

2013

What are the toxicological effects of mercury in Arctic biota?

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Dietz, Rune; Sonne, Christian; Basu, Niladri; Braune, Birgit; O'Hara, Todd; Letcher, Robert J.; Scheuhammer, Tony; Andersen, Magnus; Andreasen, Claus; Andriashek, Dennis; Asmund, Gert; Aubail, Aurore; Baagøe, Hans; Born, Erik W.; Chan, Hing M.; Derocher, Andrew E.; Grandjean, Philippe; Knott, Katrina; Kirkegaard, Maja; Krey, Anke; Lunn, Nick; Messier, Francoise; Obbard, Marty; Olsen, Morten T.; Ostertag, Sonja; Peacock, Elizabeth; Renzoni, Aristeo; Rigét, Frank F.; Skaare, Janneche Utne; Stern, Gary; Stirling, Ian; Taylor, Mitch; Wiig, Øystein; Wilson, Simon; and Aars, Jon, "What are the toxicological effects of mercury in Arctic biota?" (2013). *USGS Staff -- Published Research*. 763.
<http://digitalcommons.unl.edu/usgsstaffpub/763>

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Review

What are the toxicological effects of mercury in Arctic biota?

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HIGHLIGHTS

- Unpublished and published data were compiled for Arctic fish, birds, and mammals.
- These data were compared to available toxicological threshold limits.
- Toothed whales, polar bears, and some bird and fish species exceeded the limits.
- Increasing mercury concentrations are observed for some Arctic species.
- These exceeded thresholds and increasing Hg trends are of concern.

ARTICLE INFO

Article history:

Received 20 April 2012

Received in revised form 7 November 2012

Accepted 10 November 2012

Available online 8 December 2012

ABSTRACT

This review critically evaluates the available mercury (Hg) data in Arctic marine biota and the Inuit population against toxicity threshold values. In particular marine top predators exhibit concentrations of mercury in their tissues and organs that are believed to exceed thresholds for biological effects. Species whose concentrations exceed threshold values include the polar bears (*Ursus maritimus*), beluga whale (*Delphinapterus leucas*), pilot whale (*Globicephala melas*), hooded seal (*Cystophora cristata*), a few seabird species, and landlocked Arctic char (*Salvelinus alpinus*). Toothed whales appear to be one of the most vulnerable groups, with high concentrations

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Keywords:

Fish
Birds
Mammals
Heavy metals
Exposure
Threshold levels

of mercury recorded in brain tissue with associated signs of neurochemical effects. Evidence of increasing concentrations in mercury in some biota in Arctic Canada and Greenland is therefore a concern with respect to ecosystem health.

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1. Introduction

Previous Arctic Monitoring and Assessment Programme (AMAP) assessments have reported that the highest biological mercury (Hg) concentrations in the marine environment were found within the upper trophic levels (Dietz et al., 1998a, 1998b; AMAP, 2005). Because of this Hg effects assessments relating to these species (i.e., with the highest presumed exposure) were carried out in the present AMAP assessment using data for species inhabiting this ecological niche in the Arctic and at lower latitudes. A recent review reported that Hg concentrations have increased in Arctic animals over the past 150 years, resulting in more than 92% of the Hg body burden in higher trophic level species being of man-made origin (Dietz et al., 2009). This indicates that Arctic species are exposed to higher Hg concentrations today than in historic times.

Two approaches have generally been taken in identifying and estimating the risk of possible effects of Hg or other contaminants in Arctic species. The first involves a comparison of concentrations in Arctic species against known detrimental levels or toxicity thresholds. In most cases, the detrimental levels are derived from laboratory studies, semi-field studies or observations of affected animals in the wild, with varying levels of study design rigor and certainty with respect to the actual cause or causes. Extrapolation is routinely used in toxicology but difficulties in extrapolation relate generally to differences in sensitivity, where the same types of effects are seen but at different doses, or to differences in structure and function. These scenarios are also complicated by dose (exposure) reconstruction, and range from being high in certainty to very gross estimates.

Laboratory animals are most often exposed to a single contaminant at high doses for short periods of time, and it is difficult to extrapolate the toxic effects seen at high acute doses to possible adverse effects at lower but chronic exposures. Wild animals are generally exposed to lower concentrations of Hg or other contaminants than laboratory animals, and they are exposed to mixtures of contaminants. In addition, captive animals tend to be housed under optimal conditions while

free-ranging animals are subjected to a variety of stressors that may lower their resilience to toxicants. Differences in species sensitivities to the effects of contaminants make it difficult to know which of the tested species best represents those in the Arctic (e.g., Ross, 2000; O'Hara and Becker, 2003).

This review critically evaluates the existing Hg data in Arctic biota based on the AMAP Hg assessment by Dietz et al. (2011b) and compares this with toxicity threshold values. Details on Hg concentrations, species and references are provided in the Supplementary material and locations in Fig. 1.

2. What role does mercury speciation play in uptake and toxic effects?**2.1. Mercury uptake and demethylation**

More than 95% of the methylmercury (MeHg) in food items is taken up by mammals, whereas the corresponding proportion for inorganic Hg is thought to be lower than 15% (Berlin, 1986; WHO, 1993; Mori et al., 2012). Methylmercury is transported through the intestinal mucosa, and lymph and blood vascular portal systems transport it into the organs where it may be demethylated, stored, or excreted. In marine mammals, the liver is the organ with the highest reported Hg concentrations (Dietz et al., 1998a). Studies show that demethylation occurs here in marine mammals and birds (Dietz et al., 1990, 2000a). For terrestrial mammals, including polar bears, kidney has the highest Hg concentrations and hence may be the main target organ (AMAP, 2011). Some high trophic level predators, such as polar bears and pinnipeds (fin-footed mammals such as seals), may use other strategies, such as excretion of MeHg into growing hair and excretion through urine and feces (e.g., Dietz et al., 2006a; Brookens et al., 2007, 2008; Cardona-Marek et al., 2009). Birds utilize a similar excretion strategy via feathers (e.g., Dietz et al., 2006b). Hair and feathers may represent a means to limit the bioavailability of MeHg to the central nervous system (Basu et al., 2009).



Fig. 1. Circumpolar map showing regions from which Hg data was available for the present effect assessment of Arctic wildlife (not all fish locations are shown). See Supplementary material for details of Hg concentration levels, species and references. Map source: [Letcher et al. \(2010\)](#).

2.2. Mercury–selenium relationships and interactions

A strong positive correlation between the concentrations of Hg and Se in tissues (e.g., liver, kidney) of many fish-eating wildlife species, especially predatory marine mammals is well documented (Koeman et al., 1973; Koeman and van deVen, 1975; Smith and Armstrong, 1978; and others). The Hg–Se relationship is a toxicant–nutrient interaction that has relevance for both basic biology and environmental risk assessment; however, important physiological details of the relationship are still unclear.

High trophic level mammals and birds may be partially protected against MeHg toxicity (particularly in the liver and for polar bears also in the kidney) due to binding of inorganic Hg with Se in an approximate 1:1 molar ratio, respectively (Dietz et al., 2000a, 2011b). This complex probably represents a direct covalent (or other strong) interaction of Hg and Se. In some wild aquatic predatory bird and mammal species, it has been shown that MeHg predominates in the liver at low total Hg (THg) concentrations whereas at higher

concentrations an increasingly large percentage of THg is present as inorganic Hg associated with Se, and some studies have identified this complex as HgSe (tiemanite) (Koeman and van deVen, 1975; Dietz et al., 1990, 1998a, 1998b, 2000a, 2000b; Scheuhammer et al., 1998, 2008; Wang et al., 2001; Woshner et al., 2001a, 2001b, 2008; O'Hara et al., 2003; Arai et al., 2004; Ikemoto et al., 2005; Dehn et al., 2005, 2006; Eagles-Smith et al., 2009; Moses et al., 2009; Routti et al., 2011).

3. Is there any evidence that tissue mercury concentrations at present are harmful to Arctic biota?

3.1. Cerebral exposure and potential neurological effects of mercury on Arctic marine mammals

Mercury has the potential to cause neurotoxicity in Arctic biota and human residents and this is of major concern; especially for women of childbearing age and the developing fetus (e.g. [US EPA](#),

1997; ATSDR, 1999; Clarkson and Magos, 2006; Mergler et al., 2007; Grandjean et al., 2010). Besides humans, Hg is also neurotoxic to wildlife and Hg-associated poisoning events have been documented in some fish-eating species, such as mink (*Mustela vison*) and common loons (Scheuhammer et al., 2007; Basu et al., 2009; Pilsner et al., 2010).

While all chemical forms of Hg have intrinsic neurotoxic properties, environmental public health is most concerned with organic Hg and in particular MeHg exposure. Methylmercury biomagnifies through aquatic and marine ecosystems including food chains in the Arctic (Atwell et al., 1998). Methylmercury can cross the blood–brain barrier (Aschner and Aschner, 1990), and the brain is considered the primary target organ of MeHg toxicity in higher organisms (WHO, 1993). At sufficient concentrations, MeHg may disrupt a range of neurological processes within the brain owing to its high affinity for protein thiols (Clarkson and Magos, 2006). Characteristic outcomes of MeHg poisoning in both humans and mammalian wildlife include structural degeneration of the occipital cortex and the cerebellum, which leads to paresthesia (numbness, tingling), ataxia (incoordination), sensory impairment, and memory loss (ATSDR, 1999; Clarkson and Magos, 2006; Basu et al., 2007a; Basu and Head, 2010). There is some concern that Hg concentrations in Arctic wildlife and humans may be approaching those that cause impacts on behavior and health. For example, an associative study on 43 Inuit children (Qaanaaq, Greenland) reported that Hg exposure may be related to subtle neurological deficits in a few cases examined (Weihe et al., 2002). Balancing the risks/benefits of Hg exposure via dietary pathways is an immense challenge as fish and marine mammals are the primary means by which Hg is transferred to humans and high trophic level wildlife but are also an excellent and critical source of nutrients for Arctic consumers.

