions of concern, there was no evidence linking marginal productivity to *p,p′*-DDE, PCB or aryl hydrocarbon receptor-active PCB congener exposure in osprey eggs. However, in another osprey study by Toschik et al. (2005) from the Delaware River and Bay, the concentrations of *p,p′*-DDE, heptachlor epoxide, chlordane and PCBs were predictive of hatching success, suggesting that in this area, contaminants continue to be a stressor on osprey productivity. Moreover, in an area along the lower portion of the Columbia River, the number of osprey nests increased from 94 nests in 1997 to 255 nests in 2004 (Henny et al., 2008). These authors concluded that this increase was associated with higher reproductive rate in recent years and lower levels of most OC pesticides, PCBs and PCDFs. In this study, a comparison between observed egg residues in 2004 and effect level information for ospreys suggests that very few nests were affected by OCs.

The dioxin congener TCDD was added to hepatocyte cultures from bald eagle embryos to determine their sensitivity to induction of CYP1A and porphyrin accumulation (Kennedy et al., 2003). There was no porphyrin accumulation, but both CYP1A catalytic activity EROD assay and immunodetectable CYP1A were induced by high concentrations of TCDD. This suggests that bald eagles are relatively insensitive to some of the effects of TCDD and related dioxin-like compounds, which was consistent with recent field data on bald eagles.

2.4. Marine and freshwater fish

Due to the fact that most fish are relatively short lived, and occupy low trophic positions in aquatic, high-latitude food chains, the levels of POPs/OHCs in fish are generally low, although as we have shown (Table 4), there are exceptions. Local hot-spots in fresh water systems with high contaminant levels within a spatially limited area may be found. A well-known example of this in the high Arctic is the high OHC levels in the Arctic charr population residing in Lake Ellasjøen, Bjørnøya (Bear Island) south of Svalbard. This local “hotspot” is

thought to be caused by transport of contaminants by seabirds from the marine environment and their deposition in the guano (Evenset et al., 2005). Indeed some of the highest PCB levels (>5 μg/g muscle ww) in the Arctic ecosystem have been recorded in tissues of Arctic charr from this lake (Skotvold et al., 1998, 1999; Evenset et al., 2004) (Table 4). To our knowledge, it is likely others sites may exist, e.g., high OHC levels have been reported in fish from Lake Nordlaguna on Jan Mayen in Svalbard (Gabrielsen et al., 1997, 2007).

Compared to avian and mammalian top-predators, very limited data exists on possible effects of POPs/OHCs in fish in the Arctic. Evaluation of the possible risk posed by contaminants on fish species and/or populations in the Arctic must, therefore, be based on the few environmentally relevant experimental effect studies with PCB that have been carried out with Arctic fish (Jørgensen et al., 2006). Furthermore, possible risk is also supported by results from effect studies on other fish species, and data from one comparative study on Arctic charr from Lake Ellasjøen (high POP levels) and Lake Øyangen (low POP levels), Bjørnøya (M. Vijayan, unpublished data). It must be emphasized that the mechanisms of actions of the various POPs, constituting the suite of contaminants found in Arctic animals, have been reviewed in fish before (Hahn et al., 2004) and it is beyond the scope of this review.

2.4.1. Toxicokinetics and biotransformation enzyme systems

As previously mentioned, threshold levels for CYP1A induction may be considered an indicator of thresholds for biological effects. In environmentally realistic experimental studies with Arctic charr given technical PCB mixtures (Aroclor 1260/1254) the lowest observable effect level (LOEL) for hepatic CYP1A induction was reported to be 1 μg PCB/g ww (Jørgensen et al., 1999, 2002a). This LOEL was consistent for both catalytic activity (EROD) and CYP1A protein content (Jørgensen et al., 1999). However, recently a significant CYP1A protein induction in Arctic charr was seen with a liver PCB concentration as low as 200 ng/g ww, when the fish were emaciated after the long winter fasting period (Vijayan et al., 2006). This shows that lipid mobilization, and associated changes in tissue distribution and bioavailability of lipophilic pollutants, may strongly affect the biological activity of these pollutants during periods of negative energy balance. For instance, a high content of storage lipids (triglycerids) in the liver must be considered to lead to a decreased cytoplasma:lipid equilibrium of the lipophilic compound, thereby reducing the concentration of PCB at the site of action (cytoplasm) and the corresponding CYP1A expression.

LOEL for hepatic CYP1A induction may, therefore, differ between species with different strategies for lipid deposition. For instance, hepatic CYP1A induction was more than 3-fold lower in Atlantic cod than in rainbow trout (*Oncorhynchus mykiss*) despite a substantially higher TCDD concentration in the fatty liver of the cod relative to the lean liver in trout (Hektoen et al., 1994). Taking into consideration the substantial temporal variations in body fatness within fish species in the Arctic, and differences between these species in their body fat distribution, it appears difficult to set a common threshold level for hepatic CYP1A expression for all fish species. Further, seasonal adaptations are associated with endocrine changes and compensatory mechanisms associated with long-term cold acclimation in ectothermic fish, which may also affect the activity of hepatic biotransformation enzymes (Jørgensen and Wolkers, 1999). However, existing data indicate that LOEL for hepatic CYP1A induction is far below 1 μg PCB/g ww, at least in very lean fish. In support of this, a significantly higher hepatic CYP1A activity was found in out-migrant juvenile chinook salmon (*O. tshawytscha*) from an urban estuary with liver PCB concentration of 450 ng/g ww than in conspecifics with lower liver PCB concentrations from other estuaries (Stein et al., 1995).

2.4.1.1. Experimental data on PCB toxicokinetics and effects in Arctic fish. Relatively little is known about PCB effects in arctic fish. Few studies have taken into account the seasonal fluctuations in the fat deposition and mobilization that is inherent to the high Arctic animals, including fish (see below). To our knowledge, there are just a few experimental studies that have addressed the impact of environmentally realistic levels of PCBs, associated with the seasonal feeding and fasting cycles, in Arctic fish (Jørgensen et al., 2006). These studies used the technical PCB mixture Aroclor 1254 as the contaminant because PCBs are the dominating organic pollutant in the Arctic wildlife and fish (Tables 1–4). Also, the congener composition found in Arctic fish is similar to that of Aroclor 1254 (Gundersen et al., 2000; Muir et al., 1988).

It is well established that inter-species differences in adiposity may have consequences for the tissue distribution of lipophilic POPs (Hektoen et al., 1992) and the sensitivity of a given fish toward lipophilic POPs (Lassiter and Hallam, 1990; Geyer et al., 1993). Many animals in the Arctic exhibit marked seasonal cycles of "fattening" and emaciation, and an important question was, therefore, if and how such temporal changes in adiposity affect the toxicokinetics of lipophilic pollutants as well as the sensitivity of the animal toward such pollutants. Contamination in animals with marked seasonal changes in food intake and body fatness follows a pattern with successive cycles of POP deposition (season with high food intake) and disposition (season with low food intake or anorexia). In the experimental studies, the fish were, therefore, first contaminated by oral administration and thereafter held both with and without food for several months in order to i) attain a realistic scenario of deposition and disposition, and ii) test the effect of fasting and emaciation on dose-response relationships (Jørgensen et al., 2006).

2.4.1.2. POP toxicokinetics associated with winter fasting and emaciation. In one experimental set-up with anadromous Arctic charr, PCB disposition and hepatic CYP1A activity was studied during their overwinter fasting (Jørgensen et al., 2002a). The fish were orally contaminated after their summer feeding in September, after which they were left without food until May the following year to mimic their natural feeding habit. Irrespective of the dose administered, only 15% of the body burden of PCB was lost between October and May. The rate of loss corresponded to a PCB half-life in excess of 800 days, which is much greater than the <120 days recorded previously for fish (Niimi and Oliver, 1983). The long half-life of PCB recorded in this study may be an effect of the low water temperatures prevailing in the Arctic throughout winter, but may also reflect previous findings that the Arctic charr have a low capacity to eliminate PCB compared to other fish (Bright et al., 1995; Andersson et al., 2001).

The low rate of elimination of PCB recorded in arctic charr will result in an increased bioaccumulation of OHCs in this species, and an increased risk of redistribution toward vital organs during periods of fat mobilization. Indeed, in the group given an environmentally realistic PCB dose (1 μg PCB/g fish) in September, a 9-fold increase in mean brain PCB concentration during winter (from 0.857 μg/g ww measured in the fish sampled in October to 5.780 μg/g ww in those sampled in May) was observed (Jørgensen et al., 2002a). This increase, most of which took place during the last part of the winter, was accompanied with a net loss of PCB from the muscular and skeletal lipid depots, and a net input to metabolically active and vital tissues such as the liver and brain. The dramatic increase in brain PCB concentration probably reflects the energy demand, and associated substrate repartitioning, to this tissue during fasting, and emphasizes the risk seasonal emaciation may pose to animals contaminated with persistent, lipophilic pollutants. The reported 2-fold increase in liver PCB concentration recorded during winter was much lower than in the brain. However, liver is a major organ of xenobiotic biotransformation and, consequently, the input of PCB to this organ may have been counteracted by a concurrent elimination of PCB. This assumption is supported by the observation that the activity of liver biotransformation enzymes (i.e. CYP1A) increased 12-fold from October to May in the group treated with 1 μg PCB/fish in September.

