



## CONTAMINATION OF MERCURY IN FISH AND ITS TOXICITY TO BOTH FISH AND HUMANS: AN OVERVIEW

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### ABSTRACT

Heavy metals are considered the most important form of pollution of the aquatic environment because of their toxicity and accumulation by marine organisms. The fish may be more greatly affected by anthropogenic pollution sources. Fish are highly exposed from the heavy metals, like mercury (Hg), leading to severe toxicity, both in the fish and human beings. The fish accumulate substantial concentrations of Hg in their tissues, and thus the fish are the single largest sources of Hg for humans through fish eating. The organic forms of Hg (e.g., methyl Hg) are more toxic than the inorganic forms due to ease of absorption into the human system. Communities that relied on fish intake for daily nutrient sustenance may be at risk from chronic, high exposure to methyl Hg, as well as other persistent organic environmental pollutants. The organic Hg compounds are most toxic to central nervous system (CNS), and may also affect the kidneys and immune system. The main symptoms of Hg poisoning in humans include kidney damage, disruption of nervous system, damage to brain functions, DNA and chromosomal damage, allergic reactions, sperm damage, birth defects, and miscarriages. The greater concern for Hg exposure is not to adult human, but to developing foetus. The methyl Hg content of fish varies by species and size of the fish as well as harvest location. The FDA level of concern for Hg in fish is 1 ppm. The fish with levels higher than this should probably be avoided by everyone.

**Keywords:** Contamination, environmental pollutants, fish, heavy metals, humans, mercury (Hg), toxicity.

### INTRODUCTION

Fish are exposed from different environmental pollutants, drugs and chemicals, including 'heavy metals'. The most important heavy metals causing severe toxicity to fish are arsenic, lead, mercury, cadmium, copper, chromium, iron, manganese, nickel, zinc, tin, etc.<sup>1</sup>. Heavy metals are considered the most important form of pollution of the aquatic environment because of their toxicity and accumulation by marine organisms<sup>2</sup>. The natural aquatic systems may extensively be contaminated with heavy metals released from domestic, industrial and other man-made activities. The fish are widely used to evaluate the health of aquatic ecosystems because pollutants build up in the food chain, and are responsible for adverse effects and death in the aquatic systems<sup>2-3</sup>. The heavy metals contents in aquatic environment have increased because of different activities, such as industrial, domestic and agricultural. With increasing heavy metals in the environment, these elements enter the biogeochemical cycle. The heavy metals can enter from contaminated water into fish body by different routes and accumulate in the organisms. These metals concentrated at different contents in organs of fish body<sup>2,4</sup>.

The fish accumulate substantial concentrations of Hg in their tissues, and thus can represent a major dietary source of this heavy metal for humans. Hence, the fish are the single largest sources of Hg for humans. The primary sources of Hg contamination in humans are through eating fish<sup>2,5</sup>. Prevalence of Hg in the environment leads to biomagnification in the food chain. The organic forms of Hg, such as methyl Hg, are more toxic than inorganic forms due to ease of absorption into the human system<sup>6</sup>. The levels of Hg in bluefish are high enough to cause potential adverse health effects in sensitive birds and mammals that ate them and to provide a potential health risk to humans who consume them. The fish larger than 50 cm fork length

average levels above 0.3 ppm, suggesting that eating them should be avoided by pregnant women, children and others who are at risk. The fish consumption is the only significant source of methyl Hg exposure for the public. Communities that relied on fish intake for daily nutrient Sustenance may be at risk from chronic, high exposure to methyl Hg, as well as other persistent organic pollutants. Similarly, high-end fish consumers, whether recreational or and subsistence, are at risk from Hg exposure<sup>2,7</sup>.

The methyl Hg accumulation in seafood and fish products is a growing global concern that poses severe health risks to the public. While Hg occurs naturally, large amounts enter the environment from anthropogenic sources. Human exposure to Hg begins with the production of many useful products. As the only metal on earth that can be found in a liquid form at room temperature, Hg and its compounds have many uses. Due to its special properties, including high density and high rate of thermal expansion, Hg is often used in barometers and thermometers. It can also be combined with other metals to create special alloys called amalgams. Gold and silver amalgams have been used in dentistry for fillings, and tin amalgams are used to make mirrors. The Hg can be found in many different lamps, including 'black lights', and is used in the industrial production of chloride and sodium hydroxide<sup>8</sup>. Some Hg compounds are used as ingredients in skin creams, antiseptics, diuretics, fungicides, insecticides, and as a preservative in vaccines. The Hg compounds were even once used in the treatment of syphilis<sup>9</sup>.