In a recent study, THg and MeHg levels were evaluated in the lower medulla oblongata (brain stem) brain region of 82 polar bears collected by subsistence hunters in Greenland (Basu et al., 2009). In that study, concentrations of THg of less than 1 µg/g were found (mean = 0.36 ± 0.12 µg/g dw; range 0.11 to 0.87 µg/g). In this same brain region, MeHg comprised 83% of the THg present. Krey et al.

(2012) documented that brain MeHg comprised 100% of the brain total mercury in Canadian polar bears from Nunavik (Fig. 2). In a previous study of eight ringed seals from northern Quebec, the mean THg concentration in the cerebral cortex was 0.09 ± 0.05 µg/g ww (wet weight) (Basu et al., 2006a). Similar THg values (0.13 ± 0.03 µg/g ww) were found in the brain tissue of six harp seal (*Phoca groenlandica*) pups collected from the Grise Fjord and Pangnirtung region of Nunavut (Ronald et al., 1984). Canadian beluga exhibited brain concentrations that are an order of magnitude greater than those in polar bears and seals (Lemes et al., 2011).

At a neurochemical level, MeHg may cause a range of sub-clinical effects and so neurochemical biomarkers have recently been used to assess the early risks of Hg to several fish-eating wildlife species that accumulate high levels of Hg. For example, changes in the levels of muscarinic cholinergic receptors (increased) and N-methyl-D-aspartate (NMDA) glutamate receptors (decreased) were related to concentrations of brain Hg in wild mink (Basu et al., 2005, 2007b), common eagles, and bald eagles (Scheuhammer et al., 2008). Several of these neurochemical effects have been substantiated in laboratory studies involving captive mink experimentally fed environmentally realistic MeHg doses (Basu et al., 2006b, 2007b). These results suggest that Hg at ecologically relevant levels may be exerting subtle, sub-clinical neurological changes in the 3 to 5 µg/g dw range (dry weight concentration in brain tissue) in several fish-eating wildlife species.

Neurochemical biomarkers have recently been applied in studies on Arctic biota (Basu et al., 2009). Despite relatively low concentrations of Hg in the lower brain stem of polar bears, significant negative correlations were found between both MeHg and THg concentrations and synaptic NMDA (N-methyl-D-aspartic acid) glutamate receptors similar to observations in other organisms (Fig. 3). In these polar bear tissues, concentrations of several chlorinated and brominated organic chemicals were also measured; however, statistical analyses showed that these were not correlated with any of the neurochemical biomarkers (Basu et al., 2009). In a captive mink study, ingestion of food containing MeHg levels as low as 0.1 ppm (corresponding to brain Hg concentrations ranging from 1 to 2.2 µg/g ww) was linked to decreased

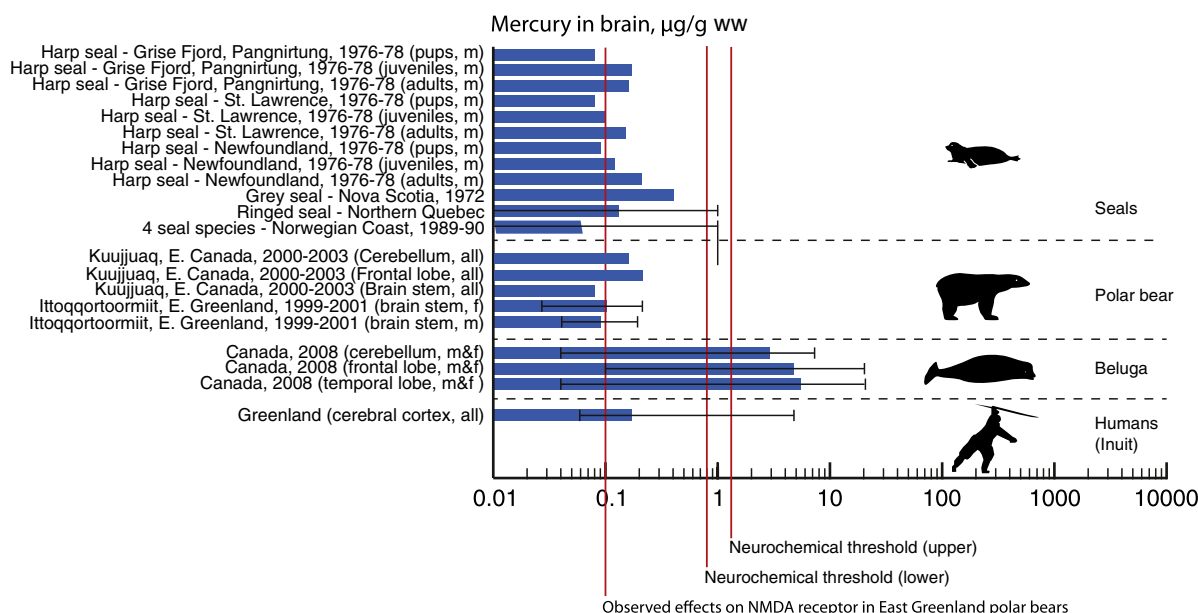


Fig. 2. Overview of mean mercury concentrations in brain from Arctic biota and humans. Red lines indicate the mean mercury concentrations in East Greenland polar bear brain stem that were associated with lower N-methyl-D-aspartate (NMDA) receptor levels and the mercury-associated neurochemical effect threshold in the 3 to 5 µg/g dw range based on previous studies on fish-eating mammals (Basu et al., 2006b, 2007b) and birds (Scheuhammer et al., 2008). For detailed data see Table S1. In cases where minimum and maximum concentrations are available these are indicated by range bars.

NMDA receptor concentration, fmol/mg

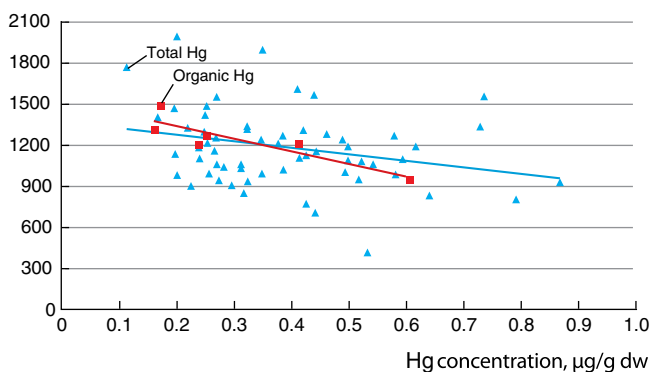


Fig. 3. Significant correlation between glutamate N-methyl-D-aspartate (NMDA) receptor levels and both total mercury ($n=60$; $r=-0.34$, $p<0.01$) and methylmercury ($n=6$; $r=-0.89$; $p<0.05$) in the medulla oblongata brain region of free-ranging East Greenland polar bears.

Source: adapted from Basu et al. (2009).

NMDA receptor levels (Basu et al., 2007b). A decreased level of brain glutamate NMDA receptors is potentially of ecological and physiological concern because glutamate is the main excitatory neurotransmitter, and glutamate receptors have essential roles in multiple facets of animal health, behavior, reproduction, and survival (Siegel et al., 2006). Changes to these receptors may represent one of the earliest and most sensitive biochemical indicators of MeHg exposure and effect.

3.2. Mercury-related histopathology of Arctic marine mammals

Few studies have investigated the histopathology (i.e. microscopic cellular and interstitial lesions) of Hg in Arctic wildlife. It is important to understand that all Arctic marine mammals are contaminated with a range of toxic substances including organic chemicals and mercury, and that the lesions found are similar to those being due to age, pathogen exposure and chemical contamination. Therefore; it can be hard to distinguish between the exact effects from these three groups of stressors despite observed significant relationships.

3.2.1. Liver exposure and effects

The functions of the liver are to serve as lymphatic and intestine drainage, to support metabolic processes and to synthesize plasma proteins and coagulation factors, as well as being an endocrine/immunological modulator and storage site of energy (glycogen) (Janeway et al., 2001; Ganong, 2005; Klaassen et al., 2007). In addition, the liver is the key site where xenobiotic compounds are biotransformed (Janeway et al., 2001; Ganong, 2005; Klaassen et al., 2007). Studies of Hg driven liver damage have been conducted both in the laboratory and in the field (Kelly, 1993; MacLachlan and Cullen, 1995; Rawson et al., 1993; Thompson, 1996; AMAP, 1998, 2005; Klaassen et al., 2007). In the Arctic, investigations of histopathological lesions in liver tissue from Arctic wildlife have focused on polar bears, pilot whales, bowhead whales, beluga and ringed seals (e.g., Woshner, 2000; Woshner et al., 2002; Sonne et al., 2007, 2010). Liver lesions were found in these five species, and where statistically significant associations were found between histochemical endpoints and Hg and Cd concentrations.

Liver is a major tissue where exposure to POPs and Hg elicits an effect via three biochemical pathways: induction of the sER (smooth endoplasmic reticulum, including CYP-450); disruption of the ADP.ATP pathway; and free radical oxidative stress of the cell membrane resulting in hypoxia and hepatomegaly (enlarged liver) as the first signs of liver toxicosis (Kelly, 1993; MacLachlan and Cullen, 1995; Klaassen et al., 2007). As such, liver weight may be a preliminary indicator (invasive biomarker) for POP and Hg exposure, and effects in Arctic marine mammals. However, non-specific histopathological changes such as intracellular hepatocytic steatosis (foamy cytoplasm), inflammation (lymphocytic and multinuclear cells) and necrosis may also occur, but cannot be used as specific contaminant biomarkers (Kelly, 1993; MacLachlan and Cullen, 1995; Klaassen et al., 2007).

