EFFECTS OF MERCURY ON WILDLIFE: A COMPREHENSIVE REVIEW

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Abstract—Wildlife may be exposed to mercury (Hg) and methylmercury (MeHg) from a variety of environmental sources, including mine tailings, industrial effluent, agricultural drainwater, impoundments, and atmospheric deposition from electric power generation. Terrestrial and aquatic wildlife may be at risk from exposure to waterborne Hg and MeHg. The transformation of inorganic Hg by anaerobic sediment microorganisms in the water column produces MeHg, which bioaccumulates at successive trophic levels in the food chain. If high trophic level feeders, such as piscivorous birds and mammals, ingest sufficient MeHg in prey and drinking water, Hg toxicoses, including damage to nervous, excretory and reproductive systems, result. Currently accepted no observed adverse effect levels (NOAELs) for waterborne Hg in wildlife have been developed from the piscivorous model in which most dietary Hg is in the methyl form. Such models are not applicable to omnivores, insectivores, and other potentially affected groups, and have not incorporated data from other important matrices, such as eggs and muscle. The purpose of this paper is to present a comprehensive review of the Hg literature as it relates to effects on wildlife, including previously understudied groups. We present a critique of the current state of knowledge about effects of Hg on wildlife as an aid to identifying missing information and to planning research needed for conducting a complete assessment of Hg risks to wildlife. This review summarizes the toxicity of Hg to birds and mammals, the mechanisms of Hg toxicity, the measurement of Hg in biota, and interpretation of residue data.

Keywords—Review Wildlife Methylmercury Analytical methods

INTRODUCTION

The purpose of this review is to summarize the current state of knowledge about the effects of mercury (Hg) on wildlife, to provide an extensive reference list, and to add information from the literature about the cellular and biochemical mechanism of methylmercury (MeHg) toxicity from laboratory animal, aquatic animal, and in vitro work, when such findings are pertinent to impacts on wildlife. In this way, we hope to derive useful MeHg toxicologic benchmarks for wildlife, and to identify areas where adequate information is lacking. The literature search for this review drew on major computer databases for references concerning the effects of Hg on wildlife. The general search criterion was “effects of MeHg on terrestrial wildlife.” Using this search strategy, more than 800 references were retrieved and screened. Because MeHg is the form relevant to wildlife exposures, inorganic Hg effects have been included only for comparative or illustrative purposes. We preferentially selected studies reporting the results of dietary exposure, or oral administration at environmentally realistic doses. Residue-type field surveys are useful for documenting the extent of wildlife exposure, but have not been included here unless they help to provide a quantifiable exposure and effect. Studies conducted on wildlife species rarely are able to use large sample sizes; therefore, conclusions drawn from wildlife work are strengthened when supported and supplemented by similar investigations employing domestic or laboratory animals. Studies with domestic or laboratory species, aquatic organisms, or humans have been included if they provided information on a relevant toxicity endpoint for which no data was available from a wildlife species. Acceptable endpoints were those that affect growth, viability, or reproductive or developmental success, including behavior, immunologic effects, neurologic impairment and neurohistologic lesions, and teratology.

Reviews also have been presented recently by Heinz [1], and Thompson [2]. This review includes a discussion of the mechanisms of MeHg toxicity, which has not been included in previous wildlife reviews, and a overview of Hg and MeHg analysis methods in matrices of interest to wildlife toxicologists.

MECHANISM

Methylmercury toxicity in mammals is primarily manifested as central nervous system damage; including sensory and motor deficits and behavioral impairment [3,4] Animals initially become anorexic and lethargic. Muscle ataxia, motor control deficits, and visual impairment develop as toxicity progresses, with convulsions preceding death [5–7]. Smaller carnivores are more sensitive to MeHg toxicity than are larger species, as reflected in shorter time to onset of toxic signs and time to death. Dietary concentrations of 4.0 to 5.0 μg/g MeHg were lethal to mink and ferrets within 26 to 58 d, whereas otters receiving the same concentration survived an average of 117 days [3,8].

Methylmercury is readily transferred across the placenta, and concentrates selectively in the fetal brain. Mercury concentrations in the fetal brain were twice as high as in the maternal brain for rodents fed MeHg [9]. Reproductive effects of MeHg in mammals range from developmental alterations in the fetus, which produce physical or behavioral deficits after birth, to fetal death [10–14]. Sundberg and Oskarsson [15]...
reported speciation of Hg in the milk and offspring of rats exposed to dietary MeHg. The lack of comparable data from mammalian wildlife species certainly constitutes one of the more glaring gaps in our knowledge.

**Neurotoxicity**

Methylmercury damages primarily the cerebellum and cerebrum [16]. The neurotoxic effects of MeHg in adult mammals include ataxia, difficulty in locomotion, neurasthenia (a generalized weakness, impairment of hearing and vision, tremor, and finally loss of consciousness and death [1,14,17]). Lesions in the cerebral and cerebellar cortex accompany these clinical signs. Necrosis, lysis, and phagocytosis of neurons results in progressive destruction of cortical structures and cerebral edema. O’Connor and Nielsen [5] found necrosis, astrogliosis, and demyelination in the cerebral and cerebellar cortex of otters that received 0.09, 0.17, and 0.37 mg/kg/d MeHg for 45 to 229 d. In adult mammals MeHg is preferentially taken up by glial cells; these seem particularly susceptible to MeHg damage [18]. Low concentrations (10⁻⁵ M) of MeHg inhibit the ability of cultured rat brain astrocytes to maintain a transmembrane K⁺ gradient, resulting in cellular swelling [19]. These findings support the suggestion of Clarkenson [20] that inhibition of cell membrane Na⁺, K⁺, adenosine triphosphatase (ATPase) is the primary mechanism of MeHg toxicity. Aschner and his coworkers [21] further showed that the particular sensitivity of glial cells to MeHg was due to a neutral amino acid carrier system that enhances transport of MeHg into these cells. In an investigation of the protective effect of glutathione against MeHg toxicity in cultured mouse neuroblastoma cells, Kromidas et al. [22] proposed that MeHg produces damage to microtubules by oxidation of tubulin sulf-hydrils and peroxidative injury.