The Hg is a naturally occurring heavy metal and a waste product of industries such as coal-burning power plants. Once Hg enters the water, it is consumed by microorganisms, which are eaten by small fish, and these, in turn, by bigger fish. At each step up the food chain, the Hg is retained in the muscle meat of the fish, resulting in the highest concentrations of Hg in large, long-lived predatory fish, such

as swordfish and shark. The Hg has a toxic effect on the human nervous system, and can cause problems with learning, coordination and several other severe disorders leading to death. The Hg is particularly dangerous for pregnant women (who can pass the Hg to the foetus through the placenta), breastfeeding women (who can pass the Hg to the baby through breast milk) and young children, whose nervous systems are developing. Taking these matters in view, this review article emphasizes about the contamination and toxicity of Hg occurring in fishes which ultimately causes the death of fishes as well as humans by eating/exposure of such Hg-contaminated fishes.

### Source and exposure of Mercury

The Hg is widespread in the environment as a result of natural and anthropogenic releases. Everyone is exposed to small amounts of Hg over the course of a lifetime<sup>10</sup>. Most atmospheric Hg is elemental Hg vapor and inorganic Hg. The Hg present in waters, soils, plants and animals is typically present in organic or inorganic forms. The organic Hg is primarily in the form of methyl Hg. The Hg is released into surface waters from natural weathering of rocks and soils, and from volcanic activity. It is also released from human action, e.g., industrial activities, fossil fuel burning and disposal of consumer products (i.e., Hg thermometers, fluorescent bulbs and dental amalgams). The global cycling of Hg via air deposition occurs when Hg evaporates from soils and surface waters to the atmosphere. From the atmosphere, the Hg is redistributed on land and surface waters; then absorbed by soils or sediments. Once the inorganic Hg is released into the environment, the bacteria convert it into organic Hg, which is the primary form that accumulates in fish and shellfish<sup>11</sup>. The Hg vapor is emitted to the atmosphere through both natural and anthropogenic sources. The natural sources of Hg vapor include volcanoes, as well as rocks, soils and water surfaces. The Hg is also found naturally in cinnabar, the major ore for the production of Hg. Anthropogenic sources of Hg vapor include emissions from coal-burning power plants, municipal incinerators and through the recycling of automobiles<sup>9</sup>. It is estimated that 50 to 70% of the total emission of Hg to the environment is a result of human activity. About 1,000 times as much, about 2,600 tons, is emitted from anthropogenic sources<sup>12</sup>. The Hg emitted from all these sources is then cycled through the ecosystem. Once in the atmosphere, Hg vapor is slowly converted by oxidative processes to divalent Hg, which is then returned to the earth's surface by rainfall, where it accumulates in soils and in surface waters. Some of the Hg load is then converted back into Hg vapor and returned to the atmosphere. However, another fraction of the Hg load is washed into rivers, streams and eventually the ocean, where it accumulates in aquatic sediments. It is here that inorganic Hg is converted to methyl Hg by microorganisms living in the sediments by a process called 'methylation'<sup>9</sup>. This methyl Hg then enters the food chain when it is absorbed by phytoplankton species. The phytoplanktons are eaten by plankton consumers, which then are eaten by larger and larger fish. The methyl Hg accumulates in the tissues of fish and shellfish via a process called 'biomagnification', through which the methyl Hg concentration increases as it moves up from one trophic level to the next. Within each organism, the methyl Hg bioaccumulates as the organism consumes more and more organisms containing methyl Hg. Thus, smaller fish that are lower down in the food chain have lower concentrations of Hg in their tissues, while larger fish that are

higher up in the food chain have higher concentrations. For example, sardines contain about 0.01 ppm of Hg, while sharks contain from 1 ppm to as much as 4 ppm<sup>13</sup>. The fish with the highest levels of Hg include sharks, swordfish and king mackerels. Large marine mammals such as whales have levels similar to these fish.

