Chapter 42
Mercury in Fish: History, Sources, Pathways, Effects, and Indicator Usage

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Abstract Methyl mercury is highly toxic to humans, particularly to the developing nervous system. Virtually all mercury in muscle tissue of naturally-occurring edible fish is in the form of methyl mercury, and fish consumption is the most common route of human exposure to methyl mercury. The monitoring of mercury in fish thus provides reliable indication of potential exposure of humans to mercury, and regulatory guidelines based on threshold levels of effects due to such exposure provides the best mechanism for effective avoidance of mercury toxicosis in populations throughout the world. This chapter traces the development of the use of mercury in fish as an indicator of potential harm to human health from early recognition of the dangers associated with methyl mercury, to the first records of major toxicity events attributable to fish consumption, through the sources of environmental contamination by mercury today, both natural and anthropogenic, and an overview of the mercury species, environmental conditions and pathways leading to uptake and bioconcentration of mercury in fish.

Keywords Mercury • Methyl mercury • Fish consumption • Bioconcentration • Indicator • Regulatory guidelines

42.1 Introduction

The concentration of mercury (Hg) in edible fish tissue is today perhaps the most broadly-applied indicator of potential harm to human health from any xenobiotic substance. Organic mercury, in particular monomethyl-Hg (CH_3Hg^+ or MeHg), is the most toxic form of mercury commonly found in the environment, and consumption of contaminated fish is the most common route of human exposure to MeHg. Virtually all Hg (>95 %) in muscle tissue of naturally-occurring (and commonly consumed by humans) fish is in the form of MeHg (Bloom 1992). Today, fish and products derived from fish and sea mammals are virtually the only sources of MeHg to humans (Clarkson 1997).

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This chapter reviews the early history of organic-Hg toxicity events, the origin of our recognition of the value of fish as the primary indicator in determining potentially harmful human exposure to MeHg, the primary pathways of uptake by fish, bioaccumulation and bioconcentration of Hg in fish, factors that exacerbate or mitigate the uptake of Hg in fish, the toxic effects of Hg to the fish themselves, as well as to piscivorous species both wildlife and human, and how these translate into regulatory standards and action levels, or consumption advisories. This chapter is an overview of MeHg poisoning with a focus on the principal vector to humans and wildlife. It is not intended to be a comprehensive review of the literature relating to each subject, but it is my intent within each section to provide adequate references to assist students who wish to pursue more focused studies in greater detail.

42.2 Historical Background

42.2.1 Organic Mercury Poisoning

The earliest known deaths attributed to exposure to organic mercury, involving dimethyl mercury, occurred at St. Bartholomew's Hospital in Smithfield, London in the course of research on the valency of metals and metallic compounds. Details of the research that led to the lethal exposures were reported by Frankland and Duppa (1863); yet, inexplicably, their publication made no mention of the poisoning and deaths of two technicians involved in the research. The two technicians were apparently directly exposed to dimethyl Hg for periods of 3 months and 2 weeks, respectively. According to hospital reports, both men exhibited symptoms associated with ataxia and died 2 weeks and 12 months, respectively, after the onset of symptoms. Clinical details were reported in two internal hospital reports (Edwards 1865, 1866), which include the statement, "That the symptoms were due to the inhalation of [mercuric methide] is rendered almost certain." However, circulation of these reports was limited; Hunter et al. (1940) commented that "The story of these deaths has been handed down verbally from one generation of chemists to another."

Despite these early fatalities, a detailed clinical description of the toxicity of organic mercury to humans was not published in the scientific literature until shortly before a massive poisoning event, traced to the consumption of contaminated fish, occurred in Minamata, Japan. Hunter et al. (1940) reported four cases of human poisoning by inhalation of MeHg compounds that occurred in a factory where fungicidal dusts were manufactured. In all four subjects, only the nervous system was involved; symptoms included generalized ataxia, dysarthria (speech slurred, slow, and difficult to understand), astereognosis (unable to distinguish form of objects by touch), gross constriction of visual fields, inability to perform simple tasks, weakness of arms and legs, and unsteadiness in gait. Symptoms known to occur in cases of metallic Hg poisoning, salivation, stomatitis and erethism (abnormal physical sensitivity), were generally absent. All recovered with varying

degrees of disability; the most severe, a 23-year-old man (Case 4), remained totally disabled 3 years after the onset of symptoms.

Hunter et al. (1940) also undertook four experiments with animals, which included a pathological study. The first three experiments exposed rats to methyl mercury nitrate through gavage feeding or vapor inhalation. The fourth experiment exposed a female monkey (*Macacus rhesus*) to MeHg vapor using the same box as previous inhalation experiments with rats, albeit at a much lower dose in proportion to body size. Symptoms in both exposed rats and monkey mimicked the general ataxia, involving severe neurological symptoms, as observed in human exposures. Neurological symptoms were far more severe in the monkey than in the rats, suggesting that primates may be more susceptible to organic mercury compounds than rats. Animals that survived through later stages of intoxication showed degeneration of the cells in the granular layer of the middle lobe of the cerebellum. This is of particular interest because similar cerebellar cortical atrophy was found when the first human exposure to MeHg (Case 4 above) came to necropsy, following the exposure that occurred 15 years before his death (Hunter and Russell 1954).

42.2.2 Minamata Disease

Minamata Disease (MD) was first described by McAlpine and Araki (1958) as "an unusual neurological disorder caused by contaminated fish," which attacked villagers living near Minamata Bay in Kyushu Island, Japan between 1953 and 1956. During this period, 40 families were affected, "causing death in more than a third of its victims and serious disability in most of those who survived." In addition, numerous animals in the immediate area died with similar neurological symptoms, including 24 cats, 5 pigs, 1 dog and many crows. The brains of 10 of the cats showed the granular layer of the cerebellum especially affected. Although the cause could not then be established, the authors noted that certain metals including MeHg had been shown to cause some of the neurological symptoms of the disease. In all cases, the disease was directly correlated with the consumption of fish caught in Minamata Bay. It was strongly suspected that the fish were contaminated by pollutants contained in the effluent from a chemical factory owned by Chisso & Company, which, in 1950, had diverted its former open sea discharge through a newly constructed channel discharging directly into Minamata Bay. The factory utilized a process discovered in 1881 in which mercuric sulfate was used as a catalyst in the conversion of acetylene to acetaldehyde (Clarkson 1997). MeHg compounds were produced as byproducts of the catalytic process, which were at first recycled but later discharged directly into Minamata Bay because of soaring recycling costs (Kondo 1999). The causative agent of MD was verified in 1959 as MeHg poisoning by a Kumamoto University team (Study Group of Minamata Disease 1968). During the life of the plant, an estimated 600 tons of Hg were discharged (Harada 1982). In 1965, a second outbreak of MD occurred far to the north of Minamata Bay in the Agano River area of the Niigata Prefecture. Again,