The behavioral deficits produced by exposure to MeHg are known mostly from work with nonwildlife species, although an early article by Burton et al. [23] describes Hg-induced behavioral changes in Peromyscus. The behavioral teratology of MeHg in rodents was summarized by Shimai and Satoh [24]. Rats and mice exposed via the diet or by gavage at various times during gestation period showed retarded righting reflex, impaired or retarded swimming ability, decrease in spontaneous activities, impaired maze and avoidance learning, and deficits in operant learning [25]. Behavioral effects on a carnivorous species are reported only for the domestic cat [26]. The use of primates to study the behavioral teratology of MeHg has permitted more extensive investigations. Infant crab-eating macaques (Macaca fascicularis) born to females exposed to 50 or 70 μg/kg/d MeHg had blood MeHg levels of 1.69 ppm at birth and 1.04 ppm at the time of testing. The exposed macaques had significant deficits of visual recognition memory, compared to controls [27]. Cynomolgus monkeys (crab-eating macaques, M. fascicularis) born to females given by 50 μg/kg/d MeHg showed more nonsocial passive behavior, and less social play than nonexposed monkeys [28]. Adult macaques dosed with 0.24 to 1.0 mg/kg MeHg at twice-weekly intervals for up to 73 weeks first experienced constriction of the visual field, as has been reported by MeHg-intoxicated humans, an effect that was reversible if exposure was discontinued. At higher or more prolonged doses visual field constriction became permanent, and visual thresholds were altered, reflecting damage to neurons in the visual cortex [29]. Rice [30] exposed female monkeys to 10 to 50 μg/kg/d MeHg, bred them, then administered the same doses to the young, producing both a pre- and postnatal exposure. Infant Hg blood levels were 0.46 to 2.66 ppm at birth, decreasing to a steady-state concentration of 0.20 to 0.60 ppm by the time of behavioral assessment (fixed interval and discrimination reversal performance). Surprisingly, only small differences occurred in test performance in the young monkeys, even though the monkey receiving the highest doses exhibited clear signs of MeHg toxicity. Rice suggested that discrimination reversal might not be a sufficiently sensitive test in this species [30]. Cynomolgus monkeys to which Rice and Gilbert [31] administered 50 mg/kg/d MeHg for the first 7 years of life showed high-frequency hearing loss at 14 years, although no further exposure to MeHg occurred in the intervening 7 years. Ikeda et al. [32] reported that 100 to 300 μg/kg/d for 2 to 6 months was required to produce neurologic signs in rhesus monkeys (macaca mulatta). Although MeHg-induced behavioral impairments in birds have been documented (discussed below) comparable investigations with mammalian wildlife species have not been reported. Future effort should be directed to understanding the effect of low-level chronic MeHg exposure to sensory and behavioral function in wildlife species.

**Biochemical and enzyme effects**

Cholinesterase (ChE, acetylcholinesterase [ACHE] and butryrycholin esterase [BCE]) activities decreased in Coturnix quail receiving a diet containing 5 ppm MeHg for 18 weeks. Dietary concentrations of 0.05 or 0.5 ppm alone did not inhibit ChE activity, but potentiated the ChE inhibition of coadministered parathion. Quail receiving the highest concentration of MeHg had liver total Hg residues of 35.8 ppm, wet weight [33,34]. Great blue heron nestlings were fed fish containing 0.31 to 0.87 ppm Hg in fish, resulting in liver Hg concentrations of 1.32 to 1.71 ppm by the end of the nesting period; however, no depression of brain ChE activity resulted from this exposure [35]. In rhesus monkeys given 0.4, 4.0, or 50 μg/kg/d MeHg for 150 d, no significant difference occurred in ChE activity, even at the highest dose [36].

**Glutathione and glutathione enzymes**

The MeHg-induced swelling of cultured rat brain astrocytes reported by Aschner et al. [19] mentioned earlier could be prevented if the cells were exposed to MeHg as its glutathione conjugate. Protection from MeHg-induced embryotoxicity in mice was provided by administering N-acetyl-L-cysteine, a precursor of glutathione, either simultaneously or following MeHg exposure [37]. Di Simplicio and coworkers [38] measured the activities of several glutathione enzymes in liver and kidney against a variety of substrates in mice given MeHg with or without the protective coadministration of sodium selenite. They described a complex interaction of glutathione in tissues in which MeHg-induced damage and tissue repair occurred together. Similar results in mice were reported by Yasutake and Hirayama [39].