In the wild, only a few studies have associated metal exposure to pathological changes in the liver. For example, high Hg concentrations of 61 $\mu\text{g/g ww}$ in the liver of Atlantic bottlenose dolphins (*Tursiops truncatus*) were associated with liver abnormalities (Rawson et al., 1993). The histopathological changes found in the liver of Arctic marine mammals (i.e., Arctic beluga, polar bear, bowhead whale, pilot whale and ringed seal) are similar to those observed in other Hg-exposed marine and laboratory mammals (Woshner, 2000; Woshner et al., 2002; Sonne et al., 2007, 2010). The latter, however, showed that histopathological changes could also be ascribed to age and dietary composition

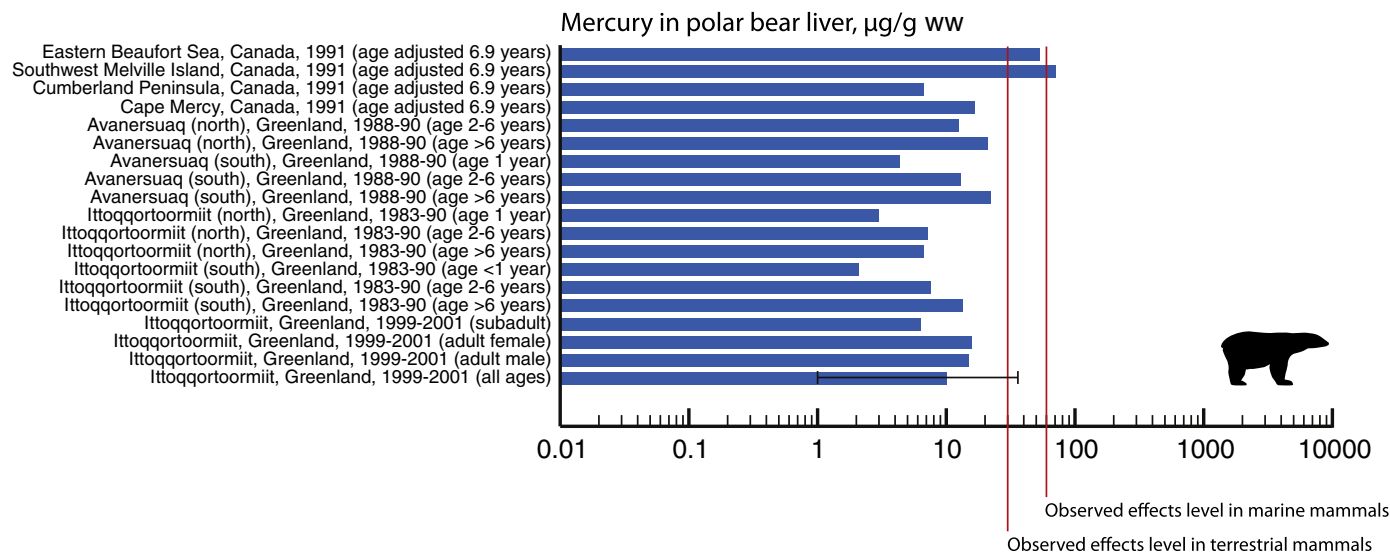


Fig. 4. Mercury concentrations in polar bear liver for selected regions of the Arctic and selected periods (for full datasets see Table S2). The lethal/harmful effect level for terrestrial free-ranging wildlife (30 $\mu\text{g/g ww}$; Thompson, 1996) and the observed effect level for marine mammals associated with liver lesions in bottle-nosed dolphins (61 $\mu\text{g/g ww}$; Rawson et al., 1993) are also shown. In cases where minimum and maximum concentrations are available these are indicated by range bars.

(lipid content), creating uncertainty in ascribing the lesions specifically to Hg.

Fig. 4 shows the mean liver Hg concentrations in polar bears of several age classes from various Arctic locations. Using an estimated toxic threshold value for terrestrial mammals of 30 µg/g ww (Thompson, 1996) only polar bear means from the eastern Beaufort Sea and Southwest Melville Island (age adjusted to 6.9 years) exceeded this threshold. Bears from Southwest Melville Island likewise exceeded the toxic threshold value of 61 µg/g ww for marine mammals (Rawson et al., 1993).

The only population where the mean value exceeded the threshold value for toxic effects in marine mammals (61 µg/g ww; Rawson et al., 1993) was for hooded seals (*Cystophora cristata*) from Davis Strait sampled in 1984 (mean 78 µg/g ww; no later data available from this region) (Fig. 5). Several other species and populations, such as ringed seals (>5 years) from Grise Fiord (in 1998) and hooded seals from the Greenland Sea (in 1999) had mean concentrations that approached the terrestrial mammal toxic threshold value of 30 µg/g ww (Thompson, 1996).

Fig. 6 shows the mean Hg concentrations in liver tissue from baleen and toothed whales. All baleen whale populations had liver Hg concentrations far below the toxic threshold levels. However, pilot whales from the Faroe Islands had liver concentrations above the 61 µg/g ww toxic threshold value (Hoydal and Dam, 2009; Sonne et al., 2010) for marine mammals provided by Rawson et al. (1993). Beluga from the St Lawrence River and Point Lay had mean liver concentrations close to the 30 µg/g ww toxic threshold value for terrestrial mammals provided by Thompson (1996).

3.2.2. Renal exposure and effects

Renal (kidney) lesions are of a health concern since this organ has endocrine functions, acts as a blood filter that clears metabolic waste

products such as urea, and maintains calcium and phosphorus homeostasis, blood pressure, water and electrolyte levels as well as activates vitamin D (Ganong, 2005). Kidney lesions have been reported in whale species and polar bears from the Arctic (cf. Woshner, 2000; Woshner et al., 2002; Sonne et al., 2007, 2010; Rosa et al., 2008) resemble those reported for gray seals (*Halichoerus grypus*) and ringed seals and bottlenose dolphins living in the heavily metal and organohalogen polluted regions such as the Baltic Sea (Lavery et al., 2009; Bergman et al., 2001). However, some work has shown that age and micro-pathogens (e.g., bacteria and parasites) are important co-factors in the development of kidney lesions in Arctic marine mammals which must be considered when evaluating metal toxicosis (Woshner, 2000; Woshner et al., 2002; Sonne et al., 2007, 2010; Rosa et al., 2008).

Fig. 7 shows Hg concentrations in renal tissue from polar bears. It is clear that for two populations from Southwest Melville Island and the eastern Beaufort Sea (sampled prior to 1991), kidney mean concentrations exceeded the toxic threshold value for marine mammals (61 µg/g ww). These values were, however, calculated from tissue ratios from Greenland bears as no kidney data were available from these regions. If, on the other hand, the terrestrial toxic threshold value of 30 µg/g ww is used then polar bears from East Greenland also exceeded the threshold level. The increases observed in Hg concentration in polar bear hair in recent years indicate that kidney concentrations have increased in some of the northern populations (Dietz et al., 2006a, 2009, 2011a). The prediction of the northeastern Canadian bears as being at risk of Hg toxicity fits well with the liver and hair data described above and in AMAP (2011).

Mean Hg concentrations in renal tissue for various seal species showed that none of the seal populations have renal Hg concentrations that reach the 61 µg/g ww toxic threshold value for marine mammals or the 30 µg/g ww toxic threshold value for terrestrial

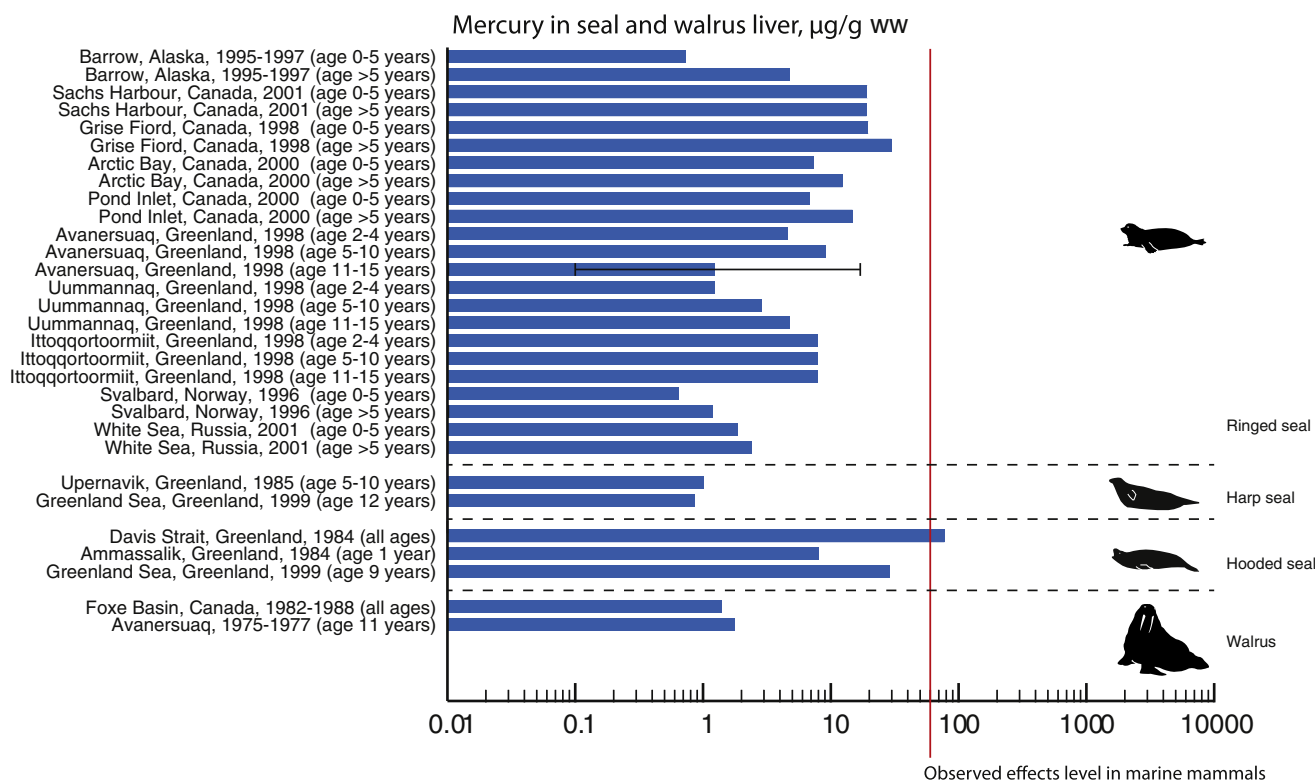


Fig. 5. Mercury concentrations in seal and walrus liver for selected regions of the Arctic and selected periods (for full datasets see Table S3). The observed effect level for marine mammals associated with liver lesions in bottle-nosed dolphins (61 µg/g ww; Rawson et al., 1993) is also shown. In cases where minimum and maximum concentrations are available these are indicated by range bars.