There was also a strong (80%) decrease in the liver triacylglycerol concentration during winter in these fish (Jørgensen et al., 2002a). Lipids are stored as fat droplets in specialized cells in the liver of salmonid fish (Robertson and Bradley, 1992) and lipid mobilization may lead to an increased cytoplasma:lipid equilibrium of PCB (Bertelsen et al., 1998). This may lead to a higher bioavailability of PCB for the activation of cytosolic aryl hydrocarbon receptor and the associated induction of liver CYP1A expression. These results pointed to a dramatic increase in the toxicity of persistent, lipophilic pollutants with fasting and lipid mobilization. Also, these studies emphasize that nutritional status must be taken into account when liver CYP1A enzyme induction is used as a biomarker in risk assessments.

2.4.2. Endocrine, immunological and metabolic effects

Little is known about the effect of contaminants on the physiological responses to environmental stressors in fish in the Arctic. A series of laboratory studies to address this aspect was carried out with either fed or four month fasted Arctic charr that were exposed to Aroclor 1254 (Jorgensen et al., 2006). Subsequently, these fish were exposed to stressors, including an acute handling disturbance (Jørgensen et al., 2002a) and a disease challenge with *Aeromonas salmonicida* (inducing furunculosis in fish) (Maule et al., 2005). The results showed that extended fasting resulted in a dose-related effect of PCB on stress response in charr. Specifically, plasma cortisol levels in unstressed fish were lower in all PCB treated groups compared to the untreated controls in the fasted fish (Jørgensen et al., 2002a). Also, the acute stressor-induced plasma cortisol elevation was muted by PCB exposure in a dose-related manner in these fish. As elevation in stressor-induced plasma cortisol response is an evolutionarily conserved adaptive response (Vijayan et al., 2005; Hontela and Vijayan, 2008), the muted response with PCB exposure suggests reduced capacity for the animal to cope with secondary stressors. The attenuated cortisol response may be related to a decrease in the interrenal tissue sensitivity toward adrenocorticotropic hormone stimulation, interrenal exhaustion or altered turnover of the hormone, all of which have been reported in fish exposed to PCBs (Vijayan et al., 1997; Hontela and Vijayan, 2008). Unlike the fasted fish, in fed fish the high PCB dose elevated pre-stress plasma cortisol concentrations, whereas no effects of the high PCB dose were seen on post-stress cortisol levels. This clearly suggests that PCBs effect is strongly influenced by the nutritional state of the animal. In addition, other changes that were associated with extended fasting and PCB in Arctic charr included disruption of the brain glucocorticoid receptor upregulation (Aluru et al., 2004) and lower plasma glucose concentration and activities of several liver enzymes involved in intermediary metabolism (i.e. lactate dehydrogenase, alanine aminotransferase, glucose-6-phosphate dehydrogenase) (Vijayan et al., 2006). These data revealed that even the low dose of PCB, which resulted in a tissue burden of ~200 ng/g liver w.w., impact metabolism in fasted but not fed arctic charr (Vijayan et al., 2006). This demonstrates that PCB content well within the levels found in arctic fish attenuate the animals ability to cope with stress and disrupt metabolic pathways (e.g. amino acid catabolism and gluconeogenesis) vital for animal performance, including growth and metabolism.

In the disease challenge experiment it was found that skin mucus lysozyme activity was reduced in all fasted PCB groups before they were challenged with *A. salmonicida* and that mortality during the disease experiment increased in a dose-dependent manner with PCB in fasted Arctic charr (Maule et al., 2005). These finding corresponds to other studies which have demonstrated that PCB can decrease resistance of fish to bacterial and viral pathogens, and modulate adaptive immune responses both in laboratory and field studies (Thuvander and Carlstein, 1991; Thuvander and Darnrud, 1999; Arkoosh and Collier, 2002). Based on these results we hypothesize that PCBs impact the immune integrity of the most contaminated fish in the Arctic.

It is very important to emphasise that these experiments demonstrated PCB impact at liver concentrations as low as 200 ng/g ww in fasted fish (Vijayan et al., 2006), and that the effects comprised a wide range of bodily functions, including immune, endocrine and metabolic mechanisms (Vijayan et al., 2005). These PCB levels are below the threshold for CYP1A induction reported earlier (Jørgensen et al., 1999) and supports the notion that this threshold, and those associated with biological effects, may be far below 1 μg PCB/g ww in fasted animals. It is also important to emphasize that nutritional status affect dose–response relationships substantially. For example in the disease challenge experiment, a high PCB dose which resulted in a liver PCB concentration of approximately 9 μg PCB/g ww did not effect disease resistance in fed fish, whereas a 30-fold lower tissue PCB concentration affected fish that had been fasted (Maule et al., 2005). Based on these studies, it appears that the existing dose–response relationships for PCBs derived from laboratory animals, maintained in a positive nutritional state, may not be applicable for Arctic animals.

2.4.3. Effects on smoltification and seawater preference

Many Arctic animals undertake directed migrations in order to cope with the strong spatial and temporal variations in food availability and feeding opportunity that is typical for the Arctic environment. For example, some freshwater fish (i.e. members of the family *salmonidae*) leave their oligotrophic freshwater environments in spring and migrate to the sea where they utilize the abundant food resources of the Arctic oceans. The Arctic charr, which is the northernmost distributed salmonid fish, and a very important food source for many high-Arctic communities, undertake annual migrations to the sea to feed every summer, whereby they accumulate resources for winter survival and sexual maturation (Dempson and Kristofferson, 1987). Prior to seaward migration, these fish undergo a preparatory process termed parr-smolt transformation (or smoltification), by which they develop seawater tolerance (ability to hypoosmoregulate in full-strength seawater) and metabolic adaptations that enhance survival, food utilisation and energy accumulation during the short residence in the sea (Hoar, 1988). Since seawater entry may cause severe osmotic stress to these fish, a successful smoltification is pivotal for survival, growth and energy allocation during the feeding residence in seawater (Usher et al., 1991), as well as subsequent reproduction after the return to freshwater (Dutil, 1986). In the Arctic charr, the endocrine-orchestrated smoltification process is completed during a period when these fish are emaciated and therefore are considered to be particularly vulnerable to POPs/OHCs.

Possible effects of PCB on smoltification in anadromous Arctic charr were studied in semi-wild charr that were hatched in captivity and released in a natural system where they established an anadromous (sea migrating) life strategy (Jørgensen et al., 2004). Upon return to freshwater after the feeding residence in the sea, they were captured and maintained in captivity under natural light and temperature conditions and exposed to different concentrations of Aroclor 1254 (Jørgensen et al., 2004). Thereafter, several indices of the smoltification process were investigated throughout winter and spring. In order to mimic their natural life-style, the fish were not fed during this period. Subsequently, the fish were transferred to seawater during summer, where they were fed, and back to freshwater again in late summer where they were held until maturation. The results showed that the charr that were exposed to the high PCB dose had either a transient or permanent reduction in plasma levels of hormones involved in the regulation of the smoltification process, including growth hormone (GH), insulin-like growth-factor I (IGF-I), T_4 and T_3, during winter and spring. This reduced endocrine response in the high PCB group corresponded with an impaired hypoosmoregulatory ability in seawater in May and June. Also, these fish showed reduced growth and survival in seawater

(Jørgensen et al., 2004). The effect of PCB on seawater tolerance and performance in this study was thought to be due to disruption in hormone dynamics. However, such dysfunctions may also occur at much lower tissue PCB burdens than seen in this study. For instance, plasma T_4 concentrations were reduced in coho salmon (*O. kisutch*) fed Aroclor 1254 that amounted to a liver PCB concentration of < 1 μg/g ww (Folmar et al., 1982).

In a recent experiment, aqueous exposure of Atlantic salmon to 10 μg Aroclor 1254/l during the yolk-sac stage resulted in a dramatic reduced preference for seawater (motivation for seaward migration) at the smolt stage a year later, whereas exposure during the smoltification period reduced both seawater preference, gill Na^+, K^+-ATPase (indicator of hypoosmoregulatory ability) and plasma levels of hormones involved in the regulation of the smoltification process (triiodothyronine and cortisol) (Lerner et al., 2007). The total body burden of PCB in the salmon exposed during the smoltification period (516 ng/g ww) is well within the range detected in Arctic fish. It is worth noting that the effect of exposure to PCB may vary depending on the developmental stages, and that short-term exposure during early life stages may have long-term impacts on behavioral mechanisms that are of utmost importance for growth and maturation in fish living in the high north. One key aspect of smoltification is thought to be a role for thyroid hormone in imprinting the odour of their home stream (Hoar, 1988). Indeed, Leatherland and Sonstegard (1980) reported reduced plasma T_4 and T_3 titers in rainbow trout (*O. mykiss*) fed a mixture of Aroclor 1245 and 1254. Consequently, PCB-related effect on the thyroid axis may also affect the ability of these fish to return to their natal river.