**Immunotoxicity**

Mercuric compounds have been demonstrated to be immunotoxic in several investigations. In a study in which rat dams received 3.9 μg/g diet MeHg during pregnancy, natural killer cell activity was reduced 42% in offspring exposed in utero and via lactation. A decline in T-cell activity in some cell types was also noted [40]. Human peripheral blood cells exposed in vitro to low concentrations of both Hg and MeHg showed a dose-dependent reduction in T-cell proliferation, and
in monocyte and macrophage viability. Cell death was preceded by disruption of cell membranes and an increase in intracellular Ca\(^{2+}\). The effect of MeHg was 5 to 10 times greater than the effect of Hg effect [41,42]. However, even inorganic Hg administered chronically to mice in drinking water as HgCl\(_2\) caused immune cell impairment and disruption of enzyme activity at doses too low produce kidney damage [43]. Methylmercury is more immunotoxic than Hg because MeHg exerts a double influence on Ca\(^{2+}\) modulation. In rat T lymphocytes, the rapid increase in Ca\(^{2+}\) concentration caused by MeHg resulted from both influx of extracellular Ca\(^{2+}\) and mobilization of Ca\(^{2+}\) from intracellular stores; the HgCl\(_2\)-induced slow rise in Ca\(^{2+}\) was due only to influx [44].

Chronic exposure to MeHg at levels too low to cause overt signs of toxicity may render an animal susceptible to infection that it might otherwise resist [43,45]. The finding by Spalding et al. [46] that great white herons dying of chronic, multiple diseases had greater body burdens of Hg than those dying of acute diseases suggests the importance for wildlife of mercurial compounds’ immunotoxicity.

**Genotoxicity**

Both Hg and MeHg cause chromosome breakage, an effect that is mitigated by H\(_2\)SeO\(_4\) [47,48]. In cultured lung and brain cells from rats, Chinese hamsters, and humans, brain cells were more susceptible to MeHg DNA strand breakage and cytotoxicity than were lung cells [47–50]. De Flora et al. [51] reported in an extensive review of the genotoxicity of mercury that Hg compounds often exerted clastogenic effects in eukaryotes, especially by binding SII groups and acting as spindle inhibitors, thus causing e-mitosis and resultant aneuploidy and/or polyploidy. Methylmercury compounds were more active than inorganic Hg salts.

**MAMMALS**

The results studies of the effects of MeHg on mammals are summarized in Table 1. Controlled feeding studies employing wildlife species provide the highest quality data. O’Connor and Nielsen [5] fed rations with 2, 4, or 8 ppm MeHg to 11 adult male river otters, 3 per dose level and 2 controls. Actual MeHg consumption was quantified as 0.09, 0.17, and 0.37 mg/kg body weight/d. At the lowest observed adverse effect level (LOAEL) dose of 0.09 mg/kg/d, two of three otters developed anorexia and ataxia between day 168 and day 199. Histologic findings included neuronal necrosis and demyelination, mainly in the neocortex and cerebellum. Wobeser et al. [6] fed mink feed contaminated with fish containing 0.44 ppm MeHg for 145 days. The fish comprised 1.1, 1.8, 4.8, and 8.3 and 15 ppm MeHg for 93 d. Mink receiving 1.8 ppm and greater concentrations developed the same signs of Hg toxicity, irrespective of dose, but the time to onset of signs was proportional to dose received. Mink receiving 1.1 ppm did not display clinical signs during the observation period, but at necropsy were found to have neurologic lesions. The authors maintained that clinical manifestations of MeHg toxicity would have developed at this those had the exposure period been longer. This argument is supported by the findings of Wren et al. [14], who fed diets containing 1 ppm MeHg to mink to determine the effects of chronic exposure. The diet was fed daily until a female mink died at 10 to 12 weeks, after which the diet was fed to the surviving mink on alternate days, effectively reducing the dose to 0.5 ppm/d. These findings suggest that 1.0 ppm should be regarded as the dietary LOAEL for mink and that a brain or muscle concentration of 5.0 ppm is the criterion for MeHg toxicity in mink. Ronald and coworkers [53] fed fish containing 0.25 or 25 mg/kg MeHg to harp seals. The 0.25 mg/kg exposure produced lethargy and weight loss in the seals; 25 mg/kg was lethal to seals exposed for 20 to 26 d.

**Toxicokinetics and biotransformation**

Ingested Hg may be either inorganic or organic, although it is usually in the form of MeHg in higher trophic level feeders. Inorganic Hg may be monovalent (mercurous) or divalent (mercuric). Methylmercury is readily absorbed from the gastrointestinal tract (90–95%), whereas inorganic salts of Hg are less readily absorbed (7–15%). In the liver, Hg binds to glutathione, cysteine, and other sulfhydryl-containing ligands. These complexes are secreted in the bile, releasing the Hg for reabsorption from the gut [54]. In blood, MeHg distributes 90% to red blood cells and 10% to plasma. Inorganic Hg distributes approximately evenly or with a cell:plasma ratio of ≅2 [55]. O’Connor and Nielsen [5] found that length of exposure was a better predictor of tissue residue level than dose in otters, but that higher doses produced an earlier onset of clinical signs.