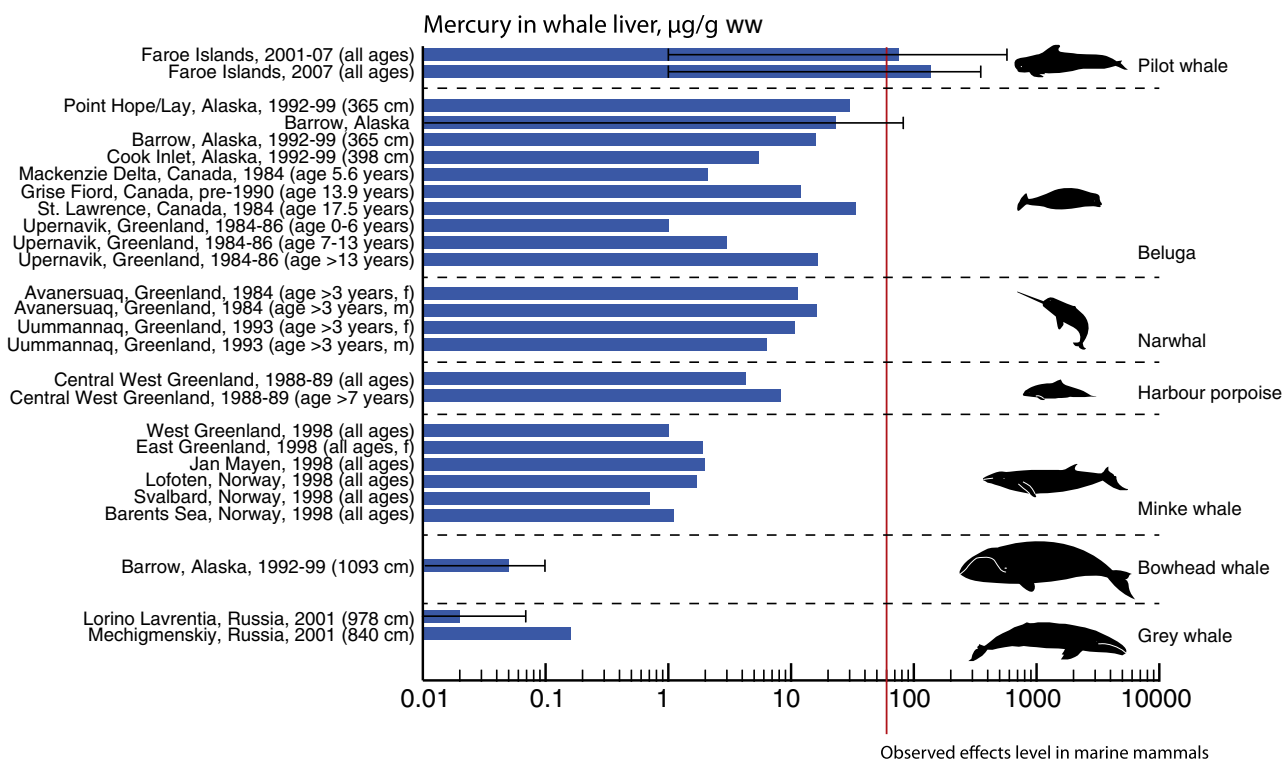


Fig. 6. Mercury concentrations in whale liver for selected regions of the Arctic and selected periods (for full datasets see Table S4). The observed effect level for marine mammals associated with liver lesions in bottle-nosed dolphins (61 µg/g ww; Rawson et al., 1993) is also shown. In cases where minimum and maximum concentrations are available these are indicated by range bars.

mammals. All baleen whale populations had lower kidney Hg concentrations than the toothed whales. No whale population had kidney concentrations that reach the 61 µg/g ww toxic threshold for marine mammals or the 30 µg/g ww toxic threshold value for terrestrial mammals (Figs. 8 and 9).

3.3. Blood mercury in high trophic level Arctic species in comparison with human health guidelines

Because blood represents one of the few minimally invasive monitoring matrices for live vertebrates, and because multiple organs are being exposed through blood, this matrix is widely used in toxicology

studies. Mercury concentrations in blood are mainly in the methylated form (MeHg) and represent post-absorptive processing (diet), and release (mobilized) of stored sources (e.g., MeHg in muscle, liver) (Ronald et al., 1977).

Blood Hg concentrations for polar bears were in the same range as for harp seals from St. Lawrence, northeastern Canada and West Greenland, but greater than the levels in the Labrador harp seals (Fig. 10). Only blood Hg concentrations in Inuit women from Qaanaaq, north-western Greenland, were similar to levels in polar bear. Blood Hg concentrations showed the lowest concentrations in western Hudson Bay and comparable concentrations between Alaska and East Greenland (Cardona-Marek et al., 2009; Dietz et al., 2000b). Total Hg concentrations

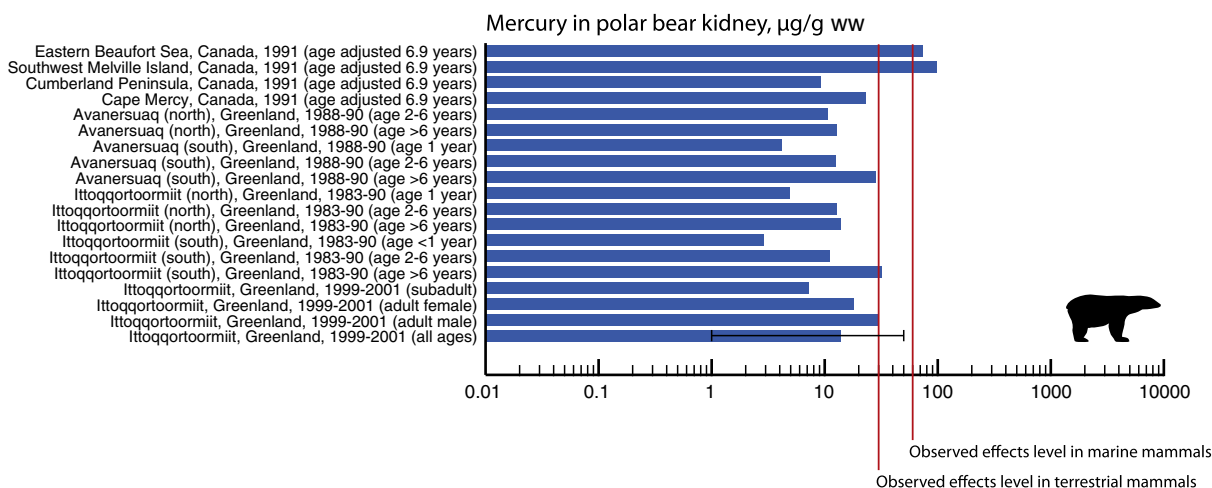


Fig. 7. Mercury concentrations in polar bear kidney for selected regions of the Arctic and selected periods (for full datasets see Table S2). The lethal/harmful effect level for terrestrial free-ranging wildlife (30 µg/g ww; Thompson, 1996) and the observed effect level for marine mammals associated with liver lesions in bottle-nosed dolphins (61 µg/g ww; Rawson et al., 1993) are also shown. In cases where minimum and maximum concentrations are available these are indicated by range bars.

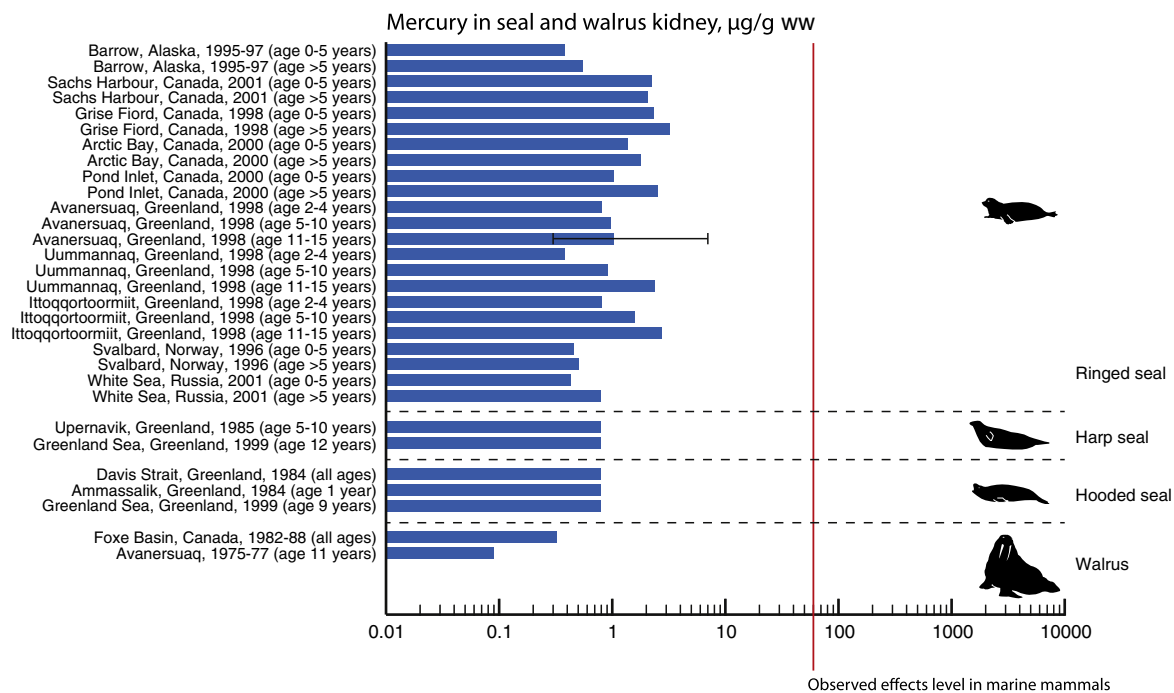


Fig. 8. Mercury concentrations in seal and walrus kidney for selected regions of the Arctic and selected periods (for full datasets see Table S3). The observed effect level for marine mammals associated with liver lesions in bottle-nosed dolphins (61 µg/g ww; Rawson et al., 1993) is also shown. In cases where minimum and maximum concentrations are available these are indicated by range bars.