2.4.4. Reproduction

To the best of our knowledge, no environmentally relevant experimental studies on the effect of POPs/OHCs on reproduction in high-latitude fish have been reported. There are, however, results in other studies with fish exposed to PCB suggesting that adverse effects may occur in fish in the Arctic. In two separate experiments, Nile tilapia (*Oreochromis niloticus*) larvae and adults were dietary exposed to different doses of Aroclor 1254 (Coimbra and Reis-Henriques, 2005, 2007). Tilapia larvae was fed 50 ng Aroclor/g feed for 40 days following the absorption of the yolk sac, whereas adult fish (< 1 year old) was fed three doses of Aroclor (0, 0.5 and 4.5 μg/g feed) for 10 and 20 days. In the former experiment, tissue concentrations of PCB after the exposure period were in the order 10–30 ng/g tissue ww. Although no data exists on POP levels in larvae of Arctic fish, egg POP concentration tends to be around 50% of those found in adult, mature females (Miller, 1994), and hence, the concentration in tilapia larvae are relevant for the contaminant load that can be found in young life-stages of Arctic fish. Briefly, the experiment with tilapia larvae revealed both ovary and testicular alterations and a decline in T_4 plasma concentrations 18 months after the intermittent PCB exposure (Coimbra and Reis-Henriques, 2007).

The tissue concentration of PCB in the adult tilapia exposed to Aroclor were not reported (Coimbra and Reis-Henriques, 2005), but using a realistic assimilation efficiency (80%) a tissue concentration of about 1 μg/g ww seems likely. Hence the body burden of PCB is within the burdens found in Arctic fish (Table 1). This short-time exposure to a realistic PCB body burden caused depressed plasma progesterone and testosterone levels in males. In the adult fish exposed to the high-dose PCB, morphological alterations were seen in the testicular and germinal tissues. In Atlantic croaker (*Micropogoinas undulates*) exposed to Aroclor 1254 during gonadal recrudescence, there was a loss of *in vitro* pituitary gonadotropic response to luteinizing hormone-releasing hormone stimulation (Khan and Thomas, 1997). Although brain PCB concentration appeared high in these fish (~13 μg/g ww), it is important to remember that a realistic PCB burden (1 μg/g tissue ww) caused a brain PCB concentration that was not much lower (~6 μg/g ww) in Arctic charr after the winter fasting.

Further evidence which points to PCB-derived effects on reproduction in the most polluted Arctic fish stems from a field study on Arctic charr in Lake Geneva (Monod, 1985). In that study, eggs from18 feral, mature female charr were collected and fertilized individually with males captured from the same lake. From each spawn the eggs were divided in two parts; one which was incubated and later recorded for embryo development and mortality and one which was analyzed for PCB. Egg PCB concentrations from the sampled females ranged from 100 to 500 ng/g ww or 13 to 78 μg/g lw; concentrations which probably would be found in the gonads of some individuals of Arctic charr from Lake Ellasjøen at Bjørnøya. There was a significant positive correlation between mortality in the early embryonic phase and PCB concentration in this study, when PCB concentrations were expressed on a lipid weight basis, but not when they were expressed on a wet weight basis (Monod, 1985). The explanation for this paradox is possibly that a high PCB concentration on a lipid weigh basis reflects low lipid contents in these eggs, and a higher bioavailability of PCBs during the early embryonic development. This, again, illustrates that lipid status and feeding cycles should be taken into account when studying the effects of lipophilic pollutants in the Arctic.

In conclusion it seems that low PCB levels in eggs (< 500 ng/g ww) affect their survival after fertilization and that larvae exposed to very low PCB levels (10–30 ng/g ww) may suffer from reproductive dysfunctions later in life. In an epidemiological investigation in the Great Lakes, there was a negative correlation between lake trout (*S. namaycush*) egg PCB concentration (124–314 ng/g w.w.) and egg and fry survival (Mac and Edsall, 1991). Although the eggs in the latter study were exposed to many other chemicals, it is clear that PCB levels far below 1 μg/g ww in early life stages (eggs, larvae) impact reproduction later in life. These studies also support the proposal that early life stages of fish are more vulnerable to pollutants than adult stages, which complicates the determination of threshold concentration for contaminants further.

2.4.5. A special case of DDT and toxaphene in Arctic fish

The levels of *p,p′*-DDT are generally below those of PCB in the arctic biota, but occasionally levels similar to, or above, those of PCB can be found (Tables 1, 3 and 4), as has been the case for Greenland shark (Fisk et al., 2002). In Arctic charr from Bjørnøya, the *p,p′*-DDT concentration in muscle was approximately 6-fold lower than PCB concentrations, but still relatively high in the individual with the highest concentration (423 ng/g ww; Evenset et al., 2004). Little relevant experimental evidence is available for evaluating if these *p,p′*-DDT levels may pose a threat to fish in the Arctic. In a study with maturing brook trout fed technical DDT for a period of 156 days (Macek, 1968), the whole fish contained 0.78 (controls) to 7.60 μg/g ww *p,p′*-DDT (high dose fish) at the end of the contamination period. There were no observable effects of DDT exposure on the adult fish during the contamination period. However, cumulative mortality of eggs and fry were higher if one or both gametes came from DDT-treated fish than when both gametes were from untreated controls (Macek, 1968). Of the various *p,p′*-DDT metabolites, *p,p′*-DDE was found to be the most prevalent in arctic charr from Ellasjøen, Bjørnøya (Evenset et al., 2004). This metabolite, which is considered to be anti-androgenic, did not affect plasma sex steroid levels or gonadal development in summer flounder (*Paralichthys dentatus*) injected with very high doses (15, 30 and 60 μg/g fish weight) of *p,p′*-DDE (Mills et al., 2001; Zaroogian et al., 2001). The tissue *p,p′*-DDT levels obtained in the experiment with brook trout (Macek, 1968) correspond to those that have been found in Greenland shark (Fisk et al., 2002). However, *p,p′*-DDT concentrations in the shark were measured in the fatty liver, and the concentrations at target sites were not estimated. Data on toxicokinetics of *p,p′*-DDT associated with fasting and emaciation, to the best of our knowledge, has not been reported. It is possible that fish in the Arctic (e.g. Greenland shark) is

affected by *p,p′*-DDT, but too little data is available to suggest threshold concentrations for effects.

Not many environmental realistic, experimental studies on toxaphene toxicity have been reported. In an experiment with Arctic charr, groups were orally administered a low and a high dose of toxaphene, after which several physiological parameters were compared between toxaphene and control groups 60 days later (Blanar et al., 2005). Toxaphene levels in the muscle of these fish ranged at the time of sampling between 0.03 (control fish) and 920 ng/g ww (high dose fish). The toxaphene level in the high and low dose groups seems to be very high compared to the levels observed in fish in the Arctic in general (<100 ng/g tissue ww; de Wit et al., 2004), but comparable to levels observed in Yukon Flats in Alaska, where burbot (*Lota lota*) liver contained up to 420 ng toxaphene/g liver ww (Mueller and Matz, 2000). The short-term exposure to toxaphene did not affect post-stress plasma cortisol levels, or vitamin A and E levels, in Arctic charr. On the other hand a similar exposure (104 days) with a dose of toxaphene, causing a muscle toxaphene concentration between 300 and 600 ng/g ww, markedly decreased fish growth (Blanar et al., 2005). Taken into consideration the short-lasting contaminant exposure these fish were exposed to, the threshold for toxaphene effects must be below the tissue levels obtained in these fish and probably below the highest levels of toxaphene found in Arctic fish. However, pertinent studies, including fed and fasted animals, are necessary before a threshold concentration of this chemical eliciting a toxic effect in Arctic fish can be established.

2.4.6. Comparative studies on Arctic charr in Lake Ellasjøen and Øyangen at Bear Island

POP/OHC contamination in wild animals constitute a mixture of industrial pollutants such as PCBs and chlorinated pesticides such as *p,p′*-DDT (in addition to other pollutants such as heavy metals etc.), and this mixture of pollutants represents a toxic burden that is difficult or impossible to imitate in laboratory experiments. Comparative studies on wild populations suffering from different pollutant loads and the multitude of stressors characterizing high-latitude environments are therefore needed for a reliable assessment of possible impacts.

In contrast to the situation with high pollutant loads associated with accidents and discharge from local industrial activities, the high pollutant load in Arctic charr from Lake Ellasjøen, represents a local up-concentration of long-range transported POPs/OHCs to the main deposition area in the Norwegian Arctic (Pacyna and Oehme, 1988; Evenset et al., 2004). Further, the Arctic charr population in Lake Øyangen, located only 6 km north of Lake Ellasjøen, has substantially (10–40 times) lower contaminant loading than Arctic charr from Lake Ellasjøen (Evenset et al., 2004). Consequently, these lakes on Bjørnøya provide a natural system for assessing biomarker responses and effect parameters related to long-term contaminants exposure in fish living under similar environmental conditions. Further, the biomarker responses and effects documented in the experimental studies with PCB in Arctic charr (Jørgensen et al., 2006), represents a useful background for the validation and interpretation of results obtained in comparative studies with these two charr populations, since PCB represents the dominating POP in these fish.