Methylmercury readily crosses the blood–brain barrier, whereas inorganic Hg does so poorly. The transport of MeHg into the brain is mediated by its affinity for the anionic form of sulfhydryl groups. This led Aschner and Aschner [56] to propose a mechanism of molecular mimicry in which the carrier was an amino acid. Transport of MeHg across the blood–brain barrier in the rat as MeHg-L-cysteine complex has since been described [57]. Demethylation occurs in brain tissue, as evidenced by the observation that the longer the time period between exposure to MeHg and measurement of brain tissue residue, the greater the proportion of inorganic Hg [58–60]. Methylmercury is converted to mercuric Hg in other tissues, but the rate of demethylation varies with tissue. In humans exposed to dietary MeHg for 2 months, inorganic Hg constituted 16 to 40% of total Hg in liver, 7% in blood, and 22% in plasma. In monkeys (M. fascicularis) given 50 µg/kg body weight MeHg for 12 months, the half-life (t\(_{1/2}\)) in brain was 35 d. However, the proportion of inorganic Hg increased with increasing time after exposure [61]. Rice et al. [62] determined the t\(_{1/2}\) of MeHg in macaque blood to be 14 d, and estimated the brain t\(_{1/2}\) to be between 38 and 56 d. Chen et al. [63] administered MeHg to rhesus monkeys for 3.5 to 12 months. As the time between dosing and sacrifice increased, liver Hg declined and kidney Hg increased. Under these exposure conditions, the monkeys of Chen and coworkers did not exhibit neurologic symptoms, and blood chemistry remained within normal limits.

Both inorganic and organic Hg are excreted primarily in feces; 98% of the dose was recovered in the feces as inorganic Hg and 15% was recovered as organic Hg. Urinary excretion accounted for less than 5% of the dose, although urinary excretion of inorganic Hg increased with increasing time after exposure. Incorporation into fur or hair is also an important
route of excretion for both methyl and mercuric Hg [64]. On an average of species and tissues, the biological half-life of MeHg in mammals is about 70 d; for inorganic Hg the half-life is about 40 d.

All forms of Hg cross the placenta, but MeHg concentrates selectively in the fetal brain. Fetal red blood cells contain 30% more MeHg than do maternal red blood cells [65]. Methylmercury concentrations in the fetal brain were twice as high as in the maternal brain in rodents fed MeHg [9]. Reproductive effects of MeHg in mammals include developmental alterations that produce behavioral deficits after birth, impaired fertility, and fetal death. Chang and Annau [11], Eccles and Annau [12], and Shimai and Satoh [24] reviewed the behavioral toxicology of MeHg in mammals. Swimming ability, operant learning, avoidance, maze learning, and development of reflexes were affected at the lowest dosages, followed by changes in spontaneous activity, visual function, vocalization, and convulsions at successively higher exposures.

Further exposure may occur after birth. When hamster females were given 1.6 μmol/kg/d of radiolabeled MeHg the day after giving birth to young, 0.12 nmol/g of radiolabeled Hg was recovered in the milk 1 d later, 80 to 90% as MeHg. Pups continued to accumulate Hg in the tissues for 10 to 12 days, after which tissue concentrations declined, except in fur and kidneys, where concentrations increased throughout the 4-week study period. The investigators calculated that 5% of the dose administered to the dam passed to the young in the milk [66].

**BIRDS**

Mercury concentrations in avian eggs and tissues and related effects are summarized in Table 2. The biokinetics and toxicology of organomercurials in birds, particularly of MeHg, have been more extensively studied than those of Hg in the inorganic form. This is due to the greater toxicity and bioaccumulation of the methylated form compared to inorganic forms. Intestinal absorption of inorganic Hg is limited to a few percent, whereas absorption of MeHg is nearly complete [67]. The half-life of Hg in seabirds has been estimated to be about 60 d [68]. Inorganic Hg exerts its greatest effect on the kidneys, whereas MeHg is a potent embryo and nervous system toxicant. Methylmercury readily penetrates the blood–brain barrier in birds, as in mammals, producing brain lesions, spinal cord degeneration, and central nervous system dysfunctions. Symptoms of acute MeHg poisoning in birds include reduced food intake leading to weight loss; progressive weakness in wings and legs; difficulty flying, walking, and standing; and an inability to coordinate muscle movements [67]. Brain residues are most diagnostic for acute Hg poisoning. Kidney disease and kidney lesions also are strongly associated with elevated dietary Hg [46, 69–71]. Determination of Hg concentrations in brain, liver, and kidney of birds found dead is desirable if Hg poisoning is suspected. In some species, especially Procellariformes, demethylation of Hg appears to be a significant detoxification strategy.

In addition to well-identified acute effects of Hg at high concentrations, significant adverse effects also occur at lower tissue Hg concentrations representing chronic Hg exposures. In great white herons liver Hg contamination >6 ppm correlated with mortality from chronic diseases [72]. Reproduction is one of the most sensitive toxicologic responses, with very low dietary concentrations causing effects [73–76]. Concentrations in the egg are typically most predictive of Hg risk to avian reproduction, but concentrations in liver have also been evaluated for predicting reproductive risk. The documented effects of Hg on reproduction range from embryo lethality to sublethal behavioral changes in juveniles at low dietary levels; Effects of Hg include reduced hatchability due to increases in early mortality of embryos, eggshell thinning, reduced clutch size, increased numbers of eggs laid outside the nest, and aberrant behavior of juveniles, and potentially may include impaired hearing of juveniles [73,77–80].

**Hg in avian diets**

Barr [75] indicated that reductions in egg laying and territorial fidelity were associated with mean prey Hg concentrations of 0.3 to 0.4 ppm fresh weight; common loons established few territories, laid no eggs, or one egg and raised no progeny in waters where the mean Hg concentrations of prey exceeded 0.4 ppm fresh weight. The dietary concentrations of MeHg that are required to produce significant reproductive impairment are about 1.5-fold those required to produce overt toxicity in adult birds of the same species [81]. Overall reproductive success in birds can decrease by 35 to 50% due to dietary MeHg exposure insufficient to cause obvious signs of intoxication in adults. Heinz [73] fed 0.5 mg/kg dry weight MeHg (0.1 mg/kg wet weight) to three generations of mallards. Females laid fewer eggs and produced fewer ducklings. Barr [75] made the same observations in the field study mentioned previously where reductions in egg laying and in nest-site and territorial fidelity of the common loon in northwestern Ontario were associated with maximum Hg residues in eggs of 1.39 mg/kg wet weight. The loon diet contained from 0.2 to 0.3 mg/kg wet weight Hg. Heinz [73] also found that ducklings in his multigeneration laboratory feeding study were less responsive to taped maternal warning calls and were hypersensitive to fright stimulus.