the cause of the poisoning was the production of acetaldehyde and discharge of waste MeHg byproducts into the Agano River and the consumption of contaminated fish. In all, 2,920 cases of MD in the two areas were officially recognized before the acetaldehyde process was discontinued in Japan and elsewhere (Kondo 1999).

42.3 Sources, Speciation and Pathways of Hg in Fish

Hg in the global aquatic environment comes primarily from atmospheric deposition (Livett 1988; Fitzgerald et al. 1991; Iverfeldt 1991), either direct from wet and dry deposition or indirect through Hg deposition on watersheds or floodplains, which is subsequently transported to surface water bodies. The form in which it deposits is primarily as Hg^{++}, or HgII, which can be biotransformed to MeHg which, in turn, is efficiently taken up by organisms at the base of the food chain. Trophic transfer and resultant concentrations in higher trophic level organisms are influenced by food web dynamics, including length of the food chain. A portion of Hg entering the environment from both natural and anthropogenic sources is reemitted as gaseous elemental Hg, or Hg^0, which is eventually redeposited, reemitted, etc. This cyclical history must be considered when constructing source attribution budgets.

42.3.1 Natural Sources

The earth's crust naturally contains approximately 50 ppb Hg, varying from an average of 40 ppb in limestone to an average of about 160 ppb in the A soil horizon. Most natural waters contain <2 ppb Hg (Adriano 1986). Natural sources of Hg to the atmosphere include geological, vegetative and aquatic degassing, biomass burning, and volcanic (explosive, passive & calderas) and geothermal emissions. Oceanic and soil degassing are probably the most important contributions to the global atmospheric burden of Hg (Pirrone et al. 2010; Norton et al. 1990). Considerable uncertainty exists concerning the proportion of natural sources of Hg, as opposed to anthropogenic sources, contributing to the total atmospheric burden. Seigneur et al. (2003) reported the contributions of natural Hg emissions, direct anthropogenic emissions, and re-emitted anthropogenic emissions to be roughly equal. Thus, by these estimates, one-third of the total annual Hg emissions, estimated at 6,000–6,600 metric tons, would be attributed to natural sources. More recent models estimate the contribution from natural sources to be on the order of 10 % of an estimated annual total of 5,500–8,900 metric tons currently being emitted and re-emitted to the atmosphere from all sources (UNEP 2013).

42.3.2 Anthropogenic Sources

The earliest evidence of anthropogenic releases of Hg to the atmosphere is associated with mining. Cinnabar (HgS) has been used for the production of vermillion since about 1500 BCE, with early mining sites in China, Spain, Greece, Egypt, Peru, and Mexico (Rapp 2009). On the Iberian Peninsula, mat deposits built by the seagrass *Posidonia oceanica* provide a paleorecord of Hg fluxes to the marine environment going back 4,315 years (Serrano et al. 2013). The first European Hg increase attributable to an anthropogenic source was identified in the *P. oceanica* record at about 2500 BP, coinciding with the beginning of intense mining in Spain. Lake-sediment cores collected near Huancavelica, Peru demonstrate the existence of a major Hg mining industry at Huancavelica spanning the past 3,500 years (Cooke et al. 2009). Artisanal and small-scale gold mining (ASGM) is the largest source of global anthropogenic Hg emissions today (e.g., Cleary 1990) followed closely by coal combustion. Other large sources of emissions are non-ferrous metal production, cement production, disposal of waste from mercury-containing products, hazardous waste sites, and sewage treatment plants (UNEP 2013). The global distribution of estimated Hg emissions in 2010 from anthropogenic sources, ranked from highest to lowest regional emitters, is shown in Table 42.1.

Note that estimates of regional and total anthropogenic Hg emissions change with pollution control technologies, regulatory limits and enforcement, fuel choice, phase-out of Hg containing products, increased usage, etc. This is illustrated by comparing global inventories over different time periods. For example, in 1995, approximately 11 % of the total global anthropogenic emissions originated in North America (Pacyna et al. 2003). In the 2010 inventory given in Table 42.1, the estimated contribution from North America had decreased to 3 %, primarily due to advances in emission control technologies, particularly with respect to coal combustion. On the other hand, inventory data from South America show a clear increase from approximately 3 % of total global anthropogenic Hg emissions in 1995, to 4 % in 2000, 7 % in 2005, and 12.5 % in 2010 (Pacyna et al. 2003, 2006, 2010; UNEP 2013). This increasing trend, the largest global increase in Hg emissions over the 15-year period of record, is due almost entirely to ASGM (Cleary 1990). Indeed, as noted by Pacyna et al. (2010), "at least 100 million people in over 55 countries depend on ASGM – directly or indirectly – for their livelihood, mainly in Africa, Asia and South America."