in the blood of southern Beaufort Sea polar bears did not differ much by year (2005, 2007), age, or sex. Cardona-Marek et al. (2009) assessed sub-adults (3 to 5 years) and dependent young (1 to 2 years), and found a considerable amount of Hg in both blood and hair. Mercury in dependent young was suggested to be via maternal sources of Hg (i.e., during gestation and/or lactation) (Knott et al., 2012). This is an

important exposure route for Hg in young animals, and indicates an important elimination route for Hg in young animals, and indicates an important elimination route for reproductive females (Knott et al., 2012). Concentrations of THg in adult polar bears ranged from 7 to 210 µg/L for blood, with adult females having a greater concentration of THg in hair than adult males, again indicating a cohort of concern exposed to higher Hg (i.e., the fetus and neonate) as reported by Cardona-Marek

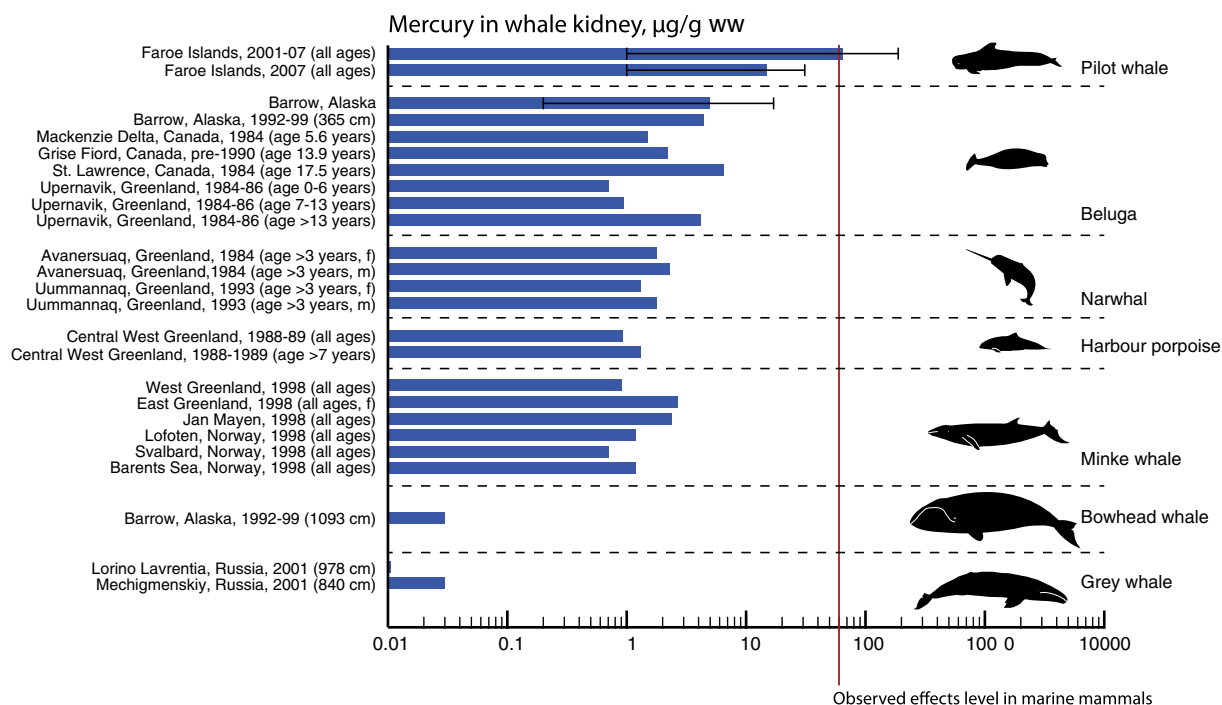


Fig. 9. Mercury concentrations in baleen and toothed whale kidney for selected regions of the Arctic and selected periods (for full datasets see Table S4). The observed effect level for marine mammals associated with liver lesions in bottle-nosed dolphins (61 µg/g ww; Rawson et al., 1993) is also shown. In cases where minimum and maximum concentrations are available these are indicated by range bars.

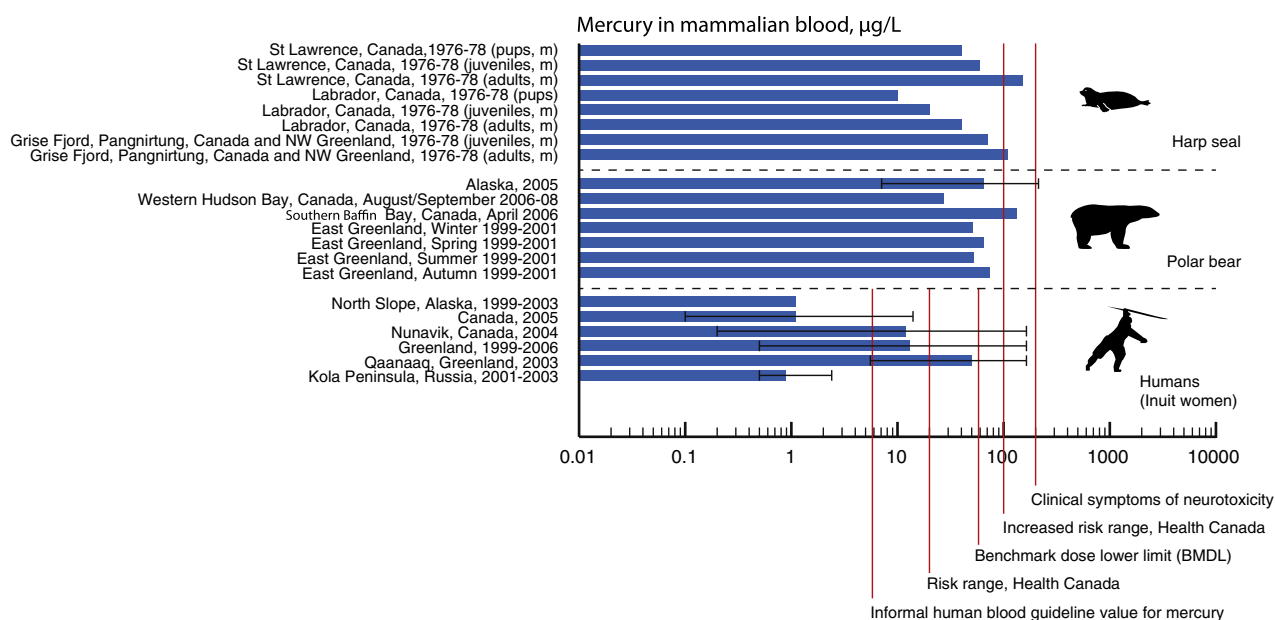


Fig. 10. Mean blood mercury concentrations in Arctic marine mammals, Arctic Inuit populations and guideline levels for wildlife and humans. For sources and raw data see Table S5. In cases where minimum and maximum concentrations are available these are indicated by range bars.

et al. (2009). The explanation for this difference may be due to a higher dietary exposure of pregnant or lactating female polar bears as they may eat more high protein and high Hg-exposed tissues than males, who tend preferentially to eat blubber which is low in Hg. Also, Alaskan female bears may target species higher in Hg (smaller pinnipeds), while males may target larger species with less Hg (bowhead whales (scavenged), bearded seals and walrus) simply based on larger males taking larger prey. The implication of maternal transfer of Hg to polar bear offspring is unknown and further research should examine the potential of Hg accumulation (and resulting effects) on the developing organism. A seasonal difference has been reported for polar bear blood with spring and autumn Hg concentrations being higher than during summer, when limited sea ice is available on which to hunt, and during winter when females hibernate and seals are harder to access (Dietz et al., 2011b).

In the absence of polar bear-specific guidelines for Hg in blood, Hg blood concentrations are compared to those derived for humans. The blood guideline established by Health Canada for Hg considers concentrations below 20 µg/L in human blood to be within an acceptable range (Health Canada, 1984). Individuals with Hg concentrations between 20 and 100 µg/L have been determined to be at 'increasing risk', whereas individuals with blood Hg concentrations that exceed 100 µg/L are considered to be 'at risk'. Following the observations at Minamata Bay, Japan where thousands of people suffered from MeHg poisoning, it was concluded that 200 µg Hg/L whole blood may be considered a value associated with clinical symptoms of neurotoxicity (Clarkson and Magsos, 2006). Based on a review of human epidemiological data from studies from the Faroe Islands and New Zealand, the NAS/NRC (U.S. National Academy of Sciences/U.S. National Research Council) derived a benchmark dose lower limit (BMDL) of 58 µg/L Hg in cord blood. The U.S. National Research Council re-evaluated the Hg risk assessment (NRC, 2000). The NRC report suggested that a ten-fold uncertainty factor should be applied in the development of a tolerable daily intake (NRC, 2000). Based on this evaluation an informal blood guideline value for Hg of 5.8 µg/L in blood has been developed (see AMAP, 2003, 2011). When this guideline value is applied to the polar bear, it is clear that most bears possess blood Hg levels that would be of health concern in humans. It should

be emphasized that variable sensitivity to Hg exists across species and that the human 5.8 µg/L guideline is highly conservative. For example, primates with blood Hg levels exceeding 1000 µg/L did not show any signs of clinical toxicity (Clarkson and Magsos, 2006).