**Hg in avian liver, brain, and kidney**

Correct interpretation of tissue residue data requires characterization of the various species of Hg. The kidney is a major reservoir of inorganic Hg in birds as well as in mammals. In renal tissue Hg will bind to metallothionein. Not surprisingly, the major toxic effects of inorganic Hg are kidney damage when Hg-induced necrosis of proximal tubular cells occurs [82]. Spalding et al. [46] found that liver Hg concentrations >6 ppm correlated with malnutrition and mortality from chronic disease in great white herons; however, the authors cautioned against overinterpreting these results because only dead birds were examined. Zillioux and coauthors [83], in their review of the literature, found that concentrations in liver between 1 and 2 ppm (wet weight) Hg may be associated with behavioral effects, whereas liver Hg concentrations of about 11 ppm (wet weight) and above were associated with high embryo/duckling mortality and brain lesions. Spalding and Forrester [84] suggested that neurologic effects may be associated with liver Hg levels in birds as low as 5 ppm (wet weight). Gochfeld [85] reported abnormal feather loss in the young of common terns having liver concentrations of 3 to 14 ppm. Zillioux et al. [83] concluded that a conservative residue threshold for major toxic effects in waterbirds is 5 ppm (wet weight) in liver. In contrast, apparently normal seabirds have been found with extraordinarily high Hg concentrations in liver, but these concentrations have been primarily inorganic Hg [86]. In the majority of wild birds sampled, liver concentrations of Hg are usually higher than kidney concentrations. However, in Hg poisoning some
Table 1. Effects of mercury and methylmercury (MeHg) on mammals and associated tissue residues

<table>
<thead>
<tr>
<th>Species</th>
<th>Tissue</th>
<th>Tissue concn. (ppm, wet wt.)</th>
<th>Dose (mg/kg or ppm)</th>
<th>Route/form</th>
<th>Exposure/duration</th>
<th>Effect/comments</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog (<em>Canis familiaris</em>)</td>
<td>Liver (total Hg)</td>
<td>0.1–0.25 mg/kg</td>
<td>0.25 mg/kg/d, 5 of 7 d</td>
<td>MeHg, in caps with food</td>
<td>90 d</td>
<td>Stillbirths</td>
<td>[13]</td>
</tr>
<tr>
<td></td>
<td>Liver (MeHg)</td>
<td>18.1</td>
<td></td>
<td>Oral, during pregnancy</td>
<td></td>
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<tr>
<td></td>
<td>Hair</td>
<td>170</td>
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<tr>
<td></td>
<td>Liver</td>
<td>40.2</td>
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<td></td>
<td>Kidney</td>
<td>21.6</td>
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<td></td>
<td>Brain</td>
<td>11.3</td>
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<td></td>
<td>Muscle</td>
<td>15.1</td>
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<td></td>
<td>Heart</td>
<td>8.92</td>
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<td></td>
<td>Lung</td>
<td>10.8</td>
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<tr>
<td>Cat (<em>Felis catus</em>)</td>
<td>Brain</td>
<td>0.85</td>
<td>0.55 with 2.9 mg/kg selenium</td>
<td>Dietary, 93.5–154 µg/d</td>
<td>188 d</td>
<td>No difference in maze learning or handling response but less than half object contact on open field test</td>
<td>[26]</td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>1.27</td>
<td></td>
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<tr>
<td></td>
<td>Liver</td>
<td>11.9</td>
<td></td>
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<td></td>
<td>Muscle</td>
<td>1.59</td>
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<tr>
<td>Cat</td>
<td>Brain</td>
<td>0.5</td>
<td></td>
<td>Dietary</td>
<td>7–11 months</td>
<td>Proliferation of smooth endoplasmic reticulum; degeneration of hepatic mitochondria</td>
<td>[10]</td>
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<tr>
<td></td>
<td>Kidney</td>
<td>4.0 mg/kg body wt.</td>
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<tr>
<td></td>
<td>Liver</td>
<td>125 mg/kg body wt.</td>
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<tr>
<td></td>
<td>Muscle</td>
<td>80 mg/kg body wt.</td>
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<tr>
<td>Pig (<em>Sus</em> spp.)</td>
<td>Liver</td>
<td>0.5</td>
<td></td>
<td>Oral, during pregnancy</td>
<td></td>
<td>Stillbirths</td>
<td>[13]</td>
</tr>
<tr>
<td>Crab-eating macaque (<em>Macaca fascicularis</em>)</td>
<td>Liver</td>
<td>0.4 µg/kg body wt.</td>
<td>MeHg, in apple juice</td>
<td>150 d</td>
<td>No clinical symptoms, no significant difference in cholinesterase activity</td>
<td>[36]</td>
<td></td>
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<tr>
<td></td>
<td>Kidney</td>
<td>4.0 µg/kg body wt.</td>
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<tr>
<td></td>
<td>Liver</td>
<td>50 µg/kg body wt.</td>
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<tr>
<td>Rhesus monkey (<em>Macaca mulatta</em>)</td>
<td>Liver</td>
<td>0.5 mg/kg</td>
<td>Oral, d 20 to 30 of pregnancy</td>
<td></td>
<td>Abortions, maternal toxicity</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kidney</td>
<td>22.91</td>
<td>125 µg/kg body wt./d</td>
<td>MeHg, in apple juice</td>
<td>3.5 months</td>
<td>No clearance period; liver and kidney histologic alterations</td>
<td>[62]</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>21.32</td>
<td></td>
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<tr>
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<td>Kidney</td>
<td>26.4</td>
<td>80 µg/kg body wt./d</td>
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<tr>
<td></td>
<td>Liver</td>
<td>30.32</td>
<td>80 µg/kg body wt./d</td>
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Table 1. Continued