42.3.3 Atmospheric Hg Speciation and Deposition

Mercury is emitted to the atmosphere in gaseous forms, as Hg^0 and HgII (also known as reactive gaseous Hg, or RGM) and as particulate Hg, or Hg_p. The majority of Hg emissions to the atmosphere is as Hg^0, including soil, vegetative, and oceanic degassing, volcanic and geothermal emissions, mining operations, biomass burning and approximately half of fossil fuel emissions (Pacyna et al. 2006). The atmospheric residence time for Hg^0 is approximately one year

Table 42.1 Mercury emissions from various regions, in tones per year, with the range of the estimate, the percentage of total global anthropogenic emissions, and the primary and secondary regional sources of emissions[a,b]

Region	Emissions (range), tones	%	Primary and secondary regional sources
East and Southeast Asia	777 (395–1,690)	39.7	1° Coal combustion; 2° ASGM
Sub-Saharan Africa	316 (168–514)	16.1	1° ASGM; 2° Coal combustion
South America	245 (128–465)	12.5	1° ASGM; 2° Non-ferrous metals
South Asia	154 (78.2–358)	7.9	1° Coal combustion; 2° Large-scale gold
CIS and other Eastern European countries	115 (42.6–289)	5.9	1° Coal combustion
			2° Non-ferrous metals
European Union (EU27)	87.5 (44.5–226)	4.5	1° Coal combustion; 2° Cement production
Undefined	82.5 (70–95)	4.2	Global total from contaminated sites
North America	60.7 (34.3–139)	3.1	1° Coal combustion; 2° Product waste
Central America and Caribbean	47.2 (19.7–97.4)	2.4	1° ASGM; 2° Non-ferrous metals
Middle Eastern States	37.0 (16.1–106)	1.9	1° Coal combustion; 2° Cement production
Australia, NZ and Oceania	22.3 (5.4–52.7)	1.1	1° Large-scale gold; 2° Non-ferrous metals
North Africa	13.6 (4.8–41.2)	0.7	1° Non-ferrous metals; 2° Product waste
Grand Total	**1960 (1,010–4,070)**	**100**	

[a]UNEP (2013)
[b]Estimates based on 2010 inventory

enabling distribution on a global scale. The majority of Hg^0 is eventually oxidized to HgII, which is soluble and subject to washout. HgII is also emitted directly to the atmosphere from various industrial processes including fossil fuel combustion (primarily coal), municipal waste incineration, cement production, as well as crematoria. HgII and Hg_p, have much shorter atmospheric residence times, often depositing on a local or, at most, a regional scale from point sources. Other species of Hg are generally present at de minimis levels in the atmosphere and will not be considered further here.

42.3.4 Methylation and Uptake of Hg in Fish

Deposited HgII is the primary substrate for methylation by sulphate- and iron-reducing bacteria and/or methanogenic archaea under anoxic conditions found in sediments, as well as in periphyton and wetland catchment areas, and is

highest in sediments moderately enriched by organics and sulfate (Poulain and Barkay 2013; Hamelin et al. 2011; Gilmour et al. 1992; Driscoll et al. 1994; Sunderland et al. 2006 [see also reviews by Zillioux et al. 1993; Porcella 1994 and references therein]). The efficiency of MeHg production varies greatly among species and between geobiological niches, however. Benoit et al. (2003), in an extensive review of MeHg production and degradation, made the case that sulfate-reducing bacteria (SRB) are the key Hg methylators in aquatic ecosystems. They cited studies using specific metabolic inhibitors where inhibition of methanogens increased Hg methylation, while inhibition of sulfate reduction dramatically decreased MeHg production in saltmarsh sediment (Compeau and Bartha 1985). In addition, Oremland et al. (1991), citing Mcbride and Edwards (1977), reported that "Hg methylation was not detected in whole cells of methanogens or in methanogenic sewage sludge suggesting that methanogens are not active in this reaction." However, Hamelin et al. (2011) presented findings that suggest "that methanogens rather than SRB were likely the primary methylators in the periphyton of a temperate fluvial lake." Parks et al. (2013), although acknowledging that SRB are the main producers of MeHg in nature, provided genetic evidence for "a common mercury methylation pathway in all methylating bacteria and archaea." Kerin et al. (2006), in a paper relating mercury methylation to dissimilatory iron-reducing bacteria (DIRB), implied that, since current models for methylation are based on relationships between methylation and sulfate reduction, the potential significance of methylation by iron reduction in certain environments may be undervalued or missed entirely. Kerin concluded that "the finding that DIRB can produce MeHg suggests that Hg methylation may be important in sediments and soils where these organisms are dominant, e.g., iron-rich sediments with low concentrations of sulfate." Regardless of the methanogenic species, MeHg produced in aquatic environments is taken up rapidly by the food web, with greater accumulation in higher trophic levels. Given that some methanogenic bacteria and archaea are among the oldest life forms on the planet, and that a shared evolutionary history for methanogenesis and sulfate reduction developing about 3.5 billion years ago has been postulated (Susanti and Mukhopadhyay 2012), and that inorganic Hg has always been present in Earth's biosphere, it seems that fish have accumulated MeHg throughout their evolutionary history (Clarkson 1997).

Calculations in dilute-water lakes from the ratio of total fish Hg to total Hg and aqueous MeHg measurements indicate accumulation of MeHg in fish by a factor of three million times, accounting for the observation that fish can contain more than one part per million Hg in water with less than one part per trillion of total Hg (Zillioux et al. 1993). Although accumulation of Hg in fish can occur through uptake across both the gills and the gut, dietary uptake seems to account for more than 90 % of total MeHg uptake with assimilation rates up to 80 % or higher. MeHg binds to red blood cells and distributes via the circulatory system to all organs and tissues, although much relocates to the skeletal muscle where it accumulates bound to sulfhydryl groups in protein (Wiener et al. 2003). This process is described by a bioaccumulation factor (BAF), i.e., the ratio of tissue chemical residue to chemical concentration in an external environmental phase (water, sediment, or food).

For equilibrium partitioning at steady state, the BAF may approximate the organism-water partition coefficient (K_b), although this varies with the degree of uptake through the dietary route (the bioconcentration factor [BCF] is equivalent to K_b since it describes the ratio of tissue chemical residue directly to chemical concentration in water with no food-web exposure). The bioaccumulation process results in a biomagnification of Hg, or increase in tissue chemical residues at higher trophic levels, primarily as a result of dietary accumulation (Spacie et al. 1995), although the degree of biomagnification in a given water body varies by species and with size and age. Figure 42.1 illustrates the range of fish species variations in average Hg tissue (primarily axial muscle) concentrations as reported by the U.S. Food and Drug Administration (USFDA) and the U.S. Environmental Protection Agency (USEPA).