In the aquatic food chain, the methyl Hg biomagnifies as it is passed from lower to higher trophic levels through consumption of prey organisms. The fish at the top of the food chain can biomagnify methyl Hg approximately 1 to 10 million times greater than concentrations in surrounding waters. About all of the Hg found in fish and other aquatic organisms is in the methyl Hg form. Long-lived predatory ocean fish may have increased methyl Hg content because of exposure to natural and industrial sources of Hg<sup>10</sup>.

### Toxicity of Mercury to fish, humans and other species

While some of the Hg compounds are fairly inert, many Hg compounds are extremely toxic. In the US, some products containing Hg have been banned, have usage limits, or have special disposal requirements. These include dental fillings, vaccines, non-industrial thermometers, lamps, car starters and electronics. There are also many regulations regarding the disposal of Hg wastes. Most organic Hg compounds are readily absorbed by ingestion and appear in the lipid fraction of blood and brain tissue. The organic Hg readily crosses the blood brain barrier (BBB) and also crosses the placenta. The fetal blood Hg levels are equal to or higher than maternal levels. The methyl Hg also appears in human milk.

The organic Hg compounds are most toxic in the CNS, and may also affect the kidneys and immune system<sup>10</sup>. The methyl Hg is toxic to the cerebral and cerebellar cortex in the developing brain and is a known teratogen. The mothers, who were exposed to high amounts of Hg but were asymptomatic, gave the birth to severely affected infants. The infants often appeared normal at birth but developed psychomotor retardation, blindness, deafness and seizures over time. Since the foetus is susceptible to neurotoxic effects of methyl Hg, several studies have focused on subclinical effects among children whose mothers were exposed to high levels of methyl Hg<sup>10,14</sup>.

One form of Hg that is toxic and very harmful is elemental Hg. It is highly volatile and can easily be converted to Hg vapor, exposure to which can damage the nervous system, lungs and kidneys. This type of exposure generally only happens to industrial workers directly handling Hg compounds. They are exposed either by inhaling Hg vapor or through chronic contact with volatile inorganic Hg compounds. For most people, exposure to Hg occurs when they eat fish or shellfish contaminated with methyl Hg. This is found in nearly all freshwater and marine fish. The methyl Hg has the ability to be absorbed by the digestive tract and enter the blood stream, which, over time, can result in damage to the nervous system. The main symptoms of Hg poisoning in humans include kidney damage, disruption of the nervous system, damage to brain functions, DNA and chromosomal damage, allergic reactions, sperm damage, birth defects and miscarriages. The LD<sub>50</sub> values are as low as 1 mg/kg in small animals<sup>6</sup>.

Furthermore, both inorganic and organic forms of Hg are highly toxic to humans; however, inorganic Hg is not as easily absorbed by the body. The inorganic Hg, such as Hg vapor, is toxic if inhaled in large concentrations and can cause acute pneumonia. The inhaled gaseous Hg is absorbed into the blood. Once in the circulatory system, it can pass

through the BBB and accumulate in the brain, damaging the CNS. As the body tries to rid itself of these toxins, gaseous Hg is oxidized to divalent Hg, which accumulates in the kidneys and can cause kidney damage. The brain, kidney and lung are the target organs of elemental (gaseous) Hg; while kidney is for divalent Hg; and brain and foetal brain are for methyl Hg<sup>12</sup>. Most people are not exposed to inorganic Hg but rather absorb methyl Hg through the consumption of fish and shellfish. The methyl Hg is easily absorbed in the digestive tract, where it forms a complex with the amino acid cysteine. This new complex resembles a large neutral amino acid found in the body, methionine, and can more easily gain entry into cells. As with inorganic Hg, once in the bloodstream, methyl Hg will accumulate in the brain and cause damage to the CNS. The methyl Hg is naturally removed from the body over time. Eventually, this methyl Hg-cysteine complex is transported to the liver where it is secreted into bile, after which enzymes break the complex down into its amino acid and methyl Hg parts. Some of this methyl Hg then comes in contact with the bacteria in the intestine and is broken down into inorganic Hg and carbon. The inorganic Hg is poorly absorbed in the rest of the methyl Hg that does not interact with bacteria is reabsorbed by the body and goes through the process again. It takes about 30 to 40 hours for methyl Hg to be distributed to the tissues of the body<sup>9</sup>. This cycle is the reason it takes so long to rid the body of Hg and how it can accumulate in the blood. It can take up to a year for Hg levels to drop significantly<sup>15</sup>.