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<td>Decline in appetite, body weight</td>
<td>[53]</td>
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<tr>
<td>Kidney</td>
<td>69.5</td>
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<td>Liver</td>
<td>64</td>
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<tr>
<td>Blood (MeHg)</td>
<td>8.85</td>
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<td>Blood (total Hg)</td>
<td>9.93</td>
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<tr>
<td>Brain</td>
<td>21.8</td>
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<td></td>
<td>90 d</td>
<td>Reduced activity after 60 d</td>
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<tr>
<td>Kidney</td>
<td>50.6</td>
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<td>Liver</td>
<td>82.5</td>
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<tr>
<td>Blood (MeHg)</td>
<td>12.5</td>
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<td>Blood (total Hg)</td>
<td>13.1</td>
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<tr>
<td>Brain</td>
<td>33.3</td>
<td>25</td>
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<td>Lethargy, weight loss from day 3; death on day 20 to day 26</td>
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<tr>
<td>Kidney</td>
<td>110</td>
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<tr>
<td>Liver</td>
<td>126</td>
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<tr>
<td>Blood (MeHg)</td>
<td>21.3</td>
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<tr>
<td>Blood (total Hg)</td>
<td>28.5</td>
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the normal situation. Barr [75] documented adverse effects on common loons associated with egg concentrations of 1.39 mg/kg wet weight.

Hoffman and Moore [93] treated mallard eggs with externally applied MeHg chloride. Effects were dose related and included decreased embryo weights, developmental abnormalities, and embryonic death. With increasing concentrations abnormalities progressed in severity from mostly minor skeletal deformities to gross external ones such as micromelia, gastrochisis, and eye and brain defects as well as internal defects such as reduction in liver size. Such laboratory work is useful because it may efficiently elucidate the types of effects that can be produced, but an extrapolation of dosages in Hoffman and Moore to the field situation would be inappropriate. External Hg exposures by Hoffman and Moore had more pronounced effects at lower doses than organic Hg incorporated into the egg from diet [92], presumably because of less binding to the ovalbumin and ovoglobulin.

Reproductive effects may extend beyond the embryo to adversely affect juvenile survival rates. Mercury in the eggs of mallards caused brain lesions in hatched ducklings. Mallards were fed 3.0 ppm MeHg dicyandiamide over 2 successive years. Mercury accumulated in the eggs to an average of 7.18 and 5.46 ppm (wet weight) in 2 successive years. Lesions included demyelination, neuron shrinkage, necrosis, and hemorrhage in the meninges overlying the cerebellum [92]. In a laboratory study with pheasants, Fimbreite [77] estimated the threshold concentration in eggs for adverse effects on hatchability to be between 0.5 and 1.5 ppm. The low end of this effect range continues to be the LOAEL for Hg in the avian egg. In a field study of common terns, Fimbreite [91] estimated the threshold level for toxic effects to be between 1.0 and 3.6 ppm. Heinz [92] was able to examine more subtle behavioral effects in mallard ducklings fed MeHg. Heinz fed ducks 0.5 ppm Hg over three generations and found decreased reproductive success and altered behavior of ducklings. The mean Hg concentration in eggs associated with these observations was 0.86 mg/kg (wet weight). Hoffman and Moore applied Hg externally to mallard eggs and found dose-related effects on survival, growth, and abnormal development. The lowest dose applied that affected survival was 27 μg. Given an average mallard egg weight of 55 g, this dose corresponds to about 0.5 mg/kg.