42.3.4.1 Factors Affecting Methylation and Uptake of MeHg by Fish

Since methylation of HgII is a prerequisite for the efficient uptake of Hg in fish in most natural water bodies, an examination of the environmental factors that promote methylation, as well as demethylation, is important to understand the observed differences in Hg uptake between water bodies. Methylation and demethylation should be viewed within the context of the overall cycling of mercury species in the aquatic environment. The major compartments, fluxes, and reaction components of mercury in a lacustrine ecosystem are illustrated in Fig. 42.2.

Many authors have considered the influence of water chemistry on the uptake of Hg in fish. For example, Lange et al. (1993) reported that uptake of MeHg in largemouth bass in 53 Florida lakes was shown to be positively correlated with fish age (strongest correlation) and fish size (e.g., see Table 42.2), and negatively correlated with alkalinity, calcium, chlorophyll α, conductance, magnesium, pH, total hardness, total nitrogen, and total phosphorus. They found that pH accounted for 41 % of the variation in Hg concentration for standardized age three fish, while chlorophyll α and alkalinity accounted for 45 % of the variation. Fish Hg concentrations were significantly higher in lakes with either pH <7, alkalinity <20 mg/L as CaCO3, or chlorophyll α <10 μg/L. Also, Hickey et al. (2005) studied the effects of water chemistry on Hg in 747 fish of mixed species from 31 Ontario lakes and 11 lakes in Nova Scotia, Canada. They found that pH alone explained 77.7 % of the variation in Hg concentration in fish, while MeHg in water and dissolved organic carbon (DOC) accounted for only 2.7 % of the variation. They concluded that "reducing acid rain and mitigation of pH levels will reduce Hg levels more than will reducing Hg deposition." Although not directly addressing this relationship, it should be noted that, in a whole-ecosystem experiment where different isotopes of Hg were deposited directly to a Canadian lake surface and to upland and wetland components of its watershed and tracked over time, the Hg levels in fish responded rapidly and directly to the changes in atmospheric deposition (spike additions) when added directly to the lake surface (Harris et al. 2007; Engstrom 2007).

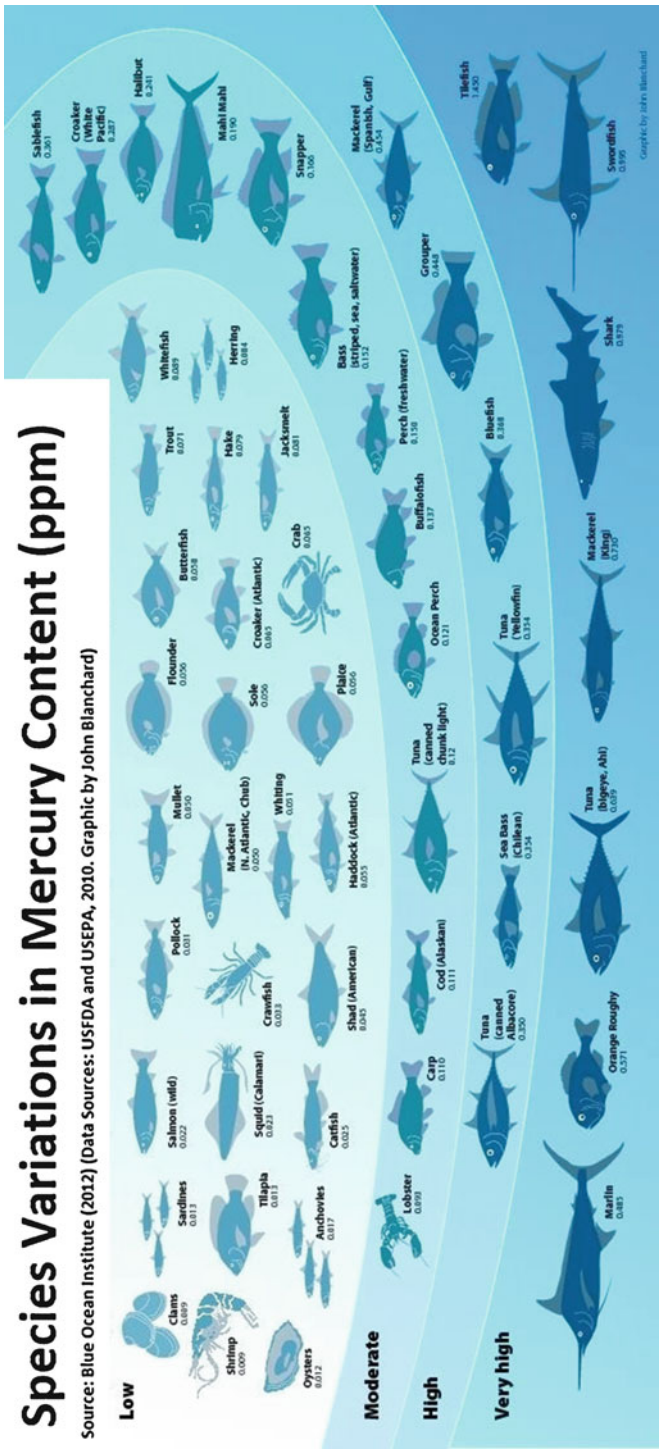

Fig. 42.1 Species variations in mercury content (ppm) (Source: John Blanchard (Sources: FDA and EPA), Sierra Magazine, Nov/Dec 2011)

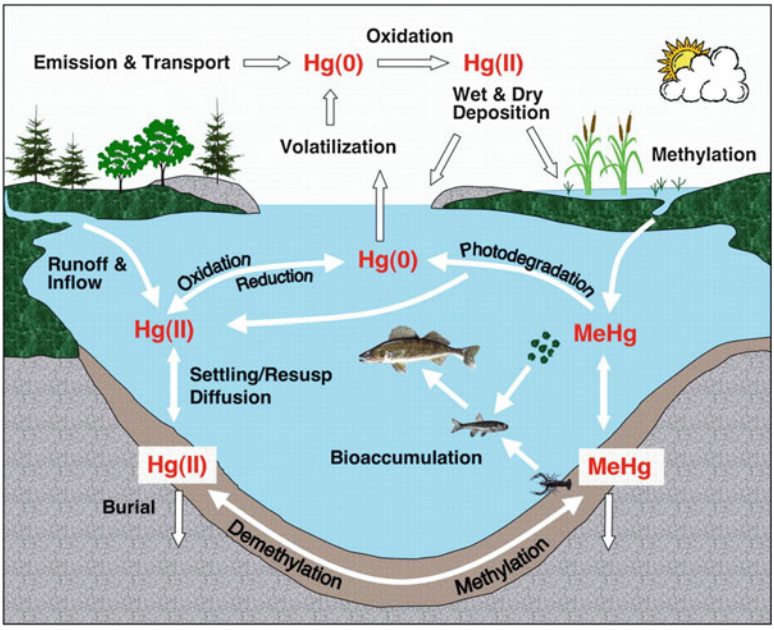

Fig. 42.2 Mercury cycling in a lake and its watershed (From: Engstrom (2007) (Reprinted with permission))