Sampling of charr from these two lakes for biomarker studies have been conducted twice. The first sampling was carried out in the late 1990 s, whereas a new sampling was undertaken in 2002. Compared to a LOEL as low as 200 ng/g ww determined for PCB related hepatic CYP1A responses in experimental studies with Arctic charr (Vijayan et al., 2006), the level of POPs in feral charr in Lake Ellasjøen should be expected to show hepatic CYP1A responses. Indeed, a strong hepatic CYP1A induction was seen in the Arctic charr sampled in Lake Ellasjøen in the late 1990 s. Actually the hepatic CYP1A activity in charr from Lake Ellasjøen was higher than the maximum levels recorded in laboratory studies with Arctic charr (Jørgensen et al., 1999, 2002a), and almost 16 fold higher than in charr from Lake Øyangen. The hepatic CYP1A induction in Lake Ellasjøen charr was stronger than expected and motivated further studies on these remote charr populations in order to reveal whether the performance of the charr in Lake Ellasjøen are affected by their contaminant load.

Logistical difficulties, including the need to capture a sufficient number of comparable fish, are a formidable challenge in ecotoxicological studies on feral fish in the Arctic. So far, it has not been possible to finance a comprehensive study on the two populations of charr and the biomarker study performed on the fish sampled in 2002 was aimed at revealing more information about whether or not the two charr populations differ in POP-related biomarker responses. The tissues sampled in 2002 comprised only 3 large males from each lake. Restricting the samples to large individuals was necessary because the lakes have two sympatric morphs of charr, small dwarfs and larger cannibalistic individuals, of which the contaminant load is highest in the latter (Evenset et al., 2005). The three fish sampled from each lake were all immature and of similar size.

The liver contaminant load was predominantly PCBs and there was a 25-fold higher mean PCBs load in the Lake Ellasjøen compared to individuals from Lake Øyangen (M. Vijayan, unpublished). This was also clearly reflected in a higher CYP1A mRNA level and protein expression in the Ellasjøen charr compared to the Øyangen charr. However, liver heat shock protein 70 (hsp70) and 90 (hsp90), two key indicators of cellular stress response (Iwama et al., 2006), gene and protein expression was not affected by the contaminants, whereas the brain levels of both these proteins were significantly higher in the Ellasjøen charr compared to the Øyangen charr (M. Vijayan, unpublished). There was also a reduction in brain glucocorticoid receptor (a key signaling molecule for stress hormone cortisol action and plasma regulation of this steroid) expression in arctic charr from Lake Ellasjøen compared to Lake Øyangen. Together, these results suggest that brain function may be more sensitive to contaminants, probably as a result of a higher accumulation of POPs in the brain than in other tissues during periods of fat mobilization.

This study is the first to suggest a tissue-specific biological effect associated with contaminant exposure in fish residing in these remote Arctic lakes. While the mechanism is unknown, further studies are warranted to understand the toxicant dynamics, specifically associated with the feeding and fasting cycles, to establish threshold levels for PCBs effects. Based on experimental studies with laboratory reared fish, our results clearly suggest that long-term or multi-generational exposure to contaminants in charr residing in these Arctic lakes may lead to impaired animal performance.

3. Climate change and other stressors in Arctic wildlife and fish

Recently, there has been focus on the effects of other non-POP anthropogenic stressors on biodiversity and ecosystem functioning in the Arctic. Global climate change is one such factor that has received focused and growing attention during the past years (Jenssen, 2006). It has been argued that the global warming will have a huge negative impact on arctic ecosystems. A central prediction is that changing climate will lead to structural changes in species composition within ecosystems (Callaghan et al., 2004; Ims and Fuglei, 2005). This will result in changes in prey availability for predators, which may influence both the accumulation and effects of POPs. For instance, over the past two decades, it has been shown that increasingly earlier breakup of the ice has been linked to lower body condition, birth and survival rates in Western Hudson Bay polar bears (Regehr et al., 2007; Stirling et al., 1999). The impacts of climate change on polar bears may also be a dynamic factor in the type, complexity and level of OHC exposure, and subsequently on OHC-related effects. For example, it was very recently reported that temporal diet variation (shift in prey seal species) (1991 to 2007) in polar bears from the Western Hudson Bay subpopulation was related to changes in the timing of the annual

sea ice breakup, and was linked to increases in the tissue concentrations of several OHCs (McKinney et al., 2009).

There are other significant anthropogenic stressors, such as overfishing, hunting, habitat destruction, increased traffic due to increased tourism, introduction of new species and pathogens to the Arctic, food deprivation, and changes in prey-predator interactions. The Arctic is characterized by extreme low environmental temperatures during winter and large seasonal fluctuations in light conditions. Arctic mammals are also challenged by large, and often unpredictable temporal variations in climate conditions and food availability, and some must take advantage of a short summer season for reproduction. These factors are also a threat for the future exploitation of harvestable bio-resources in the Arctic (fisheries, indigenous hunting).

Recent evidence suggests that a combination of POPs and other stressors may have strong adverse effects, and that even low levels of POPs may be hazardous. Hence, the effects of POPs on populations seems to be state-dependent and can increase with exposure to other stressors such as predation, pathogens and food deprivation (Relya and Mills, 2001; Sih et al., 2004; Gill and Elliott, 2003; Bustnes et al., 2006a, 2008a). Together with POPs, these non-POP anthropogenic factors have the potential of directly affecting Arctic organisms, biodiversity and ecosystem health. POPs and all of these other anthropogenic stressors do not act as single independent stressors, but that they act in concert and are dynamic. Unfortunately, there is a dearth of knowledge on the combined effects of these multiple stressor on Arctic animals.

Future environmental changes are expected to increase stress on northern wildlife and fish populations through influence on their ecosystems (Boonstra, 2004). Therefore, to understand the threats to northern ecosystems from changing physical environments, it is necessary to have knowledge about the current impact of various POPs and other pollutants. This will require more studies that deal with natural populations and and an ability to measure interactive effects of different stressors including pollutants.

4. Synthesis and summary

As has been outlined in this review, since the last AMAP assessment and related reviews (de Wit et al., 2004, 2006; Braune et al., 2005; Fisk et al., 2005; Gabrielsen et al., 2007), substantial amounts of new knowledge regarding exposure to OHCs and their degradation byproducts (Fig. 1, Tables 1–4), and effects (e.g., Table 5) have been suggested by correlations with various biomarker measurements from selected, free-ranging mammal, bird and fish populations that generally feed at the top of the Arctic marine food web (e.g., Alaska, Hudson Bay (Canada), East Greenland, Northern Norway and/or Svalbard). Based on the "weight of evidence" from reports on OHC effects in Arctic wildlife and fish, there are several key "hotspot" species and populations (Fig. 2). We also note other very recent reviews on POPs and effects in specific Arctic species and populations such as on Svalbard glaucous gulls (Verreault et al., 2010). Also, a recent paper by Sonne et al. (2009c) reported effects on