Hg in feathers: A potential monitoring tool and avian route of excretion

Almost all feather Hg is in the organic form [99]. Establishing effect levels using Hg concentrations in feathers must be considered with caution. Feathers represent a route of excretion and not a target organ. Mercury is deposited in feathers at the time of molt when feathers are actively growing and have a corresponding blood supply [100–102]. Once Hg is in feathers it is bound to the sulfide bonds of feather keratin and is not physiologically available for redistribution to target organs. Mercury content of feathers will vary with time to last molt, feather type, and age and species of the bird [103]. Feathers have the advantage of being a nondestructive exposure assessment matrix that may be resampled in the same individual, and that may also be compared with museum specimens [104]. The concentration of Hg in tissues may actually decrease during molting as Hg is mobilized from tissues into feathers [101]. In sequential feather loss patterns the first primary feather to be grown back has the greatest Hg concentration, with decreasing concentrations following [87,102,105]. Becker et al. [106] found results in three species of larids that implied that Hg in the first down of chicks was a consequence of Hg levels in the egg, whereas levels in feathers of chicks were largely due to Hg ingested in food. Lewis and Furness [107] found that in laboratory reared black-headed gulls 49% of the administered Hg was accumulated in the plumage independent of the dose administered. The percentage of the Hg body burden found in the plumage of different species has been found to vary. Species that are effective in demethylating Hg, such as members of the Procellariiformes, will tend to have a lower percentage of their total Hg body burden partitioned into the feather compartment as compared to other species. This has been interpreted as an adaptation to the slow molt of feathers in Procellariiformes with the consequent reduced opportunity for sequestration and ultimate excretion of MeHg via feathers [86]. The molt pattern of any given species will have a significant influence on variation in feather Hg concentrations between different feathers within an individual bird [104]. More variation in Hg with feather type should also be expected in more contaminated environments [106]. The exposure relative to season and feather growth may also have an important influence on Hg accumulation in other tissues if birds experience significant differences in Hg exposure between wintering and breeding grounds. For meaningful quantitative monitoring of Hg using feathers the feather/Hg pattern for a species should be established and similarly sampled among those individuals or populations that are to be compared. For historic comparisons using older museum specimens determinations of both total and MeHg in feathers may be prudent to evaluate the relative contribution of mercurials used in specimen preservation of avian study skins, if preservation methods are only vaguely recorded. In a review of effects related to Hg concentrations in feathers, Eisler [107] reported that concentrations between 5 and 40 mg/kg in feathers were linked to impaired reproduction. Sterility was observed in the Finnish sparrow hawk (Accipiter nisus) at feather Hg concentrations of 40 mg/kg. A great deal of variation is likely in feather Hg concentrations associated with adverse effects between species and between geographic areas due to Hg exposure patterns related to feather molt. Bowerman et al. [108] found mean Hg in feathers of bald eagles in the Great Lakes region of 13 to 21 mg/kg but no association between Hg concentrations and bald eagle reproduction could be made. Schreuthamer [81] suggests that feather Hg concentrations >20 mg/kg can result from diets containing Hg concentrations >1 μg/g and that these concentrations should be considered as indicative of a wetland that poses an Hg risk to birds. Schreuthamer estimated normal background of Hg in feathers of raptorial birds to be 1 to 5 μg/g.

REPTILES AND AMPHIBIANS

The toxicity of Hg and MeHg to reptiles and amphibians is almost unknown. A dose of 50 ppb applied to the embryos of the frog Xenopus laevis reduced survival by 50% after 4 d of treatment, and to 0% after 7 d. Surviving embryos showed disruption of morphogenesis, neurophysiology, and neuroimmune regulation [109]. Rao and Madhyastha [110] reported that the median lethal concentration (LC50) of HgCl to the tadpoles of Microhyla ornata ranged from 2.04 ppm (24 h) to 1.12 ppm (96 h). Wolfe (unpublished data) fed MeHg to garter snakes (Thamnophis sirtalis) in concentrations up to 200 μg/g food in the range-finding phase of a proposed feeding
study. The snakes displayed no sign of MeHg toxicity, no decrease in food consumption, and later gave birth to apparently normal young. Because no effect was seen at these high doses in the range-finding trials, the study was not completed.

**Hg AND MeHg ANALYTICAL METHODS**

**Sample preparation**

A summary of analytical methods for determination of Hg and MeHg is presented in Table 3. Biological samples such as muscle and liver tissues, hair or fur, eggshell, and body feathers have been used to determine the Hg body burden of wildlife species [111–114]. Most biological samples are obtained from wildlife captured in their habitats. Organ tissues such as skin, liver, muscle, and brain tissues are excised in the field and shipped on ice to the laboratory [113]. Normally the samples are stored in clear glass containers; however, the use of polyethylene terephthalate containers has proven to be as suitable as glass bottles [115] for shipping purposes. Eggs can be collected in the field and the contents stored under refrigeration for 2 to 3 months before analysis [111,112]. The samples are usually freeze-dried, ball-milled, and homogenized prior to digestion with a mixture of nitric and sulfuric acids.

Hair or fur samples may either be unwashed [116], or washed with acetone to reduce the fat content [117]. Some investigators have found that washing is not effective in removing naturally occurring Hg from exogenous deposition [118,119]. The digestive process may include submersion of the samples in deionized water before analysis. Addition of 50% hydrogen peroxide. The samples are diluted in deionized water alternately with acetone to remove loosely adherent external contamination [114,120]. Without washing, surface Hg from the use of Hg in the preservation of older specimens may present a compounding variable. The washing process is followed by digestion in warm nitric acid with the use of Hg vapor from the use of Hg in the preservation of older specimens. The washing process is followed by digestion in warm nitric acid with the addition of 50% hydrogen peroxide. The samples are diluted in deionized water before analysis.

**Fish and shellfish samples**

Fish and shellfish samples must be collected and analyzed when investigating Hg exposure in piscivorous species. Historically, high detection limits have caused limitations in measurement of total Hg and MeHg in aqueous and biological samples. Large amounts of organic matter and other substances accompanying biological specimens as well as contamination of samples during handling can potentially interfere with total Hg determination because of the ubiquitous presence of Hg in the laboratory environment [121].

**Hg determination**

The most commonly used technique for total Hg determination is cold-vapor atomic absorption spectroscopy (CVAAS) using electrochemical detection [122–126]. The basic approach of all cold-vapor methods is to convert the Hg in a small sample to mercuric ion, then reduce it to elemental Hg with a reductant such as stannous chloride. The Hg vapor is then measured in a modified atomic absorption spectrophotometer. Various acid mixtures have been used for the digestive process. The use of a high-pressure and high-temperature feedback microwave system has reduced the digestion time significantly [126]. The CVAAS method is applicable for drinking water, brackish water, domestic and industrial wastes, and biological samples. Other detection methods, such as inductively coupled plasma–mass spectrometry (ICP-MS), become feasible once the Hg has been released to mercuric vapor [127].