Table 42.2 The effect of size (age) on the mean Hg level in 181 king mackerel sampled in 1999 from North Carolina, South Carolina, Georgia, and Florida, USA

Size category (fork length) (in.)	Number of fish	Average (ppm)	Range (ppm)
<27	19	0.22	0.14–0.36
27–32	43	0.34	0.15–1.00
33–39	53	0.80	0.25–2.10
>39	66	1.54	0.40–3.50

Moore (2000)

A number of studies have developed statistical or inferential models in order to determine the biogeochemical factors that govern Hg bioaccumulation in aquatic food webs. For example, Pollman (2012) used a variety of multivariate modeling techniques to construct and validate empirical models relating the occurrence of Hg in fish to chemical and other potential determinants of the variability of fish tissue Hg concentrations. The modeling effort used data sets representative of over 7,700 lakes greater than 4 ha and 83,457 km of stream and riverine reaches in the State of Florida, and approaches including integrating principal components analysis with multiple linear regression and generalized linear modeling for the lake model, and classification and regression tree analysis for the streams and rivers model. The sequence of importance of independent variable contributions to the overall variability in Hg in largemouth bass was: for the study lakes, alkalinity > chlorophyll

α > urban runoff disturbance > atmospheric deposition > sulfate; and, for the study streams and rivers, pH ≫ DO % saturation > conductivity > total Kjeldahl nitrogen > sulfate > total phosphorous. Considering uncertainties in model prediction and inferred distributions, the model results for the 90th percentile concentrations for largemouth bass Hg, in mg/kg, were: streams – 1.295; small lakes – 1.319; rivers – 1.136; the Everglades – 1.071; and large lakes – 0.694. The much lower predicted fish Hg concentration in large lakes reflects both higher alkalinities and higher productivity compared to small lakes.

Chemical and biological control of microbial methylation and demethylation of Hg is complex and not fully understood. The degree of complexity is perhaps best illustrated by the central role played in the biogeochemical cycling of Hg by interactions affecting Hg methylation/demethylation among dissolved organic matter (DOM), sulfate reduction, and sulfide inhibition (e.g., Benoit et al. 2003; Hickey et al. 2005; Miller et al. 2007; Graham et al. 2012, 2013). Sulfate and sulfide exert conflicting influences on the extent of Hg methylation such that the highest methylation rates are found at sites with intermediate sulfate-reduction rates and sulfide concentration, although the point at which the highest rates occur varies with other controlling factors. Sulfate additions increase Hg methylation rates until sulfate concentration reaches the point where sulfide buildup is sufficient to inhibit microbial methylation (Gilmour et al. 1998; Graham et al. 2013; Benoit et al. 2003). Correlations between DOM and MeHg production are positive in many aquatic sediments and wetland soils with low μM sulfide levels, and DOM concentrations below 8 mg C/L. DOM can strongly enhance the bioavailability of HgII to SRB under micromolar sulfide concentrations and anoxic conditions (Graham et al. 2012, 2013); however, the degree of enhancement is influenced by DOM size, hydrophobicity, and sulfur content. The interactions of Hg with DOM in the presence of sulfide complicate the Hg-sulfide complexation as predicted by thermodynamic models such that laboratory and field studies have not always been in agreement. DOM influences numerous processes in the biogeochemical cycling of Hg including HgII complexation and transport, MeHg complexation, transport, precipitation and dissolution of Hg-S minerals, and MeHg production by microorganisms (Graham et al. 2013 and references therein). In addition, Hg complexed with DOM dominates the speciation of Hg under oxygenated conditions and may influence the ultimate Hg substrate available to SRB at the primary site of methylation in aquatic sediments, just below the oxic/anoxic interface. Reported correlations between DOM and MeHg concentration also can be negative (e.g., Hickey et al. 2005; Driscoll et al. 1995), further reflecting the biogeochemical complexity controlling these interactions.

Other factors affecting MeHg formation and uptake of Hg in fish have been reported by many authors. Examples include: food-chain structure (Cabana et al. 1994, Greenfield et al. 2001); salinity (Compeau and Bartha 1987; Farmer et al. 2010); selenium (Southworth et al. 1999; Belzile et al. 2006; Peterson et al. 2009); acid rain (Richardson and Currie 1995; Richardson et al. 1995a, b; physical attributes of lakes (Richardson 1994); sulfate loading (Gilmour et al. 1998); algal blooms (Pickhardt et al. 2002); temperature and season (Benoit et al. 2003).

As mentioned above, demethylation occurs in natural aquatic systems in concert with methylation such that MeHg uptake by fish is a function of the *net* microbial production of MeHg. Bacterial demethylation through the *mer* operon pathway has been well characterized (e.g., Robinson and Tuovinen 1984; Liebert et al. 1999; Hobman et al. 2000; Barkay 2000). The *mer* operon contains the organomercurial lyase gene that cleaves the carbon-Hg bond of MeHg, producing methane and HgII; the HgII then is reduced to Hg^{o} through a second step involving the Hg-reductase enzyme (Benoit et al. 2003; Wiener et al. 2003). Oremland et al. (1991) described an oxidative demethylation process that derives energy from single carbon substrates in a wide range of environments including freshwater, estuarine, and alkaline-hypersaline sediments and in both aerobic and anaerobic conditions. Working in three environments that differ in the extent and type of Hg contamination and sediment biogeochemistry, Dipasquale et al. (2000) found that severely contaminated sediments tend to have microbial populations that actively degrade MeHg through *mer*-detoxification, whereas oxidative demethylation occurs in heavily contaminated sediments as well but appears to dominate in those less contaminated, under both aerobic and anaerobic conditions.