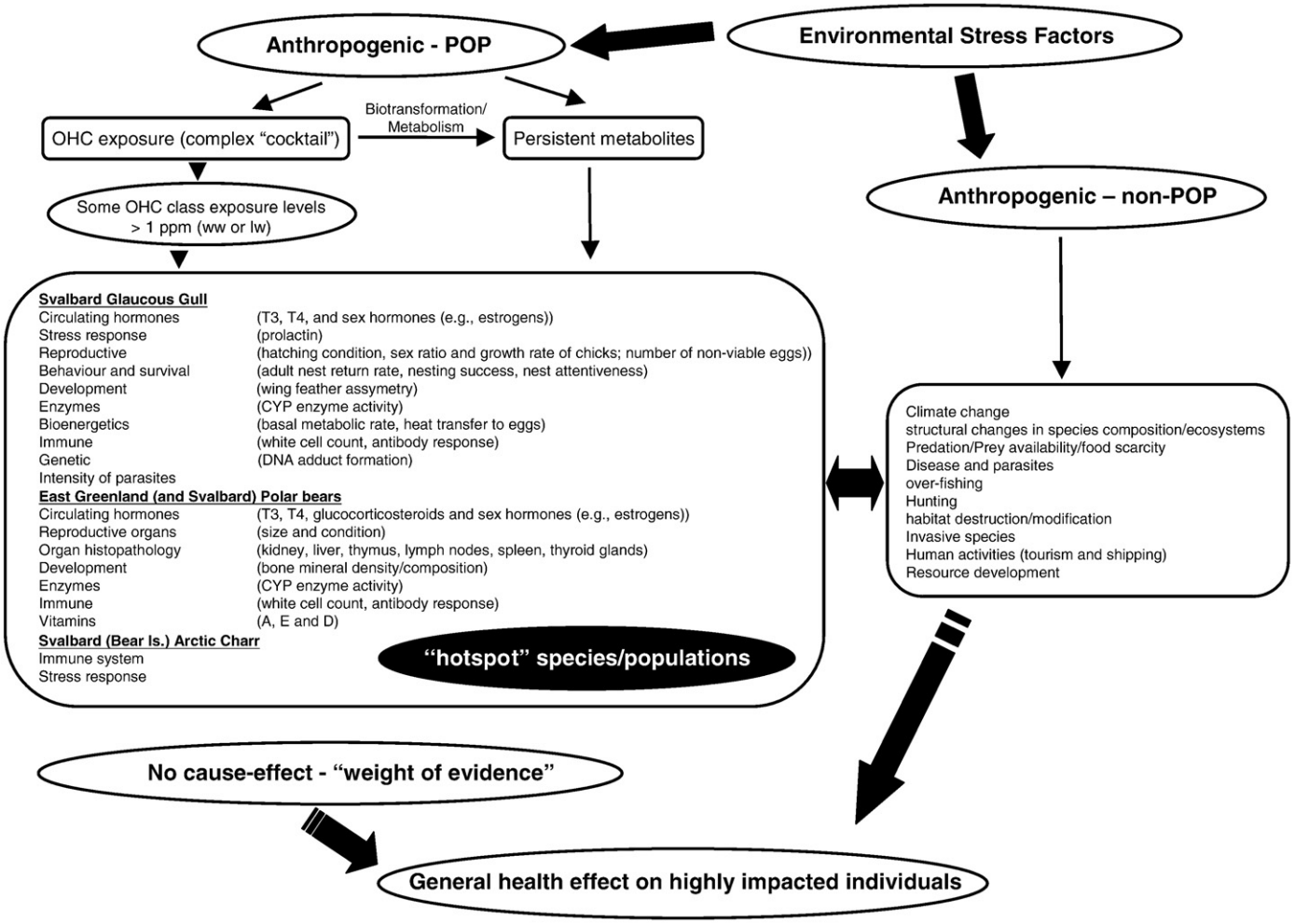

Fig. 2. Arctic species and populations ("hotspots") of concern based on "weight of evidence" of stress and effects related to OHC exposure and other stressors. Also see Fig. 1 and Tables 1–4 with respect to summary of known OHC exposure in key Arctic wildlife and fish.

reproductive performance in East Greenland polar bears and relationship to OHCs using a physiologically-based pharmacokinetic modeling approach.

4.1. A specific case of concern for endocrine-related effects

Because endocrine systems are important for Arctic mammals to respond adequately to environmental stressors, there is concern that POPs with endocrine disrupting properties may interfere with acclimatization and adaptations to the extreme Arctic environmental conditions (Jenssen, 2006). THs, sex steroid hormones and glucocorticosteroids seem to be the most vulnerable endocrine variables to effects of OHCs in Arctic wildlife and fish. Important functions of THs are the regulation of metabolic processes including thermoregulation, growth and differentiation of tissues, and neurodevelopment. THs are also important in adaptations to natural periods of fasting, to moulting, and for learning and for cognitive abilities (Jenssen, 2006). Thus, TH homeostasis disruption effected/caused by EDCs may lead to suboptimal responses to extreme temperatures, fasting, and disturbance of moulting in arctic mammals. In polar bears learning and cognitive abilities are probably important factors for successful hunting. Thus, perturbation of TH homeostasis by EDCs may impair learning and cognitive abilities and thus survival, especially of young developing polar bears (Jenssen, 2006).

Testosterone and progesterone are essential for reproduction, but they are also important in sexual behaviour. Disturbances of these hormones may affect reproduction both directly and indirectly. Glucocorticosteriods are involved in a range of physiological processes including reproduction, immune function, behaviour and metabolic adaptation to stress. Disruption of this endocrine system may lead to reduced reproduction and survival. Even though most of the reports of endocrine related effects in arctic mammals are based on studies showing significant correlations between pollutant levels and responses, the reported endocrine responses are in general accordance with those observed in controlled studies on laboratory animals (Jenssen, 2006).

Rapid climate change is likely to pose additional stress to arctic mammals, and because endocrine systems are important for enabling animals to respond adequately to environmental stress, there is concern that EDCs may interfere with acclimatization and adaptations to rapid climate changes caused by human release of greenhouse gasses (Jenssen, 2006). Thus, the weight-of-evidence clearly reinforces the risk that arctic free-ranging mammals, EDCs interfere with endocrine systems that are important for a life in the Arctic.

4.2. "Hotspot" species and populations of OHC exposure and effects

Based on the present evidence summarized in this AMAP review, it is believed that effects of biological significance related (possibly) to POP/OHC exposure are occurring in some arctic species in some specific areas including 1) polar bears may be at higher risk for infections and reproductive effects that could lead to decreased survival and a chronic stress on population health (although not yet studied) due to immune, endocrine and reproductive effects, 2) energetic stress, and other direct and indirect, climate change related factors, may modulate these impacts, 3) glaucous gulls with high POP levels may be at risk due to behavioral, immune, endocrine and reproductive effects and subsequent impacts on survival, 4) ivory gulls show potential reproductive effects, and 5) captive arctic charr experiments have demonstrated impact of environmentally realistic PCB exposure loads on metabolic, immune and endocrine systems. With respect to ivory gulls and reproductive effects, this may be related to eggshell thinning, although no broken eggs have ever been found in these Canadian and Svalbard colonies and eggs all seemed to hatch normally (Braune et al., 2007; Miljeteig et al., 2007). It should be re-emphasized that this review does not consider exposure to non-OHC substances. Hg exposure in arctic biota is singularly a major issue of concern with respect to effects and is the subject of a current but separate AMAP review exercise.

4.2.1. Mammals

In recent years, toxico-pathological studies conducted with East Greenland polar bears have reported on several correlative associations between blood and tissue (mainly adipose) OHC and Hg concentrations, and selected biomarkers of biological effects, e.g., histology, structure and size of various organs and bone mineral composition. Also, OHCs may be related to a reduced size of reproductive organs in both male and female East Greenland polar bears. Reproductive effects on steroid hormone parameters and associations with concentrations of specific OHCs have been reported in both female and male polar bears from Svalbard. Previous observations of supposed pseudohermaphroditism in female polar bears from Svalbard could not be verified from a thorough pathological examination of a single animal from the Greenland hunt with a similarly enlarged clitoris. Tissue alterations in liver and kidney have likewise been found in the East Greenland polar bears that could be linked to specific OHCs. However, no OHC-related alterations were found in lymph nodes, spleen, thymus or thyroid gland. Relationships between OHCs and THs have been reported in both male and female polar bears. Studies on effects on the skeletal system in East Greenland polar bears documented a reduction in BMD in relation to OHC concentrations. However, no relationship was found between skull pathology and organohalogens in East Greenland. Fluctuating skull asymmetry in polar bears showed variable results dependant on the analytical method used. Some of the lacking skeletal effects may have been due to sub-effect exposure to OHCs, influence of nutritional status, genetic factors or other confounding environmental factors such as climatic oscillations. Furthermore, Greenland exposure studies on captive sledge dogs have documented that daily intake of marine mammal blubber from Greenland may cause an impairment of the immune system in top predators. However, considering the potential uncertainties related to the life history and physiological condition of randomly-captured free-ranging polar bears, a major concern with these health risk assessments is the lack of confirmation of cause–effect linkages between chronic environmental POP/OHC exposure and apparent adverse biological effects. Based on ethical and practical grounds, direct dosing studies (exposure–response) to examine chemically-related stress in polar bears and other top Arctic predators are not feasible.

In Norwegian (Svalbard) and/or Russian investigations, health effect studies have been restricted to the determination of POPs/OHCs using blood samples and adipose biopsies as the polar bear is protected in these regions, although bears are still occasionally hunted in Russia. This was the case where samples were obtained during the handling of polar bears in connection with chemical immobilization and deployment of satellite collars or conventional tags. However, a substantial amount of information has been achieved from those parameters having adverse effects on hormone levels, vitamins and immune status as well as correlative associations with contaminant levels and polar bear movements within their home range. There are also new reports on tissue distribution and body burdens and associated toxicokinetics, as well as bioaccumulation and in some cases biomagnification from the ringed seal blubber diet, of major chlorinated and brominated OHCs and in connection with established metabolites in East Greenland bears. For example, OH-PCB metabolites are mainly a blood localization issue, and thus dependent on continual metabolic formation from precursor PCBs. OHC and metabolite exposure variation has as yet unknown effects and toxicological implications.

During the last five years, arctic sled dogs and foxes have been used as applicable surrogate species for the polar bear (and other

canids and ursids) as these species can be studied in captivity and/or under more controlled conditions, and with the inclusion of control groups. Recently reports have been published where sled dogs and arctic foxes have been used as surrogates for polar bears and other Arctic top predators (e.g., wolf). Specifically, over a two-year period juvenile sled dogs in West Greenland were fed either blubber from minke whale (including accumulated contaminants) or commercial pork fat for human consumption. The West Greenland minke whale has a comparable load of contaminants as West Greenland ringed seals and was considered representative of the diet of polar bears. Compared to the control animals (given a pork fat diet), the sled dogs that were fed blubber showed altered liver and kidney functions and morphology, insufficient immune response and impaired cellular immunity. For many of the parameters investigated, these effects are similar to those that have recently been reported in East Greenland polar bears. Looking at the postulated mechanism behind the effects, they appear to be linked to changes in enzymes that can transform OHCs such as PCBs and PBDEs into OH-PCB and to a lesser extent putative OH-PBDE metabolites, respectively. Based on studies in wild populations in the Canadian high Arctic and Eastern Greenland and the sled dog studies, biotransformation into these metabolites may be more important for the toxic effect than the levels of the originally accumulated (untransformed) compound.