Many adverse health effects are associated with the accumulation of Hg in the body, though these vary depending on the amount of Hg one is exposed to, time of exposure, chemical form of Hg and age of the subject. The methyl Hg, the most easily absorbed form of Hg, is a very potent neurotoxin that interferes with brain development. Once in the brain, it interferes with nerve cell differentiation and cell division by binding DNA and RNA. It can cause nerve cell death and scarring in selected areas of the brain<sup>16</sup>. With methyl Hg exposure, paresthesia is the first and mildest symptom observed, where a tingling or numbness is felt in the hands, arms, legs, or feet, but can also occur in other parts of the body. In the case of methyl Hg poisoning, this numbness is the first sign of damage to the nervous system<sup>9</sup>. Other symptoms that may follow a higher dose of methyl Hg poisoning are ataxia (stumbling or clumsy gait) and generalized weakness. Higher doses of methyl Hg poisoning may lead to dysarthria, loss of vision and hearing, tremor, and finally, coma and death<sup>16</sup>. To date, these more severe symptoms have only been observed in people who consumed fish that were contaminated directly by methyl Hg from anthropogenic sources, not from methyl Hg that accumulated through the natural methylation process<sup>9</sup>.

In the 1950's, one of the most severe incidents (known as the "Minamata Bay Incident") of industrial pollution and Hg poisoning occurred in the small seaside town of Minamata, Japan. A local petrochemical and plastics company, Chisso Corporation, dumped an estimated 27 tons of methyl Hg into the Minamata Bay over a period of 37 years. The Hg was used as a catalyst in the production of acetaldehyde, a chemical employed in the production of plastics. The methyl Hg-contaminated wastewater, a byproduct of the process, was pumped into the bay, creating a highly toxic environment that contaminated local fish. The residents of Minamata, who relied heavily on fish for food, were at risk of exposure to methyl Hg with every bite of fish they ate. The high contamination levels in the people of Minamata led to severe

neurological damage and killed more than 900 people. An estimated 2 million people from the area suffered health problems or were left permanently disabled from the contamination<sup>17</sup>. This form of toxicity in humans is now called "Minamata disease". Symptoms of this disease include sensory disorders of the four extremities, loss of feeling or numbness, cerebellar ataxia, tunnel vision or blindness, smell and hearing impairments, and disequilibrium syndrome. More serious cases lead to convulsions, seizures, paralysis and possibly death. In addition to the outbreak among the townspeople, congenital Minamata disease was observed in babies born to affected mothers. These babies demonstrated symptoms of cerebral palsy<sup>12</sup>.

#### **Fish consumption and dangerous Mercury levels**

While the danger of Hg poisoning may seem like a good reason to refrain from consuming fish, the benefits of eating fish may outweigh many of the risks. Fish is high in protein, low in saturated fats, and contains important nutrients such as heart healthy omega-3 fatty acids. Docosahexaenoic acid (DHA), one of the omega-3 polyunsaturated fatty acids found in fish oils, is important for the normal brain development and function<sup>18</sup>. It is possible that DHA may even counteract the negative effects of Hg though this relationship has not yet been proven scientifically. Eating fish has also been found to reduce the risk of heart attacks, lower blood pressure, and improve arterial health<sup>19</sup>.