The most recent cold-vapor atomic fluorescence spectroscop-
copy (CVAFS) method [128] has become increasingly important compared to CVAAS, because the instrumental detection limit of CVAFS is about 1 picogram or less and at least one order of magnitude better than CVAAS [129]. Total Hg analysis by this method requires sample digestion by a strong acid (nitric–sulfuric or nitric– perchloric–hydrofluoric) that results in conversion of organic Hg to inorganic Hg. The digested samples are introduced to the cold-vapor generator, at which point tin (II) chloride is used to effectively reduce inorganic Hg to its elemental gaseous form prior to detection by atomic fluorescence. This method can attain 95 to 105% recovery efficiency for elemental Hg [130].

Several enrichment techniques have been proposed to improve on the sensitivity of the CVAFS method. Some techniques require preconcentration of Hg on copper wire or platinum [131] and preconcentration of volatilized Hg on gold or silver [132]. Very low detection limits for total Hg in biological and environmental samples have been successfully determined by the application of a high-temperature, high-pressure microwave system combined with Hg amalgamation tube systems that reduce the amount of time, the amount of acids, and the sample size required [133].

MeHg determination

Indirect measurement. The most common indirect measurement technique is a selective digestion that allows for determination of total Hg and inorganic Hg (II) directly, and MeHg by difference [134]. The method is based on the rapid conversion of organomercurials into inorganic Hg and then followed by conversion into atomic Hg suitable for aspiration through the gas cell of a Hg vapor concentration meter (atomic absorption) by a strong alkaline solution (tin (II) chloride–cadmium chloride). Alternatively, a two-step digestion method may be performed in which total Hg is determined on nitric acid–hydrogen sulfate and Hg (II) is determined as above [128]. These methods are simple but lack species specificity and are operationally defined.

Direct measurement. Following one of several isolation techniques (extraction, ion exchange, volatilization, separation, distillation, and digestion), final determination of MeHg is accomplished by various spectrophotometry detectors. The most common MeHg determination is performed by solvent extraction combined with separation using gas–liquid chromatography followed by electron-capture detection (GC-ECD) a technique developed by Westöö [135]. A variation of this method replaces the ECD with microwave-induced plasma detection (GC-MIP) because this can be used as an Hg-specific detector [136,137]. These methods are typically tedious and complex because the MeHg bound to the tissue sample has to be extracted and purified into a small volume of solvent suitable for GC injection. The multiple steps required can reduce the yield. In addition, the EC detector, which measures the halide rather than the Hg atom, is prone to matrix interference from known and unknown halogen-containing species in the typical laboratory [138].

To overcome the difficulty with sample preparation prior to GC separation, the headspace sampling analysis method to determine MeHg was developed [136] and modified further [139,140]. These methods involve MeHg extraction from the biological sample and conversion of the MeHg into the iodide form, the most volatile MeHg halide salt. These reaction steps take place in a closed headspace vial where the MeHg iodide is then headspace-injected into a gas chromatograph equipped with a microwave-induced plasma detector (HS-GC-MIP). Quantitation is accomplished by standard addition. This method is also prone to decreased yield due to matrix interferences.

As discussed previously, the most commonly used technique for total Hg determination is by CVAAS using electrochemical detection [122]. A similar detection method was also developed by Holak [141] for MeHg determination. Methylmercury is converted into MeHg (II) chloride by hydrochloric acid treatment and isolated from the sample by elution with chloroform from a diatomaceous earth column. Prior to high-performance liquid chromatographic (HPLC) separation, the sample is back-extracted into aqueous phase as sodium thiosulfate complex. Detection is accomplished either electrochemically or by atomic absorption (AA) in a specifically constructed apparatus [141]. A few methods use CVAAS detection combined with various isolation techniques [142–145]. Some of the methods can determine total Hg and MeHg from the same aliquots. For example, Gutiérrez et al. [145] conducted an experiment that utilized a mixed solution of sodium hydroxide, sodium chloride, and cysteine to digest fish tissue followed by a selective reduction with tin (II) chloride–cadmium chloride reagent. The inorganic and organic Hg in the same sample are sequentially reduced, volatilized, and measured by CVAAS.

All of the above methods have potential problems because they lack species specificity or because matrix interferences decrease the yields. In addition, all methods that employ an acid extraction step convert dimethylmercury to the monomethylmercury form, thus diminishing the speciation information gained from that analysis [138].

The most current technique being used to determine MeHg involves aqueous phase ethylation with cryogenic GC separation and atomic fluorescence detection [128,146,147]. In this method sodium tetraethyl borate converts the nonvolatile monomethyl Hg to gaseous methyl ethyl Hg. The volatile adduct is then thermally desorbed from the column and analyzed by cryogenic GC with a highly sensitive CVAFS detection. The detection limit of this method is about 1 picogram or less and at least one order of magnitude better than for CVAAS [129,147]. Atomic fluorescence is also less prone to matrix interferences [147]. Detection limits are less critical in determination of Hg in animal tissue; however, the use of a more sensitive detector such as CVAAS allows for smaller sample size, thereby reducing matrix interference.

REFERENCES


Review of Hg effects on wildlife

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