There have been recent reports on lower trophic feeding arctic marine mammals (e.g., Alaskan/Beaufort Sea bowhead whales and gray whales) showing very low OHC concentrations in tissues (i.e., blubber) (Table 1 and 2) and with no notable indication of adverse effects on histology, physiology, enantiomer-specific OHC accumulation and biotransformation. Studies as a model mysticete species have demonstrated their importance as a subsistence resource to justify further study. However, no responses to POPs have been reported, which is contrast to studies on non-arctic populations of beluga whales and ringed seals (Tables 1 and 2).

The bowhead whale has not been as intensively studied as other marine mammals (e.g., harbour seals, beluga whales, bottlenose dolphins). There may be good reason considering the low concentrations of OHCs in tissues of this large mysticete (Tables 1 and 2) and the lack of reported evidence of adverse health effects. The levels of POPs/OHCs in whales depend on the eating habits of different species. Bowhead and gray whales, which are low in the food web, have low levels of contaminants. Recent studies have confirmed the very low OHC levels in blubber of these species, with no signs of effects on the biology on the animals. For this assessment, we conclude the bowhead whale shows no evidence of adverse health effects due to OHCs/POPs and based on lower trophic level feeding is likely of lower risk as compared to other cetaceans. However, studies are likely to continue in the context of the health assessment and as a subsistence resource.

Beluga feed at a higher level in the food web and populations in the highly polluted SLE are known to show adverse effects, including impacts on the immune system and tumors. Arctic beluga whales and other odontocetes (harbour porpoise, killer whales, etc.) are more contaminated than some of the mysticetes and are worthy of assessment. Recent studies have linked specific feeding habits (consumption of marine mammals) with higher POPs exposure in Arctic (Alaskan and Northern Norway) killer whales (Tables 1 and 2). Some have speculated these higher exposures may be compromising but logistical constraints prevent an adequate assessment. At present, it is not known whether odontocetes in the Arctic may show more subtle effects, but a previous AMAP assessment (Fisk et al., 2005) that made comparison to known effect levels in other animals concluded that levels of PCBs in some toothed whales are high enough to raise concerns. Further studies of biological impacts on toothed whales would therefore be warranted, although effect studies on Faroese pilot whales are known to be underway.

Beluga whales in the Arctic are less POP/OHC contaminated than those from the SLE. The latter populations are known to be suffering adverse effects such as on the immune system and increased neoplasia. Considering the high trophic level, circumpolar distribution, and importance to indigenous peoples, further study of arctic beluga populations is warranted to determine if more subtle effects are noted as compared to those from the SLE. Ringed seals present a similar scenario, as the beluga do, with arctic populations less contaminated than the more stressed Baltic Sea population. Reports from Baltic seals have shown gross histological lesions (e.g., uterine lesions, claw and bone lesions). In Baltic gray seals bone lesions may be associated with contaminant-mediated vitamin D and thyroid disruption. There are no new studies of biological effects on seals in the Arctic. However, based on comparisons to known effect levels in other species, the previous AMAP assessment (Fisk et al., 2005) concluded that contaminant levels at some sites (East Greenland; Fig. 1) were high enough to raise concerns about effects on the immune system, on their levels of THs and vitamin A, and on reproduction.

4.2.2. Birds

In recent years, effect studies on wild terrestrial birds having an arctic distribution have been limited to peregrine falcons. Most of these studies have concluded that the use of the pesticide DDT, which has driven many local bird populations to extinction or to the brink of extinction, has now ceased and most populations are in a recovery phase. However, these studies also provide a perspective as to the time scale needed from the ban of a persistent pollutant such as DDT to a partial population recovery, and also why some local populations may have problems re-establishing themselves. Hence, peregrine falcons may be vulnerable to a reversal of the effect of *p,p'*-DDE given that changes occur in the environment, and this may also include a change in availability of different prey items (e.g., Elliott et al., 2005). The laboratory based studies conducted on American kestrels since the 1990 s at McGill University have gained great insight into a wide range of effects and mechanisms of toxicity of environmentally relevant concentrations of major POPs/OHCs, most recently emphasized by studies on BFR (PBDE) dietary exposure of American kestrels (Fernie et al., 2005a,b, 2006, 2008). These include, among others, endocrine, immunological, developmental, reproductive and behavioral effects. In addition, several captive American kestrel studies published before 2002 (outside the scope of the present review) have reported other adverse effects on the immune system (Smits and Bortolotti, 2001), reproduction (Fernie et al., 2001a,b), courtship behavior (Fisher et al., 2001) and changes in egg composition (Fernie et al., 2000).

Similar to marine mammals, some arctic populations of seabirds feeding at the top of the marine food web are exposed to high levels of POPs. Previous assessments have concluded that levels were high enough to cause concern for a number of physiological and ecological effects. Although most of these bird species from the Arctic have not experienced population threatening declines as opposed to some terrestrial birds (e.g., falcons), subtle adverse biological effects mediated by chronic contaminant exposure have been suggested as potential stressor at the population level in glaucous gulls and ivory gulls in Svalbard and/or in Eastern Russian Arctic (Miljeteig et al., 2007), and perhaps also subspecies of the lesser black-backed gulls in Northern Norway (Bustnes et al., 2006b).

At one particular breeding location, Bear Island, halfway between the main Svalbard islands and Norway, observations were made already in the early 1970 s that breeding glaucous gulls exhibiting abnormal behaviour had alarmingly high tissue PCB and *p,p'*-DDE levels. Reports of dead or dying glaucous gulls on Bear Island have also been recorded sporadically since then. This island is a known "hotspot" for PCBs as well as numerous other OHCs (Tables 2 and 3), and studies reported in the previous assessment confirmed that POPs were associated with effects on their enzymatic system, development and behaviour (de Wit et al., 2004). Effects in glaucous gulls have now been

documented for many organizational levels of the biological systems, including endocrine, immunological, bioenergetics, genetic, enzymatic, behavioral, reproductive, metabolism, survival and developmental effects (Fig. 2). For example, some results show that specific POPs are associated with energy expenditure and potentially the ability to thermoregulate, heat transfer to the eggs during incubation and nest attendance behaviour.

There is at present increasing evidence that other marine birds may also experience deleterious effects from exposure to long-range transported POPs in the arctic environment. Observations of glaucous gulls at Bear Island and Great black-backed gulls from the northern Norwegian coast have shown that the effects of specific OHCs may be enhanced when the birds are exposed to additional stressors such as parasite infection, predation, pathogens, climate change and/or food scarcity. This suggests that a changing environment with an increasing natural and anthropogenic stress on wildlife avian populations may modulate (e.g., increase) the impact of pollutants. It is suggested that POPs can also contribute to affect the health of other arctic marine bird populations such as the highly contaminated ivory gull and great skua (*Stercorarius skua*), although this is yet to be established. At present, the species that appear to be the most vulnerable or sensitive are the predatory and fish-eating larids in which many occupy top trophic positions in their respective Arctic (or Subarctic) marine food webs (e.g., glaucous gulls, ivory gulls, lesser black-backed gulls and great black-backed gulls).

4.2.3. Fish

Arctic fish with high POP levels are either long-lived, fat marine fish, or populations of freshwater fish that live in local "hotspots". Specific examples are marine Greenland shark (Davis Strait/Baffin (Canada) and Iceland) and freshwater Arctic charr (Svalbard/Bear Is. (Bjørnøya), Norway) (Fig. 1; Tables 2 and 4). For arctic charr, there is new evidence of biological effects at Lake Ellasjøen on Bjørnøya. This lake receives a high load of contaminants from guano from a nearby seabird colony and the POP levels are much higher than in another lake on the island that receives less guano. This is reflected in the higher liver CYP1A and heat shock proteins (indicator of cellular stress) expression in Lake Ellasjøen char. In addition to these observations, there are experiments showing that environmentally relevant levels of POPs/OHCs can be redistributed from adipose tissues to critical tissues, including brain and liver in response to seasonal long-term fasting in arctic charr. Also, laboratory studies with fasted arctic charr exposed to environmentally relevant levels of POPs/OHCs suggests that the animal performances, including stress response, immune response and seawater tolerance, are affected by the contaminants.

4.3. POP exposure in relation to possible effect thresholds

There is currently no new information (post-2002; de Wit et al., 2004; Fisk et al., 2005) on specific threshold data for OHC exposure for terrestrial or marine birds or mammals residing in the Arctic. However, wildlife from the northern ecosystems are experiencing increasing stress, particularly from two sources: climate change and exposure to OHCs, which include the legacy OHCs and an increasing complexity of new organic contaminants of current production and usage (Boonstra, 2004; Muir and Howard, 2006) (Tables 2 and 3).