The greater concern for Hg exposure is not to an adult human, but to a developing foetus. As seen in the extreme Minamata case, some mothers showed no outward signs of Hg poisoning, but gave birth to children with severe brain damage<sup>9</sup>. The studies have shown a correlation between prenatal exposure to Hg and decreased ability of infants and children on neuro-behavioural tests, including tests of attention, fine motor function, language skills, visual-spatial abilities and memory. This is because the methyl Hg readily crosses the placenta through blood circulation, and foetal blood concentration of Hg is slightly higher than maternal levels. The methyl Hg can also be passed through breast milk to infants and consumed by young children in their diets. Therefore, the young children are potentially more susceptible to toxicity from Hg and the brain may be more affected as it continues to develop during the first year of life<sup>16</sup>.

The methyl Hg is 1,000 times more soluble in fat than in water, and it concentrates in muscle tissue, brain tissue and CNS. The Hg levels in fish may be in excess of 10,000 to 100,000 times the original concentration in surrounding waters. Its accumulation is fast, while depuration is extremely slow. The half-life of methyl Hg in fish is estimated at 2 yr. The Hg levels for salt water fish average 0.35 to 70.02 ppm<sup>2,7</sup>. The methyl Hg content of fish varies by species and size of the fish as well as harvest location. The top 10 commercial fish species (i.e., canned tuna, shrimp, pollock, salmon, cod, catfish, clams, flatfish, crabs and scallops) represent about 85% of the seafood market and contain a mean Hg level of about 0.1 µg/g<sup>10</sup>.

Based on the growing body of evidence concerning the health issues of methyl Hg accumulation in the body, the US 'Environmental Protection Agency' (EPA) and the US 'Food and Drug Administration' (FDA) have issued advisories targeting consumption of fish for specific groups. Their advice to women who may become pregnant, pregnant women, nursing mothers and young children up to age 6 yr. is to avoid certain types of fish high in methyl Hg, and limit

the amount of fish consumed each week. Specifically, the EPA and FDA advise these groups not to eat shark, swordfish, king mackerel, or tilefish at all because they contain very high levels of mercury (>1 ppm). They also advise these groups to eat up to 12 ounces (or 2 average meals) a week of fish and shellfish that are low in Hg. Children should only eat 6 ounces of fish. The low Hg fish and shellfish include shrimp, canned light tuna, pollock, salmon and tilapia. Albacore tuna is a commonly eaten fish but contains moderate amount of Hg. The EPA and FDA advise eating only 6 ounces of albacore tuna a week. Also, if one exceeds the suggested amount of fish or shellfish in a week, simply cut back the amount consumed the next week or two. Lastly, the EPA and FDA advise the public to check for local advisories on fish caught from local lakes, rivers and streams. These fish may be more greatly affected by anthropogenic pollution sources<sup>20</sup>. These guidelines are not aimed at adult men, or woman past child bearing age, but individuals concerned with possible exposure to Hg should follow them as well.

A study of children exposed to high levels of methyl Hg in contaminated seeds demonstrated motor retardation in children whose mothers had hair Hg levels in the range of 10 to 20 ppm. The results of another study suggest that exposure in uterus to Hg at lower levels is associated with subtle adverse effects on the developing brain (maximum level in hair was 39.1 ppm and in blood was 351 ppb). The memory, attention and language tests in that study were inversely associated with higher methyl Hg exposures in children up to 7 yr. of age<sup>10,14</sup>. In a further study, the adverse effects on development or IQ have not been found up to 66 months of age. A "Reference Dose" (RfD) for Hg has been prescribed as 0.1 µg/kg/day (µg/kg = ppb). The EPA has recently reconfirmed 0.1 µg/kg/day as RfD of Hg<sup>21</sup>. The current action level of US FDA for Hg in fish tissue is 1 ppm (1000 ppb).

## CONCLUSION

Fish are highly exposed from the Hg, leading to severe toxicity, both in the fish and humans. The organic forms of Hg, e.g., methyl Hg, are more toxic than inorganic forms due to the ease of absorption into the human system. Communities that relied on fish intake for daily nutrient sustenance may be at risk from chronic, high exposure to methyl Hg. The methyl Hg causes much more toxicity to the CNS, kidney and immune system. The main symptoms of Hg poisoning in humans include kidney damage, disruption of the nervous system, damage to brain functions, DNA and chromosomal damage, allergic reactions, sperm damage, birth defects, and miscarriages. The top 10 commercial fish, i.e., canned tuna, shrimp, pollock, salmon, cod, catfish, clams, flatfish, crabs and scallops contain a mean Hg level of

about 0.1 µg/g. The FDA level of concern for Hg in fish is 1 ppm. The fish with levels higher than this should probably be avoided by everyone. However, balancing the risks of Hg exposure and the benefits of fish consumption is essential to proper nutrition. The consumption of fish and shellfish should not be completely stopped, because the fish are important part of our diet and healthy life.