42.4 Effects

42.4.1 Effects of Hg on Fish

The effects of Hg in fish, as well as in other aquatic organisms, and piscivorous wildlife have been reviewed extensively (e.g., Eisler 1987). In two early reviews published in 1979 (Taylor 1979; Birge et al. 1979) a total of 50 discrete references that specifically addressed the issue of Hg in fish were cited. Since the completion of these two reviews, at least 447,000 publications have dealt with some aspect of Hg in fish (source: Google Scholar, extrapolated from a sample size of 1,000 citations).

Although diet is the primary route of Hg uptake in fish, most laboratory studies of Hg in fish have measured effects through gill uptake from concentrations in water much higher than typically observed in natural water bodies, where typical concentrations in lakes are measured in the low ng/L range (Watras et al. 1992). For example, Zillioux et al. (1993), in a review on the effects of Hg in wetland ecosystems, reported effects of organic Hg on fish derived from laboratory exposures at concentrations in water from 0.1 μg/L (zebrafish [*Brachydanio rerio*] – hatching success reduced) to 0.88 μg/L (brook trout [*Salvelinus fontinalis* embryo] – enzyme disruption). Sublethal exposures of fish to MeHg can result in impaired ability to locate, capture, and ingest prey, and to avoid predation (Kania and O'Hara 1974; Little and Finger 1990; Sandheinrich and Atchison 1990; Weis and Weis 1995; Fjeld et al. 1998; Samson et al. 2001, as cited in a comprehensive review by Wiener et al. 2003). However, Wiener and Spry (1996) in a review on Hg in freshwater fish concluded that reduced reproductive success was the most plausible

toxicological endpoint in wild fish populations exposed to Hg-contaminated food webs. For example, Hammerschmidt et al. (2002) reported that exposure of fathead minnows (*Pimephales promelas*) to three concentrations of dietary MeHg of 0.88, 4.11, and 8.46 μg Hg g^{-1} dry weight prior to sexual maturity, resulted in reduced spawning success rates of 63 %, 40 %, and 14 %, respectively, down from success rates of 75 % for controls. Beckvar et al. (2005) linked fish tissue residues of Hg to biological effects thresholds, primarily of growth, reproduction, development, and behavior, using literature sources screened for data consistency. Based on an evaluation of several approaches, the threshold-effect level (t-TEL) best represented the underlying data. (The t-TEL is calculated as the geometric mean of the 15th percentile concentration in the effects data set and the 50th percentile concentration in the no-effects data set.) They concluded that a whole-body t-TEL of 0.2 mg Hg/kg wet weight of tissue would be protective of juvenile and adult fish, where the incidence of effects below the t-TEL is predicted to be rare.

42.4.2 Effects of Hg on Piscivorous Wildlife

Effects of Hg on piscivorous birds and mammals were reviewed by Wolfe et al. (1998), with emphasis on the mechanisms of Hg toxicity and interpretation of residue data. In both birds and mammals, MeHg readily penetrates the blood-brain barrier producing brain lesions, spinal cord degeneration, and central nervous system dysfunctions. A residue threshold for toxicity in mink is suggested at 5.0 ppm for brain and muscle tissue. From their review of the literature, Zillioux et al. (1993) concluded that residue thresholds for significant toxic effects in wading birds occur between 1 and 3.6 ppm wet weight (w/w) in eggs and 5 ppm w/w in liver. However, a study by Frederick and Jayasena (2011) suggested that dose-related increases in male-male bonding and altered sexual display behavior in the white ibis occur at mean residue levels as low as 4.3 ppm fresh weight in feathers (approx. equivalent to 0.37 ppm in wading bird eggs, from comparative feather/egg effects data in Zillioux et al. 1993) and 0.73 ppm in blood. Many investigations on ecosystem proliferation of Hg and the effects of Hg on piscivorous wildlife have been conducted in the Florida Everglades, the largest freshwater wetland in the continental United States. For example, Frederick et al. (1999) studied the diet of great egret (*Ardea albus*) nestlings exposed to dietary Hg during the breeding seasons of 1993–1996. By collecting and analyzing Hg in regurgitated food samples from large colonies throughout the central Everglades, where fish comprised >95 % of the nestlings' diet, Frederick et al. estimated that nestlings would ingest 4.32 mg total Hg (Hg_T) during an 80-day nesting period. In live tree islands, which are the primary habitat for wading bird colonies in the Everglades, the annual Hg deposition by bird guano was estimated at 148 μg m^{-2} $year^{-1}$, about eight times the atmospheric deposition of Hg in southern Florida (Zhu et al. 2014). Feather mercury concentrations in adults and nestlings of the great egret exceeded 30 ppm in environmental samples from the Florida Everglades in the early 1990s,

when this area had the highest levels of Hg in fish in the entire USA (as high as 2.7 ppm in axial muscle tissue of largemouth bass, Wolfe et al. 2007).

During the same period, top predators of the fish-based food chain in the Florida Everglades also had high tissue Hg levels. Alligators (*Alligator mississippiensis*) collected on a transect through the Florida Everglades in 1999 were reported by Rumbold et al. (2002) with Hg_T mean concentrations ($n = 28$) in liver and tail muscle of 10.4 and 1.2 ppm w/w, respectively. A single Florida panther (*Puma concolor cori*), a critically endangered species in Florida, was found dead in the southern Everglades region with the highest Hg concentration ever reported of 110 ppm w/w in the liver; Hg toxicosis was strongly implicated in its death (Roelke et al. 1991). Other free-ranging panthers in the same region had mean hair, liver, and muscle concentrations of 56.4, 40.6 and 4.4 ppm Hg_T w/w, respectively. Roelke et al. concluded that Hg_T in panther hair greater than 57.3 ppm fresh weight would indicate toxicosis, and identified an "at risk" threshold value for Hg_T in panther hair as greater than 12.57 ppm. All of these panthers were known to be feeding on Hg-contaminated raccoons (*Procyon lotor*). Raccoons are opportunistic omnivores, but eat largely insects and crustaceans and some fish outside berry season, which peaks in January in the Everglades region. As is the case in fish, Hg in insects is essentially all MeHg (Mason et al. 2000). Roelke et al. (1991) reported a mean value of 1.8 ± 1.24 ppm Hg in raccoon muscle tissue in the central Everglades, while in a retrospective study across all of southern Florida, Porcella et al. (2004) found no statistical difference in raccoon Hg content over the past 50 years.