Because many bears are above the human 'increasing risk' (20 and 100 µg/L) and the 'at risk' (over 100 µg/L) criteria levels, this raises questions about possible implications for polar bear health. In addition, Cardona-Marek et al. (2009) reported that the highest Hg concentration in blood (213 µg/L) was from a 16-year old female captured near Barrow. The maximum concentrations observed in the East Greenland, southern Baffin Bay and western Hudson Bay populations were 287, 739 and 56 µg/L, respectively (Dietz et al., 2011b; Routti et al., 2011). The northern Arctic Canada and north western Greenland populations are likely to have even higher levels of blood Hg, as indicated in the geographical Hg exposure pattern for polar bear liver and hair (Dietz et al., 1998a, 2000a).

3.4. Comparison of polar bear hair concentrations with effect guidelines

As polar bear hair has been analyzed extensively over time and across regions, and as the Hg levels relate to effect thresholds, this matrix was used to evaluate circumpolar temporal trends in Hg exposure (Dietz et al., 2011a; Stern et al., 2012). Hair represents a good biomarker of Hg exposure since it accumulates organic Hg from blood and can be collected through minimally invasive sampling methods. Hair is a well-established research matrix for Hg among humans, from which effect guidelines have been set. As for blood, it is not known to what extent these effect levels are applicable to wildlife or polar bears in particular.

Dietz et al. (2006a, 2011a) reported that Hg concentrations in polar bear hair have increased more than 14-fold since pre-industrial times in Greenland, indicating a trend that is likely to involve anthropogenic sources. These increases are in accordance with increases in other hard tissues from high trophic level Arctic species (AMAP, 2011; Dietz et al., 2009). Polar bear hair represents a non-invasive substrate that may be collected for risk assessment.

Recent studies on polar bears from the East Greenland coast have documented Hg-associated reduction of the NMDA receptor levels and of genomic DNA methylation status in the brain stem (Basu et

al., 2009; Pilsner et al., 2010). These sub-clinical, biochemical alterations have been reported for populations with hair Hg means of about 5.4 µg/g dw. These means are comparable to the revised NOEL (no observed effect level) for Hg in human hair (6.0 µg/g dw) from the Faroe Islands as suggested by Grandjean and Budtz-Jørgensen (2007). The revised NOEL from the Faroe Island human population is half the previous NOEL (12.0 µg/g dw) set for the region (FAO/WHO, 2003). The U.S. EPA Hg guideline value of 1.0 µg/g dw for human hair is among the lowest guideline values and is based on a NOEL of 12.0 µg/g dw with a safety factor of about 10 (U.S. EPA, cited in FAO/WHO, 2003). As seen from Fig. 11 (and Table 2) some populations of polar bears like those in Svalbard and western Hudson Bay have among the lowest hair Hg median concentrations. These levels are below concentrations in which neurochemical changes have been observed in East Greenland (Basu et al., 2009) and the NOEL of 6.0 µg/g dw in humans on the Faroe Islands (Grandjean and Budtz-Jørgensen, 2007).

None of the bears from western Hudson Bay exceeded the human Hg threshold level of 12 µg/g dw. Similarly, among the bear fur samples from 1892 to 1950 sampled by Dietz et al. (2006a), none exceeded this effect level. The 12 µg/g dw NOEL level was exceeded in 4.0% to 5.1% of the bears sampled between 1973 and 2000 and between 2001 and 2008 (Table 2). For Greenland, the percent exceedance was greater for northwestern Greenland (median 2001–2008: 9.4 µg/g dw; see also Table S6) relative to East Greenland (median 2001–2008: 6.1 µg/g dw). The population with the highest Hg concentrations, and hence, the population of greatest concern was the Lancaster Sound bears sampled between 1992 and 1999. Here the effect levels of 1 and 6 µg/g dw were exceeded by 98.1% to 100% of the bears respectively, while the 12 µg/g dw effect level was exceeded by 75.9% of the bears (Table 2). In Lancaster Sound polar bears a concentration of 30 µg/g dw may have been reached in their hair by 2001, if the observed Hg increases have continued (Fig. 11).

The median values in northwestern Greenland are already close to the human guideline value of 12 µg/g dw. If the increases observed in Greenland continue, then the median concentrations will reach this

Table 1

Suggested thresholds for mercury in polar bear hair and effect guidelines in human hair.

Group	Hg µg/g dw	Symptoms	Source
Polar bear	5.4	Reduction in brain NMDA receptor level	Basu et al. (2009)
	5.4	Reduction in brain genomic DNA methylation	Pilsner et al. (2010)
Human	12	NOEL and BMDL for the Faroese population	FAO/WHO (2003)
	6	Revised NOEL and BMDL for the Faroese population	Grandjean and Budtz-Jørgensen (2007)
	1	U.S. EPA guideline values	U.S. EPA cited in FAO/WHO (2003)

level around 2030 in East Greenland and in Northwest Greenland a concentration of 20 µg/g dw will be reached by 2048, if the observed Hg increases continue (Fig. 11; Dietz et al., 2011a).

Polar bears sampled in East Greenland in ~2000 exhibiting neurochemical effects in the brain stem had mean hair Hg concentrations of 5.4 µg/g dw (Basu et al., 2009). Among East Greenland bears, in those sampled between 1973 and 2000 and between 2001 and 2008, 46.3% and 60.5% of cases, respectively exceeded the brain stem effect limit. The finding of Hg concentrations continuing to increase in some regions during the last decades, and the higher Hg levels in the northwestern Greenland and northern Canadian High Arctic populations, gives rise to concern for these populations (Dietz et al., 2011a; Rigét et al., 2011). Finally there are parts of the polar bear brain that contain even higher Hg concentrations (such as the pituitary gland, which has about 6-fold higher concentrations) than the brain stem, where more severe effects may be expected (Dietz et al., 2011b).

Future scenarios for hair Hg in hair draw attention to quite high Hg levels in polar bear fur, which have increased dramatically compared to the pre-industrial average concentration and which, in

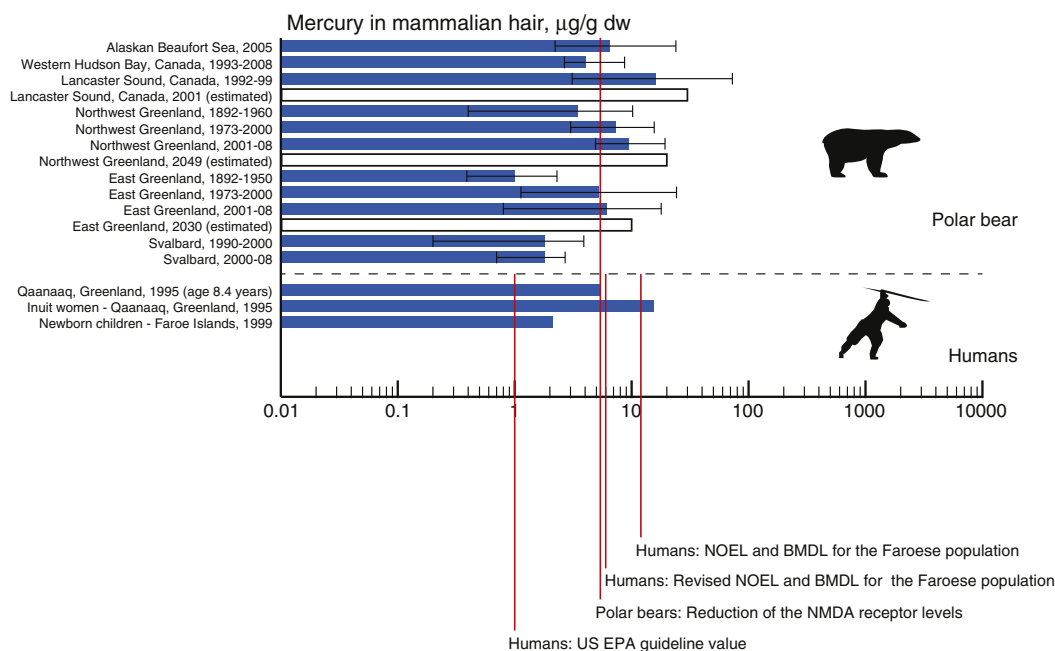


Fig. 11. Average and ranges (bars) for mercury concentrations in polar bear hair from northwestern Greenland, East Greenland, Svalbard, two Canadian management zones and the Southern Beaufort Sea. Future (relative to latest available) average values were estimated in three cases where significant upward trends were observed (open bars). Selected mean mercury concentrations in human hair are also presented, together with the effect threshold limits given Tables 1, 2 and S6, provide details on concentrations and data references. In cases where minimum and maximum concentrations are available these are indicated by range bars.

Table 2

Selected polar bear populations and periods showing their percentual exceedence of effect levels given in Table 1.