## REFERENCES

1. Madhuri S, Pandey Govind, Bhandari Rita, Shrivastav AB. Fish cancer developed by environmental pollutants. *Int Res J Pharm* 2012; 3(10):17-19.
2. Madhuri S, Sahni YP, Mandloi AK, Pandey Govind. Toxicity in fish polluted with heavy metals, chemicals or drugs. *Jigyasa* 2012; 6(2):67-71.
3. Vinodhini R, Narayanan M. Bioaccumulation of heavy metals in organs of fresh water fish *Cyprinus carpio* (Common carp). *Int J Environ Sci Tech* 2008; 5(2):179-182.
4. Dobaradaran S, Naddafi K, Nazmara S., Ghaedi H. Heavy metals (Cd, Cu, Ni and Pb) content in two fish species of Persian Gulf in Bushehr Port. *Iran Afr J Biotechnol* 2010; 9(37):6191-6193.
5. Khansari FE, Ghazi-Khansari M, Abdollahi M. Heavy metals content of canned tuna fish. *Food Chem* 2005; 93:293-296.
6. Lenntech, Home Page. <http://www.lenntech.com/periodic/periodic-chart.htm>; 2012.
7. Burger J. Risk to consumers from mercury in bluefish (*Pomatomus altatrix*) from New Jersey: Size, season and geographical effects. *Environmental Res* 2009; 109:803-811.
8. Environment Canada. Mercury and the environment. <http://www.ec.gc.ca/mercury/en/index.cfm>; 2004.
9. Clarkson TW, Magos, L. The toxicology of mercury and its chemical compounds. *Critical Rev Toxicol* 2006; 36(8):609-662.
10. Goldman LR and Shannon MW. Technical Report: Mercury in the Environment: Implications for Pediatricians. *Pediatrics* 2001; 108:197-205.
11. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for mercury. US Department of Health and Human Services, Public Health Service; 1999.
12. Honda S, Hylander L, Sakamoto M. Recent advances in evaluation of health effects on mercury with special reference to methylmercury: A mini review. *Environ Hlth Prev Med* 2006; 11(4):171-176.
13. United States Environmental Protection Agency (EPA). Mercury. <http://www.epa.gov/mercury>; 2006.
14. Grandjean P, Weihe P, White R, Debes F, Araki S, Yokoyama K, Murata K, Sorensen N, Dahl R, Jorgensen P. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicol Teratol* 1997; 19(6):417-428.
15. Center for Food Safety and Applied Nutrition (CFSAN). United States Food and Drug Administration. What you need to know about mercury in fish and shellfish. <http://www.cfsan.fda.gov/~dms/admeHg3.html>; 2004.
16. Shea, KM, Perry KL, Shah M. Health effects of methylmercury. In: Physicians for Social Responsibility publication. Washington, DC: Physicians for Social Responsibility; 2004.
17. McCurry J. Japan remembers Minamata. *Lancet*, 2006; 367(9505):99-100.
18. Sakamoto M, Kubota M, Liu XJ, Murata K, Nakai K, Satoh H. Maternal and fetal mercury and n-3 polyunsaturated fatty acids as a risk and benefit of fish consumption to fetus. *Environ Sci Technol* 2004; 38(14):3860-3863.
19. Senkowsky S. Fear of fish: The contaminant controversy. *Bioscience*, 2004; 54(11):986-988.
20. Center for Food Safety and Applied Nutrition (CFSAN), United States Food and Drug Administration. Mercury levels in commercial fish and shellfish. <http://www.cfsan.fda.gov/~frf/sea-mehg.html>; 2006.
21. Environmental Protection Agency (EPA): Integrated Risk Information System (IRIS). <http://www.epa.gov/iris/index.html>; 2012.

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