42.4.3 Effects of Hg in Humans

About 95 % of MeHg in fish ingested by humans is absorbed. In the blood, about 90 % is associated with red cells, probably bound to the sulfhydryl (SH) groups of hemoglobin. From the bloodstream, it is taken up by all tissues, and readily crosses the blood-brain and placental barriers. Early studies of the effects of MeHg on humans have been described above (Section 1.2.1). More recent studies have confirmed that the major human effects from exposure to MeHg are neurotoxicity in adults and toxicity in fetuses of mothers exposed during pregnancy. The cortex of the cerebrum and cerebellum are selectively involved in Hg toxicosis, with focal necrosis on neurons, lysis and phagocytosis and replacement by supporting glial cells. The over-all acute effect is cerebral edema, but with prolonged destruction of gray matter and subsequent gliosis, resulting in cerebral atrophy (see reviews by Clarkson 1997 and Goyer and Clarkson 2001, and references therein). However, the primary human health concern today is with more subtle effects arising from prenatal exposure, such as delayed development and cognitive changes in children. Myers et al. (2003) studied neurodevelopmental effects in a fish-consuming population in the Republic of Seychelles, investigating 779 mother-infant pairs. Mothers averaged 12 fish meals per week, with fish concentrations of MeHg similar to commercial ocean fish elsewhere. Children were followed from the prenatal period

(mean prenatal MeHg exposure was 6.9 ppm, SD 4–5 ppm) to age 9 years. Neurocognitive, language, memory, motor, perceptual-motor, and behavioral functions were assessed at 9 years. Their data did not support the hypothesis that there is a neurodevelopmental risk from prenatal MeHg exposure resulting solely from ocean fish consumption. However, other studies of prenatal exposure related to fish consumption have shown effects in children, from an inverse correlation between maternal Hg hair levels and IQ in their children (Kjellström et al. 1989) to cognitive developmental delays at the age of 4 years (Freire et al. 2010). A WHO Expert Group concluded that there may be a low risk of prenatal poisoning at maternal hair levels between 10 and 20 ppm (corresponding to blood levels of 20–40 ppb). Two independent analyses of the same data base concluded that the lowest effect level may be anywhere from 7 to over 100 ppm in maternal hair. As a point of comparison, a study conducted in the Florida Everglades, during the period of highest reported concentrations of Hg in fish, measured Hg in the hair of sport fishermen, Everglades residents, and subsistence fishermen. Of 350 participants, 119 had levels above detection limits and, of these, the mean total Hg in hair was 3.62 (SD 3.0) ppm, with a range of 2.28–15.57 ppm (Fleming et al. 1995).

42.5 Use of Fish as Indicators of Human Hg Exposure

The practice of using fish as indicators of chemical exposure is relatively new. A permissible Hg content of 0.5 ppm in fish established in 1970 by the U.S. Food and Drug Administration (USFDA) was the first regulatory action level for any element in the USA (Hall et al. 1978). This temporary action level was later revised upward to 1 ppm MeHg in fish, which "was established to limit consumers' MeHg exposure to levels 10 times lower than the lowest levels associated with adverse effects (paresthesia)" (USFDA 1995). This new action level was based on the occurrence of adverse effects in adults "because the level of exposure was actually lower than the lowest level found to affect fetuses, affording them greater protection." Nevertheless, in January 2001 the U.S. Environmental Protection Agency (USEPA) in apparent contradiction to the USFDA action, established a water quality criterion of 0.3 mg MeHg/kg fish tissue screening value for fish consumption (USEPA 2010). This was the USEPA's first issuance of a water quality criterion expressed as a fish tissue value rather than as an ambient water column value. The more restrictive USEPA criterion is intended to be protective of recreational, tribal, ethnic, and subsistence fishers who typically consume fish and shellfish from the same local water bodies repeatedly over many years. Today, action levels for fish consumption advisories are common throughout the world. Table 42.3 provides the most complete compendium of these action levels available for 53 nation states, including the 27 member states of the European Union and 12 member states of the Commonwealth of Independent States as well as general guidelines issued by the World Health Organization/Food and Agriculture Organization of the United Nations.

Table 42.3 Examples of maximum allowed or recommended levels of Hg in fish in various countries and by WHO/FAO (based on submissions to UNEP, unless otherwise noted)

Country/ organization	Fish type	Maximum allowed/ recommend levels in fish[a]	Type of measure	Tolerable intake levels[a]
Australia	Fish known to contain high levels of mercury, such as swordfish, southern bluefin tuna, barramundi, ling, orange roughy, rays, shark	1.0 mg Hg/kg	The Australian Food Standards Code	Tolerable Weekly Intake: 2.8 μg Hg/kg body weight per week for pregnant women.
	All other species of fish and crustaceans and molluscs	0.5 mg Hg/kg		
Canada	All fish except shark, swordfish or fresh or frozen tuna (expressed as total mercury in the edible portion of fish)	0.5 ppm total Hg	Guidelines/ Tolerances of Various Chemical Contaminants in Canada	Provisional Tolerable Daily Intake: 0.47 μg Hg/kg body weight per day for most of the population and 0.2 μg Hg/kg body weight per day for women of child-bearing age and young children
	Maximum allowable limit for those who consume large amounts of fish, such as Aboriginal people	0.2 ppm total Hg		
China	Freshwater fish	0.30 mg/kg	Sanitation standards for food	
Croatia	*Fresh fish* Predatory fish (tuna, sword-fish, molluscs, crustaceans)	1.0 mg Hg/kg 0.8 mg methyl Hg/kg	Rules on quantities of pesticides, toxins, mycotoxins, metals and histamines and similar substances that can be found in the food.	
	All other species of fish	0.5 mg Hg/kg 0.4 mg methyl Hg/kg		
	Canned fish (tin package) Predatory fish (tuna, sword-fish, molluscs, crustaceans)	1.5 mg Hg/kg 1.0 mg methyl Hg/kg		
	All other species of fish	0.8 mg Hg/kg 0.5 mg methyl Hg/kg		