Population	Period	Median Hg, µg/g dw	N	Percentage exceeding the hair effect levels listed in Table 1. The effects level below are expressed in µg/g dw.				Data source
				1	5.4	6	12	
Alaskan Beaufort Sea	2005	6.5	52	96.2	65.4	59.6	9.6	Cardona-Marek et al., (2009)
Western Hudson Bay	1993–2008	4.1	59	100.0	6.8	1.7	0	Dietz et al., (2011b)
Lancaster Sound	1992–1999	16.0	54	100.0	98.1	98.1	75.9	Dietz et al., (2011b)
North western Greenland	1892–1960	3.5	10	90.0	10.0	10.0	0	Dietz et al., (2006a, 2011)
	1973–2000	7.3	76	100.0	84.2	73.7	6.6	Dietz et al., (2006a, 2011)
	2000–2008	9.4	31	100.0	93.5	93.5	25.8	Dietz et al., (2006a, 2011a, 2011b)
East Greenland	1892–1950	1.0	9	55.6	0	0	0	Dietz et al., (2006a)
	1973–2000	5.2	296	100.0	46.3	38.9	5.1	Dietz et al., (2006a)
	2001–2008	6.1	124	99.2	60.5	50.8	4.0	Dietz et al., (2006a, 2011b)
Svalbard	1990–2000	1.8	203	93.1	0	0	0	Dietz et al., (2011b)
	2000–2008	1.8	28	93.8	0	0	0	Dietz et al., (2011b)

several regions, continue to increase (Dietz et al., 2006a, 2009, 2011b). However, high Hg concentration in hair is also an effective way for the polar bears to excrete Hg from the body. Other species having less fur, such as seals and walruses, and in toothed whales (beluga, narwhal, pilot whale), this excretion route is non-existent. Toothed whales are thus more at risk from Hg, and this is also reflected in their higher concentrations in brain, liver and muscle (Olsen et al., 2003; Hoydal and Dam, 2005, 2009; Sonne et al., 2010; Lemes et al., 2011).

3.5. Comparison of safe guidelines in bird eggs with Arctic seabirds

Dietary MeHg is rapidly transferred to avian eggs on a dose-dependent basis, making reproduction one of the most sensitive end-points of Hg toxicity in birds (Wolfe et al., 1998). Nearly all of the Hg transferred to eggs is in the form of MeHg, with the majority (about 85% to 95%) deposited in the egg white (Wiener et al., 2003). Mercury concentrations in the egg are a good indicator of Hg risk to avian reproduction (Wolfe et al., 1998). Some of the documented effects of Hg on avian reproduction include reduced hatchability due to increases in early mortality of embryos, reduced clutch size, and embryonic deformity (Thompson, 1996; Wolfe et al., 1998).

The currently accepted, lowest observed adverse effect level (LOAEL) for Hg in avian eggs (whole) is 0.5 µg/g ww (range 0.5 to 1.0 µg/g ww) as determined from multi-generational feeding studies in ring-necked pheasants (*Phasianus colchicus*) and mallards (*Anas platyrhynchos*) (Fimreite, 1971; Heinz, 1976). Based on a review of the literature, Thompson (1996) concluded that, overall, Hg concentrations in excess of 2.0 µg/g ww in eggs have some detrimental effects. These data point towards Hg concentrations of 0.5 to 2.0 µg/g ww in eggs as sufficient to induce impaired reproductive success in a range of bird species.

A survey of recently published concentrations of Hg in eggs (homogenates of whole egg contents including yolk and albumen/white) of Arctic birds (Fig. 12) shows that none of the mean Hg concentrations reported for eggs of a wide range of aquatic birds exceeded 2.0 µg/g ww and that only mean values for glaucous gull (*Larus hyperboreus*) and ivory gull (*Pagophila eburnea*) eggs from the Canadian Arctic, and black guillemot (*Cephus grylle*) eggs from the Canadian Arctic and the Faroe Islands approached or exceeded 0.50 µg/g ww. Braune et al. (2006) noted that two of the six ivory gull eggs sampled in the Canadian

Arctic exceeded Hg concentrations of 2.0 µg/g ww and five out of six eggs exceeded 0.50 µg/g ww, compared with the maximum concentrations for ivory gull eggs from the Russian Arctic which ranged from 0.24 to 0.48 µg/g ww (Miljeteig et al., 2009). Although mean Hg concentrations were similar in black guillemot eggs from the Canadian Arctic and the Faroe Islands, maximum Hg concentrations were higher in eggs from the Faroe Islands, ranging from 0.898 µg/g ww in 2002 to 1.31 µg/g ww in 2006, compared with maximum values of 0.60 to 0.84 µg/g ww at three colonies in the Canadian Arctic in 2004 (see Fig. 12, Braune et al., 2006; Hoydal and Dam, 2005, 2009). Knudsen et al. (2005) reported a maximum Hg concentration of 0.4 µg/g ww in glaucous gull eggs from northern Norway which is similar to the mean Hg concentrations found in thick-billed murre (*Uria lomvia*) eggs from Prince Leopold Island and northern fulmar (*Fulmarus glacialis*) eggs from two locations in the Canadian Arctic (see Fig. 12, Braune et al., 2006; Braune, 2007). Schmoltz et al. (2009) reported a maximum Hg concentration of 0.60 µg/g ww in eggs of red-throated loons (*Gavia stellata*) from Alaska compared with a maximum of 0.50 µg/g ww in eggs of common loons from Alaska (Evers et al., 2005). Burger et al. (2009) showed that the Hg concentrations found in the eggs of glaucous-winged gulls (*Larus glaucescens*) from the Aleutian Islands off Alaska were within the range known to affect avian predators although these latter authors also noted that seabirds seem to be less vulnerable to Hg than other birds. These data support the conclusion of Thompson (1996) that pelagic seabirds are not exposed to burdens of Hg that are high enough to induce measurable effects on reproduction or survival. This could well be due to the ability of some seabirds to demethylate MeHg in the liver (Kim et al., 1996) although the capacity for demethylation appears to vary among species (Kim et al., 1996; Eagles-Smith et al., 2009).

3.6. Comparison of fish effect levels with mercury concentrations in Arctic fish species

Mercury toxicology in fish was not extensively studied before the late 1990s. Indeed, it was commonly believed that fish were important mainly as vectors of MeHg transfer to humans and fish-eating wildlife. This view was partially supported by the observation that direct mortality due to MeHg exposure in fish was observed only at very high tissue Hg concentrations (over 5 µg/g ww in muscle) that

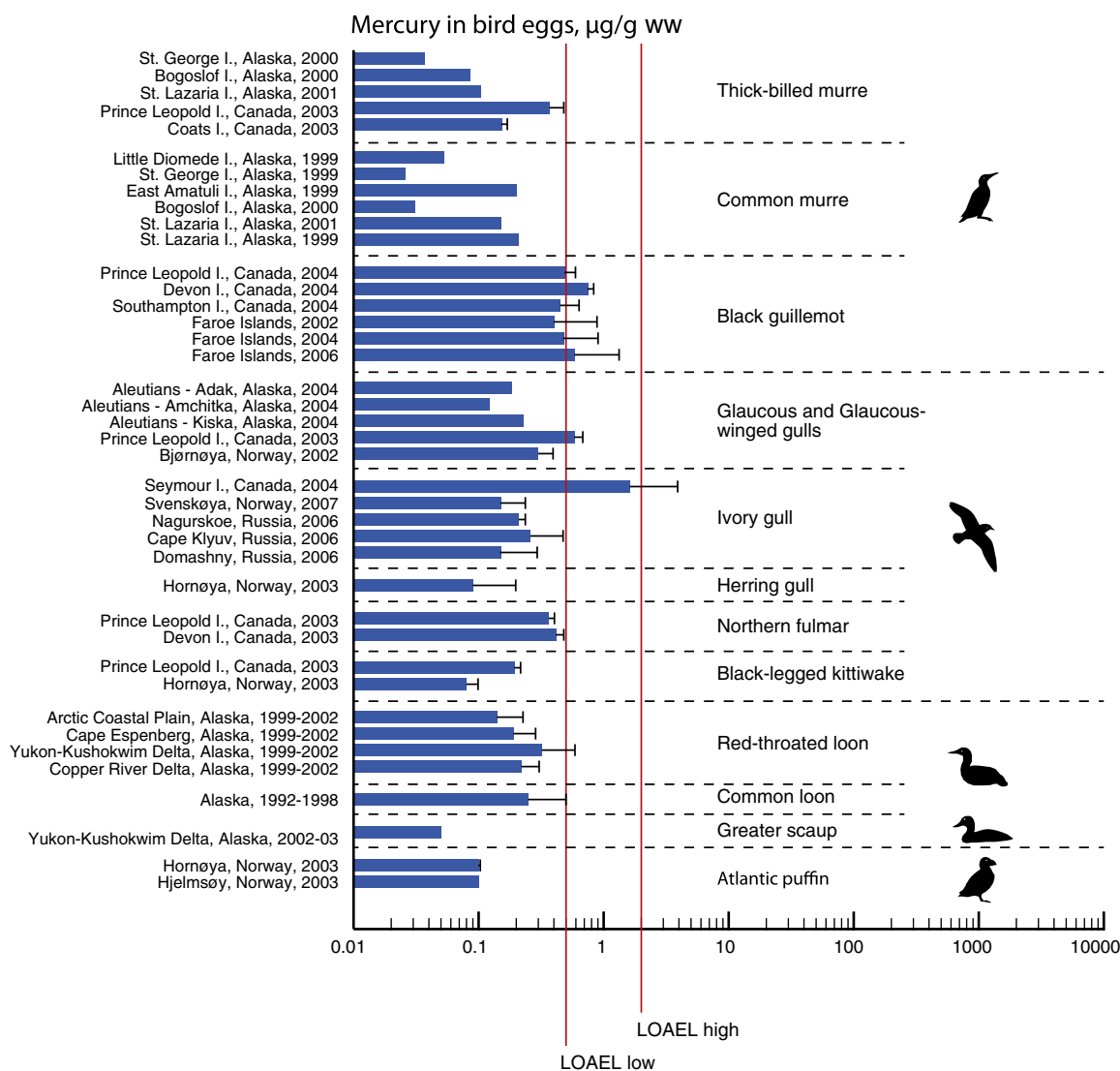


Fig. 12. Mean total mercury concentrations in eggs from a range of Arctic bird species as summarized from the literature, in comparison with effect levels for potential reproductive impairment from Thompson (1996). The bars indicate maximum range values, where available. For sources and raw data see Table S7. In cases where minimum and maximum concentrations are available these are indicated by range bars.