A great deal of caution must be exercised in establishing POP exposure level thresholds in relation to physiological and biochemical responses that manifest in an animal as a (deleterious) effect. As has been summarized, and applicable to all "hotspot" species and populations, essentially all "effects" studies to date in three key Arctic species, glaucous gull, polar bear and arctic charr (Fig. 2), have been largely based on conclusions from examination of correlative relationships between biomarker responses and POP (mainly OHC) concentrations in tissues and blood. One recent exception has been the collection of reports from a semi-captive studies with West Greenland sledge dogs and with Arctic charr. Regardless, there are other numerous factors to consider that can influence and modulate OHC/POP exposure in Arctic wildlife and fish, not the least of which is the impact of climate change as already described.

OHC/POP modulating factors include OHC metabolism, and formation of persistent OHC metabolites, which can be distinct agents of OHC-mediated effect rather than via precursor OHCs directly. Other factors include seasonal fluctuations in exposures and subsequent effects, and in relation to changes in e.g., physiological, bioenergetic and dietary condition and status of species. Thus, there are "critically" effective periods and biological/physiological considerations in terms of exposure and "sensitivity" of an effect response. There are trans-generational and age factors, survival, morphometrics and body condition. There is also the possibility of adaptive responses to POP exposure which could reduce the effect sensitivity for an exposed species or population over time. Therefore, one has to be cautious in building a "weight of evidence" and in establishing effects thresholds based on POP exposure and incorporating data from studies on non-Arctic species such as captive laboratory animals (e.g., monkeys and rats), or using *in vitro* models in attempts to establish cause–effect relationships for arctic species.

Multiple stressor effects in relation to POP exposure thresholds must also consider the changing and dynamics of POP trends (temporal, geographic) and the complexity of the types of POPs/OHCs. That is, the complexity and synergism of effects in relation to the (known and unknown) POP "cocktail" of exposure (Tables 1–4). In a situation of multiple chemical exposures, the single chemicals may act independently as in a single exposure, or a number of the chemicals may interact to modulate the effects of the total multiple exposure. An additive effect occurs when the combined effect of two chemicals corresponds to the sum of the effects of each chemical given alone. The interactions between different chemical components in a mixture may also result in either a weaker (antagonistic) or a stronger (synergistic) combined effect than the additive effect that would be expected from knowledge about the toxicity and mode of action of each individual compound. Potentiation occurs when the toxicity of a chemical on a certain tissue or organ system is enhanced when given together with another chemical that alone does not have toxic effects on the same tissue or organ system.

POP/OHC interactions may take place in the toxicokinetic phase (i.e. processes of uptake, distribution, metabolism and excretion) or in the toxicodynamic phase (i.e. effects of chemicals on the receptor, cellular target or organ). For compounds that are active as the parent compound, enzyme inhibition may reduce detoxication and thus enhance toxicity, whereas enzyme induction can enhance detoxication and thereby reduce toxicity. However, a majority of the chemicals which enter the body are metabolised (biotransformed). Metabolism can either increase (bioactivation) or decrease the toxicity of a compound, and there are a number of possible interactions that can influence the outcomes. Inducers of the microsomal CYP enzymes are well known to result in either increased production of active toxic metabolites or reduced toxicity caused by increased detoxication, depending on which enzymes and pathways are affected and the biological activity of the parent compound and its metabolites (Colborn et al., 1993; Letcher et al., 2000a; Damstra et al., 2002; Hakk and Letcher, 2003; Crofton et al., 2005; Fisk et al., 2005; Boas et al., 2006; Alexander et al., 2008).

With respect to exposure to mixtures of contaminants, most focus has been put on compounds that have a similar mode of action (simple similar action, also termed Loewe additivity and dose addition). The best examples are PCDDs, PCDFs and dioxin-like PCBs, which are aryl hydrocarbon receptor agonsists (van den Berg et al., 1998), and estrogenic mimics that are the estradiol hormone receptor agonists (Matthiessen and Johnson, 2007). The toxic equivalent factor (TEF) concept is based on the assumption that

structurally related chemicals exert their toxic effects by a similar mechanism of action (simple similar action), but they differ in potency. The TEF approach has been used for the risk assessment of mixtures of PCDD/Fs and dioxin-like PCBs in arctic animals in the two previous AMAP reports on POPs. A re-evaluation of human and mammalian TEFs for dioxins and dioxin-like compounds has recently been performed by WHO (van den Berg et al., 2006). Finally, there is a general lack of data for many new OHCs and other POPs with respect to a toxic equivalency approach for arctic wildlife and fish.

Due to release of estrogenic compounds to aquatic environments there has recently been particular focus on exposure to mixtures which contain different estrogenic compounds (Thorpe et al., 2006). Currently available information suggests that mixtures of estrogenic compounds act no more than additively (Brian et al., 2007; Matthiessen and Johnson, 2007). There is however, also concern about antiestrogenic properties of some chemicals, especially of drugs (Kawahara and Yamashita, 2000). Thus, in the environment animals can be exposed to mixtures of both oestrogenic and antiestrogenic compounds (Houtman et al., 2004). There does not seem to be any studies on the additive effects of multiple estrogenic compounds in arctic animals. In addition, other environmental factors than contaminants, such as temperature, pH, salinity and nutritional status, may influence the biological response to a chemical challenge, and thus act as confounding factors in the analysis of mixture effects.

There is also serious concern about combined effects of mixtures on the thyroid system of arctic animals. Studies on free-ranging fish, birds, seals and polar bears have shown correlative associations between pollutant levels, in particular PCBs and levels of circulating THs (Brown et al., 2004; Braathen et al., 2004; Jørgensen et al., 2004; Sørmo et al., 2005; Verreault et al., 2004). The modes/mechanisms of action of thyroid disrupters are multiple, and little is known about the combined effects of several chemicals that interfere with the thyroid homeostasis. However, it has been documented that exposure to mixtures of thyroid-disrupting chemicals may cause both dose-dependent additivity and synergism (Crofton et al., 2005), but dissimilar modes of action may also play an important role. Many POP/OHC concentrations also covary so that it is not possible to state equivocally that a certain level of POP/OHC exposure is the cause of the observed effect.

Threshold levels of individual OHCs have mainly been established in laboratory animals for effects on reproduction, neurobehavioral development, and immune suppression. There are major species differences in e.g., susceptibility, sensitivity and differing mechanisms to the effects of POPs and the environmental complexity of the mixture of POPs, and thus taking such a threshold approach may not be applicable and is difficult to establish for arctic species. There are either none or insufficient effects data for many newly identified POPs in arctic wildlife such as brominated flame retardants, perfluorinated compounds and current-use pesticides and other industrial chemicals, as well as for biologically active metabolites of some POPs such as OH-containing organohalogens (e.g., OH-PCBs). Thus, it is not yet possible to assess the effects of current levels of these contaminants in arctic biota. Results from field experiments with surrogate species have given added weight to the possible link between some POPs and specific effects. The implications of these findings are that populations of key species (e.g., east Greenland and Svalbard polar bears and Svalbard glaucous gull), and possibly other highly contaminated species, that are being affected by current levels of some POPs.

There is no information on possible effects of contaminants in fish in the Arctic at the population level. However, in general, and based on arctic charr dosing studies, it may be concluded that the levels of POPs/OHCs in fish in the Arctic are below the threshold levels for adverse effects and that only a few species and/or individuals show levels which are above thresholds for adverse biological effects. Data from experimental laboratory studies mimicking the Arctic life-style, and the few comparative data obtained from high- and low contaminated arctic charr from Bjørnøya, leads to the proposition that several arctic species of fish (e.g. Greenland shark, arctic charr, Greenland halibut and blue hake) may suffer from POP-related performance dysfunction. This conclusion is strengthened by the fact that feral animals, in contrast to laboratory contaminated animals, are exposed to multigenerational, life-long contamination and that they are contaminated with a suite of contaminants. It is also possible to conclude that for Arctic charr the threshold ΣPCB levels for adverse effects may be as low as 100 ng/g tissue ww seasonally, and even lower for early life stages (eggs, fry). However, there is a lack of studies on tissue toxicant levels, their seasonal changes in tissue distribution, and possible effects in feral fish in the Arctic, and such studies are highly needed. For example, seasonal fat deposition and fat mobilization may lead to high tissue accumulation of POPs/OHCs during the fattening period and a subsequent abnormally high inter- and intra-tissue redistribution of lipophilic pollutants during the emaciation period, which could lead to a potentiation of their toxicity. Extending to wildlife, as for fish there are also sensitive periods of development, e.g., critical development periods for young animals such as during the denning period for mammals and chick rearing periods for birds (periods where these animals use an exceptional amount of body lipids).