(continued)

Table 42.3 (continued)

Country/ organization	Fish type	Maximum allowed/ recommend levels in fish[a]	Type of measure	Tolerable intake levels[a]
European Community	Fishery products, with the exception of those listed below.	0.5 mg Hg/kg wet weight	Various Commission regulations	European Commission, Official Journal of the European Communities 7 February 2002
	Anglerfish, Atlantic catfish, bass, blue ling, bonito, eel, emperor or orange roughy, grenadier, halibut, marlin, pike, plain bonito, Portuguese dogfish, rays, redfish, sail fish, scabbard fish, shark (all species), snake mackerel or butterfish, sturgeon, swordfish and tuna.	1 mg Hg/kg wet weight	Commission regulation (EC) No. 221/2002	
Georgia	Fish (freshwater) and fishery products	0.3 mg Hg/kg	Georgian Food Quality Standards 2001	
	Fish (Black Sea)	0.5 mg Hg/kg		
	Caviar	0.2 mg Hg/kg		
India	Fish	0.5 ppm total Hg	Tolerance Guidelines	
Japan	Fish	0.4 ppm total Hg/kg	Food Sanitation Law – Provisional regulatory standard for fish and shellfish	Provisional Tolerable Weekly Intake: 0.17 mg methyl Hg (0.4 μg/kg body weight per day) (Nakagawa et al. 1997).
		0.3 ppm methyl Hg (as a reference)		
Korea, Republic of	Fish	0.5 mg Hg/kg	Food Act 2000	
Mauritius	Fish	1 ppm Hg	Food Act 2000	
New Zealand	Fish	1.6 μg MeHg/kg body weight per week	Food Standards Australian New Zealand (FSANZ)	Adopted 2003 JECFA PTWI (Karatela et al. 2011)
Philippines	Fish (except for predatory)	0.5 mg methyl Hg / kg	Codex Alimentarius	
	Predatory fish (shark, tuna, swordfish)	1 mg methyl Hg/kg		

(continued)

Table 42.3 (continued)

Country/ organization	Fish type	Maximum allowed/ recommend levels in fish[a]	Type of measure	Tolerable intake levels[a]
Slovak Republic	Freshwater non-predatory fish and products thereof	0.1 mg total Hg/kg	Slovak Food Code	
	Freshwater predatory fish	0.5 mg total Hg/kg		
	Marine non-predatory fish and products thereof	0.5 mg total Hg/kg		
	Marine predatory fish	1.0 mg total Hg/kg		
Thailand	Seafood	0.5 μg Hg/g	Food Containing Contaminant Standard	
	Other food	0.02 μg Hg/g		
United Kingdom	Fish	0.3 mg Hg/kg (wet flesh)	European Statutory Standard	
United States	Fish, shellfish and other aquatic animals (FDA)	1 ppm methyl Hg	FDA action level	US EPA reference dose: 0.1 μg methyl Hg/kg body weight per day
	States, tribes and territories are responsible for issuing fish consumption advise for locally-caught fish; Trigger level for many state health departments:	0.5 ppm methyl Hg	Local trigger level	
WHO/FAO	All fish except predatory fish	0.5 mg methyl Hg/kg	FAO/WHO Codex Alimentarius guideline level	2003 JECFA provisional tolerable weekly intake 1.6 μg MeHg/kg body weight per week
	Predatory fish (such as shark, swordfish, tuna, pike and others)	1 mg methyl Hg/kg		

From: Global Mercury Assessment, Chapter 4 (UNEP Chemicals 2002) unless otherwise noted. Revised

[a]Units as used in references. "mg/kg" equals "μg/g" and ppm (parts per million). It is assumed here that fish limit values not mentioned as "wet weight" or "wet flesh" are most likely also based on wet weight, as this is normally the case for analysis of fish for consumers

Compliance with regulatory guidelines, however, is often lacking. For example, in the study of Hg in hair of exposed populations in the Florida Everglades mentioned earlier, Fleming et al. (1995) found that, although 71 % of the 350 participants knew of the State Health Advisories concerning ingestion of Hg-contaminated fish from the Everglades, this did not change their consumption habits.

Conclusions

It would be difficult to find an indicator of potential harm more well-researched than Hg in edible fish within the HgII → methanogen → MeHg → fish → human pathway. For human consumption, the challenge is to balance regulatory guidance for protection against exposure to MeHg at potentially harmful levels with the well-known health benefits of fish consumption. Since this review has not focused on the latter, a brief summation of beneficial effects is warranted.

Clinical effects that support human health benefits of fish or fish oil intake have been shown for anti-arrhythmia, anti-thrombosis and the lowering of triglyceride, heart rate, and blood pressure. At moderate intake levels of <750 mg per day EPA/DHA (eicosapentaenoic acid and docosahexaenoic acid), the physiologic effects most likely to account for clinical cardiovascular benefits include modulation of myocardial sodium and calcium ion channels, and reduced left ventricular workload and improved myocardial efficiency as a result of reduced heart rate, lower systemic vascular resistance, and improved diastolic filling. The dose response for anti-arrhythmic effects is initially steep, reaching a plateau at intake levels of around 750 mg/day EPA/DHA. At increasing levels of intake up to at least 2,500 mg/day, beneficial effects continue to accrue with respect to triglycerides, heart rate, and blood pressure over a time course of months to years. In addition, fish or fish oil intake may provide important beneficial effects with respect to endothelial, autonomic, and inflammatory responses (Mozaffarian and Rimm 2008, and references therein).

Among piscivorous wildlife, the population and ecosystem-level risks from high environmental Hg concentrations in natural systems have proved to be demonstrably greater than the current risk to human consumers. For major health outcomes among adult humans, the benefits of fish consumption generally outweigh risks; this is true even for sensitive populations of women of child-bearing age and young children if health advisories and consumption limits are followed. Further development of the application of Hg levels in fish for the indication of potential threats to non-human species and to ecological health in general is needed.

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