were characteristic solely of highly contaminated local environments (Wiener and Spry, 1996). However, more recent studies have reported a range of toxic effects in fish at much lower Hg concentrations. It is now believed that current levels of exposure to environmental MeHg are sufficiently high to be chronically toxic to a number of predatory freshwater fish in many environments (Scheuhammer et al., 2007). For example, in some independent field studies, body condition in fish of various species was reported to be inversely correlated with tissue Hg over a range of about 0.1 to 1.0 $\mu\text{g/g ww}$ in liver or axial muscle (Munn and Short, 1997; Cizdziel et al., 2003; Drevnick et al., 2008). In a controlled feeding study, Webber and Haines (2003) reported that golden shiners (*Notemigonus crysoleucas*), with whole-body Hg concentrations averaging 0.52 $\mu\text{g/g ww}$, were hyperactive and had altered shoaling behavior relative to fish with lower Hg concentrations. Other negative effects of Hg exposure reported in fish include impacts on reproductive parameters, such as impaired spawning behavior, mediated through a disruption of normal neuroendocrine function (Hammerschmidt et al., 2002; Drevnick and Sandheinrich, 2003; Klaper et al., 2006; Sandheinrich and Miller, 2006; Crump and Trudeau, 2009). In a critical review of the recent literature, Sandheinrich and

Wiener (2010) concluded that changes in biochemical processes, damage to cells and tissues, and reduced reproduction in fish occur at MeHg concentrations of about 0.5 to 1.2 $\mu\text{g/g ww}$ in axial muscle. The lower values of this range are common in some larger freshwater piscivorous fish throughout eastern North America (Kamman et al., 2005). The principal effects of these MeHg concentrations in fish tissues are most likely to be mediated through sublethal damage to tissues and depressed reproduction (Sandheinrich and Wiener, 2010).

As shown in Fig. 13, the minimum Hg toxicity threshold in fish muscle of 0.5 $\mu\text{g/g ww}$, based on the review by Sandheinrich and Wiener (2010), is seldom exceeded in Arctic marine fish species. Similarly, a survey of Hg in the muscle of fish species from the Barents Sea reported that mean Hg concentrations did not exceed 0.25 $\mu\text{g/g ww}$ in any species (Zauke et al., 1999). Arctic freshwater species tended to have higher Hg concentrations than marine species (Fig. 13), but most species from most locations sampled between 1990 and 2008 had mean Hg concentrations in muscle of less than 0.5 $\mu\text{g/g ww}$. However, the putative toxicity threshold was approached or exceeded for some freshwater predatory species such as lake trout (*Salvelinus namaycush*), northern pike (*Esox lucius*), and landlocked Arctic char

(*Salvelinus alpinus*) from some sampling sites (Fig. 13; Evans et al., 2005; Lockhart et al., 2005). The highest mean Hg value (1.78 µg/g ww; Fig. 13) was for landlocked Arctic char sampled from Amituk Lake, Cornwallis Island, Canada; however, as discussed by Lockhart et al. (2005), this value is an adjusted (not a measured) value based on a length regression, and may be erroneously high. Nevertheless, landlocked char in general have higher Hg concentrations than sea run char (Rigét et al., 2004; Lockhart et al., 2005).

The range of fish Hg toxicity thresholds (0.5 to 1.2 µg/g ww in muscle) suggested by Sandheinrich and Wiener (2010) was based on a review of the fish toxicology literature which deals almost

exclusively with freshwater species. Although Arctic marine fish species tended to have relatively low muscle Hg concentrations, it is uncertain how well toxicity thresholds based on freshwater fish may be applied to marine species. There is far less information on the effects of MeHg on saltwater fish, and the issue of the interaction between Se and Hg in marine species adds potential complexity to the issue. As in other animal species, Se can modulate Hg toxicity in fish (Sørmo et al., 2011). In addition, there do not appear to be any Hg data for large predatory marine fish such as sharks in Arctic waters, for which Hg levels would be expected to be considerably higher than for the species shown in Fig. 13. Nonetheless, currently available data on Hg in

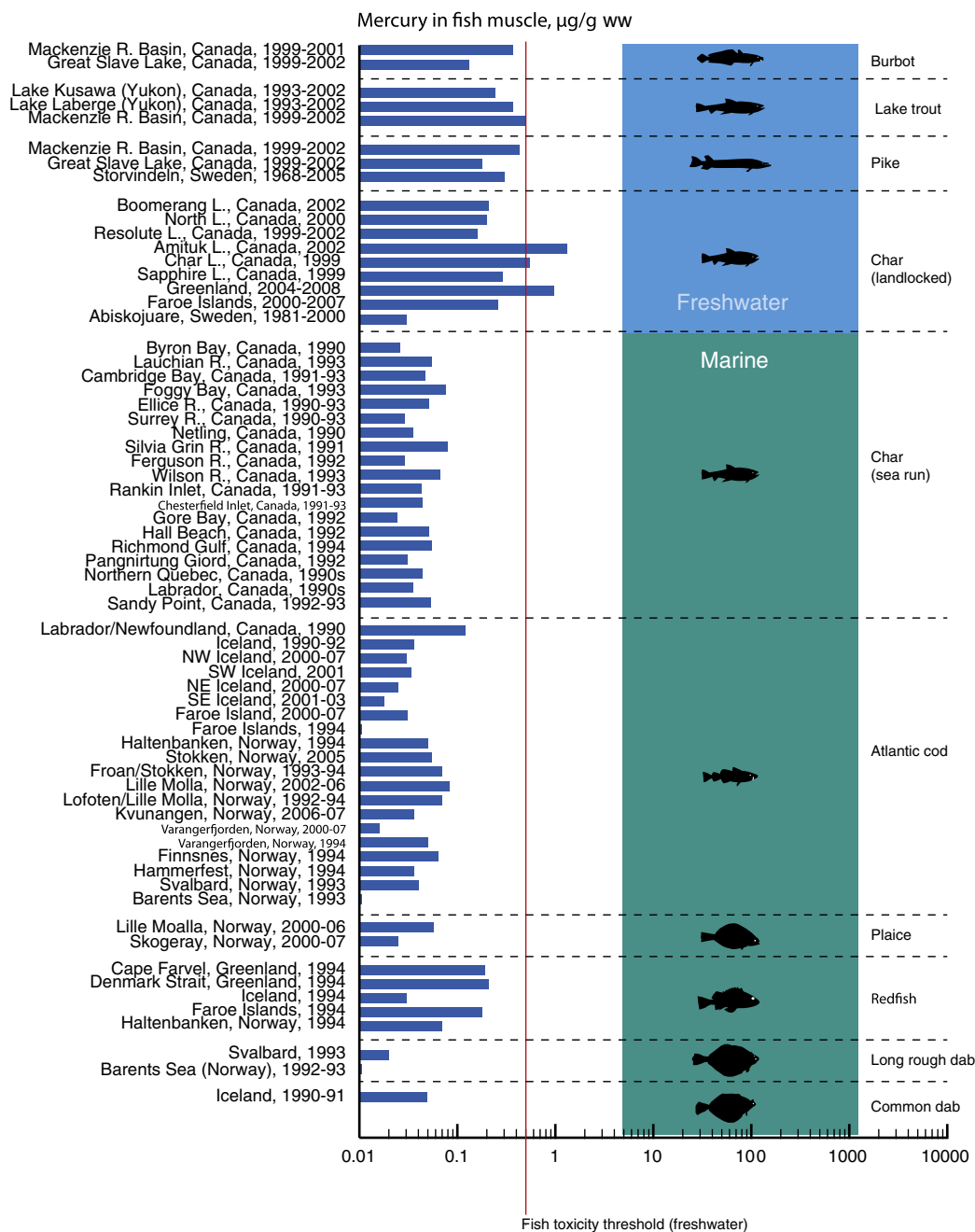


Fig. 13. Mean total mercury concentrations in muscle summarized from data for selected Arctic fish species sampled from locations in Arctic Canada, Norway, Iceland, Greenland, the Faroe Islands and Sweden. Plotted values are means for five or more individuals per location sampled between 1990 and 2009. The solid red line indicates the lowest suggested threshold in dorsal muscle for mercury toxicity in fish (0.5 µg/g; Sandheinrich and Wiener, 2010). The fish mercury data are from a range of sources (Dietz et al., 2011b). See Table S8 for further details.

Arctic fish does not indicate a significant risk of toxicity for most species analyzed to date, with the possible exception of some larger freshwater predatory species. As the vast majority of fish Hg data concern muscle concentrations, the above assessment was based on muscle levels alone. To what extent additional information could be obtained by analyzing Hg in other fish tissues such as the liver, kidney and brain remains unanswered in the present assessment.

4. Conclusions

Overall, among wildlife and fish species, the highest Hg concentrations in brain tissue are found in Arctic toothed whales, and values are in the range of demonstrated Hg-associated neurochemical effects. Despite relatively high concentrations of Hg in the liver and kidney of polar bears, brain stem values were low. However, significant correlations have been reported between brain stem Hg levels and changes in Hg-neurochemical biomarkers observed for fish-eating wildlife. Mean liver Hg concentrations and probably also kidney concentrations in polar bears from southwestern Melville Island and the eastern Beaufort Sea exceeded the general toxic threshold Hg values for terrestrial and marine mammals. Hg concentrations in the non-invasive polar bear hair are indicative of those measured in other tissues such as the brain and liver and raise concern about Hg exposure and possible health effects in some regions of the Arctic (northern Canada and Greenland) especially taking the observed temporal increases into account.

Pilot whales from the Faroe Island and in some cases beluga populations from St. Lawrence and Point Lay had mean Hg liver concentrations exceeding the threshold values for liver damage. Most bird species (with the exception of scap, murre and puffin) have Hg concentrations in eggs sufficiently high to raise concern about negative effects on reproductive success. Arctic marine fish species had Hg concentrations below suggested toxicity thresholds, but freshwater species had higher concentrations. For landlocked Arctic char the guideline limits were exceeded.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.scitotenv.2012.11.046>.

Acknowledgment

Support for this review was provided by the DANCEA (Danish Cooperation for Environment in the Arctic) program.

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