In the present effects assessment, and based on the aforementioned rationale, a different approach was taken with respect to the concept of POP/OHC exposure level thresholds for effects, as was taken in the last AMAP effects assessment (de Wit et al., 2004; Fisk et al., 2005). A pragmatic perspective on what may be considered an exposure threshold of heightened effects risk for any given OHC, class of OHC and POP in an Arctic wildlife or fish species, would be to consider the 1 ppm level in any target tissue, body compartment or egg as a general bioindicator of higher risk of a deleterious impact on health and likely via a complex and combined mode(s) of actions, regardless of whether correlative (Fig. 2) or cause–effect information is known. As has been summarized and discussed, there are several arctic species in which at least one class of OHC exceeds to 1 ppm (lw or ww) level (Tables 1–4). For example, East Greenland, Svalbard and (West and South) Hudson Bay polar bears, Alaskan and Northern Norway killer whales, several species of gulls and other seabirds from the Svalbard area, Northern Norway, East Greenland, the Eastern Russian Arctic and/or the Canadian central high Arctic, East Greenland ringed seal and a few populations of arctic charr and Greenland shark (Fig. 1). One could argue that this perspective follows the precautionary principle approach, i.e., not having scientific certainty is not a justification for not regulating (Hanekamp and Bast, 2007). A 1 ppm OHC (class) exposure threshold is a cautious definition of deleterious, OHC-associated risks to arctic wildlife and fish and promotes a preventive prescription rather than a more precautionary dimension such as regulation to control human activities to reduce or eliminate OHC exposure risks (Sandin et al., 2004).

5. Knowledge gaps and recommendations

The body of evidence is clearly growing with respect to OHC-mediated effects on arctic wildlife and fish. The trophic level that species occupy in the arctic marine food web, and their effect sensitivity, may predispose individuals to POP-mediate effects that may be adverse. POP-mediated effects data are lacking for other potentially more vulnerable species (e.g., ivory gull, glaucous gull, great skua and polar bear) and for most species during periods of physiological sensitivity (e.g., growth period, reproductive and fasting periods). There continues to be a lack of data on POP effects in Arctic wildlife and especially Russian, Canadian and Alaskan wildlife, where Russian wildlife are highly contaminated with POPs (e.g., in the White and Kara Seas) and thus are of high concern.

The very nature of POP exposure in Arctic wildlife is defined as being a complex mixture of known (Tables 1, 3 and 4) and unknown

chemicals, which includes a growing number of persistent OHC, and their degradation and metabolic byproducts (Table 2). There is clearly a need for continued characterization of unknown POPs, including OHCs, at levels that are deleterious to arctic wildlife, and with respect to the combined effects of the POPs cocktail to which they are exposed.

For marine mammals, focused attention in the immediate term should be given to the ringed seal (e.g., East Greenland) since present and temporal trends of OHC concentrations (Tables 1 and 2) in Arctic populations are showing a gradient of exposure, e.g. ranging from low in Alaska and western Canada to much higher in East Greenland, Svalbard, Western Russia and the Baltic region. Many groups, including AMAP, have identified the ringed seal as a keystone species, which supports the need to assess the overall health of seal populations, including the role contaminants may play. Focused attention for possible effects should also be given to killer whales, especially those frequenting the waters of Northern Norway, Alaska and Svalbard.

In selected species, such as top predator Svalbard and East Greenland polar bears and Svalbard glaucous gulls, there is a "weight of evidence" that suggest linkages between exposures to concentrations of known POPs and modulation/effect on biomarkers of e.g. immuno-suppression and endocrine disruption. At present these are exceptional cases as similar "weights of evidence" simply do not exist as yet for suggestive effects in other arctic species, i.e. strong linkages between contaminant exposure and effects. However, adverse effects have been found in arctic wildlife near some contaminated sites (e.g., military bases).

There is a general lack of basic ecological and physiological information for arctic wildlife that makes it difficult to assess potential changes caused by contaminants, or any anthropogenic stresses, and in the context of other environmental stressors such as climate change. This is important for determining baseline levels of hormones, vitamins, blood variables, immune factors, etc., and other factors that affect these (e.g., time of day, time of year, reproductive state, health status, fasting, etc.). It is not yet possible to conclude that changes in these imply increased risk.

Most effect thresholds established for POPs have been generated using non-arctic animals. Comparison of threshold effects levels to current levels in arctic organisms may be confounded by other stressors, e.g., seasonal physiological changes. Ideally, effects studies and risk assessment need to focus on exposure thresholds for arctic species, although this is an ethical and logistic challenge, and partial success has been achieved using surrogate and captive models, e.g., sled dogs and arctic fox for mammals (including humans). Physiological changes have been observed in seabirds (largely from Svalbard) with higher levels of OHCs, including PCBs, PBDEs and their metabolites. The impact of these changes and other sensitive effects on population dynamics should be studied. The health of wildlife near other sources of local contaminants should also be assessed.

Biological effects of new chemicals, as well as persistent metabolites such as OH-PCBs and OH-PBDEs and $MeSO_2$-PCBs and -*p,p′*-DDE have been shown. Correlative/associative evidence for, e.g., immune, endocrine and pathological effects in East Greenland polar bear has been reported. However, whether there is a health impact at the population or ecosystem level, or what the relative importance is of these contaminant stressors compared to the complexity of multiple environmental stresses, is currently unknown and unstudied. The POP stress is complex considering newly established contaminants such as PBDEs and PFCs. Interpretation of correlative hormone studies is hampered by lack of information on what other variables may affect these in wild populations. This makes drawing conclusions from some biomarker studies tenuous.

The present review has summarized a number of investigations that have revealed potential chemically-related stress in certain highly or moderately contaminated arctic terrestrial and marine bird species. However, important knowledge gaps on the mechanisms of toxicity and impact of anthropogenic or natural stressors in Arctic avian contaminants research prevent drawing a holistic picture of the current health status of these potentially more sensitive bird species. We recommend that future effect studies of POPs on terrestrial and marine birds, given the valuable information on effect mechanisms provided by the America kestrel studies, should focus on the combined effects of POPs and other anthropogenic or natural stressors. Using laboratory and/or semi-field designs, these studies should also aim to identify the effects of single classes of contaminants, including the POPs of most environmental concern (e.g., legacy OCs) but also more recently identified or suggested POP candidates (e.g., BFRs, PFCs and current-use pesticides), and their combined effects. For ethical and logistical reasons, given the demand or resources and time for e.g. semi-field study designs, and the reality that naturally complex POP exposures occur in wildlife and fish in the field, it would be most logical to consider study designs based on exposures to complex mixtures of (known and unknown) POPs via a diet that reflects the food basket of the Arctic species in question. Furthermore, populations of various Arctic avian species are showing declining trends and enhanced contaminant exposure coupled with a predicted rapid change of the Arctic climate may be important contributing factor causing these declines. We encourage especially those studies dealing with wild populations in which interactive effects of anthropogenic and natural stress parameters, and pollutant exposure can be measured.

A major challenge for understanding the impacts of POPs in wildlife is to link the effects/responses observed in animals to a specific cause, such as exposure to bioaccumulative contaminants and their precursor and degradation products. Many studies rely on correlations between tissue concentrations of contaminants and effects using a biomarker approach. Biomarkers are a measure of changes in physiological or anatomical state and indicative of potential POP-mediated effects. In some cases an effect can be defined as adverse, within the natural response variation, and can cause reversible or irreversible changes in an organism. However, in addition to logistical constraints such as selection of study site, season, and time window during the life cycle, other weaknesses include limited knowledge of the life history and general condition of randomly-captured animals. POP-related effects must be considered in the context of other or additional stressors, including anthropogenic activities, parasite infection, predation, micropathogens (disease), climate change and food scarcity. The potential adverse effects due to POPs/OHCs may be expressed as observed changes in animal performances, including impaired reproduction, altered response and stress responses (to infectious agents), but this remains to be established in Arctic wildlife and fish.

Chimate change is the dominant stressor to arctic ecosystems in biota. Climate change as an effects stressor to Arctic wildlife and fish clearly can be linked through changes in the level and type of POP/OHC exposure. This has been recently demonstrated for Western Hudson Bay polar bears, where temporal changes in sea ice conditions (1991–2007) was found to be linked to polar bear diet/food web (McKinney et al., 2009). In turn, several chlorinated and brominated OHC levels increased faster (e.g., ΣPBDE) and went from decreasing to increasing (i.e., ΣCHLs and ΣPCBs), relative to levels had diet not changed. These diet-influenced trends may continue with increasingly warmer temperatures and diminished sea ice under predicted climate change scenarios (Johannessen et al., 2004). These results indicate that there is a need to further investigate the interrelationships between climate change and effects on factors (such as diet) that can change the levels and trends of OHC exposure, and possibly on OHC-mediated effects, which are likely to be specific to Arctic regions and/or species populations.

In our recommendations we may say that we encourage/recommend to do more co-operation between scientists in the Arctic (as has been done with circumpolar polar bears) with regard to

studies on spatial and temporal trends. More harmonization of collection of samples as well as analysis done by the same laboratory will improve our impact to management people. One should consider the sample archives as sources for materials to assess metabolites, nutrients and biomarkers as well. Scientists should also indicate the tissue types and storage conditions for use in assessing impacts of contaminants (e.g., histology, serum chemistries), not just warehousing for chemical analyses only.

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