A Review of Mercury in Seafood: special focus on tuna

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Abstract

Mercury is a toxic heavy metal released into the environment from both natural and anthropogenic sources. It is of great interest to consumers as to whether it can cause neurological effects at low dose levels. The effects of organic mercury exposure at high levels have been demonstrated in several large-scale poisonings, particularly those in Japan and Iraq in the 1950s, '60s and '70s. These epidemics showed that organic mercury, in sufficient concentrations, is a potent neurotoxin that is especially harmful to the developing nervous system. Since the most common form of human exposure to organic mercury is through fish consumption, several epidemiological studies have examined the relationship between maternal fish intake and health effects in humans, especially the fetus.

Levels of mercury in fish vary depending on factors such as: trophic level in the food chain, size, and habitat location. For this reason, it is important to gather information on mercury levels in different types of fish in various parts of the world. Results of recent studies have caused the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) to issue new advisories on the fish consumption for pregnant women and young children. However, there is concern that other individuals will significantly reduce their fish consumption also, thereby decreasing the potential health benefits of seafood. This review is meant to promote understanding of current issues regarding mercury in seafood and provides a compilation of up to date information on the following topics: background information on mercury; large scale mercury poisonings; epidemiology studies and risk assessment; and studies on mercury in tuna in different geographical locations.

Background Information on Mercury

Mercury is a heavy metal with an atomic weight of 200.59 g/mole and a boiling point of 356.6°C. It was originally called quicksilver by Aristotle *circa* 350 B.C. (Hunter, 1975) because it is a dense, silvery-white liquid at room temperature. Mercury exists in three oxidation states: Hg^0 (metallic or elemental), Hg^+ (mercurous), and Hg^{++} (mercuric). In the mercuric state, it can bind to elements such as chlorine, sulfur, and oxygen to form inorganic compounds, or it can bind to 1-2 carbon atoms to form organic mercury. Mercury bound to a single methyl group is called methylmercury ($MeHg^+$ or CH_3Hg^+), mercury bound to two carbons is called dimethylmercury (DMHg or $(CH_3)_2Hg$), and mercury bound to an ethyl group is termed ethylmercury ($EtHg^+$ or $CH_3CH_2Hg^+$). It was formerly thought that organic mercury existed in fish and human bodies in the form of MeHg+ or MeHgCl, but a recent study has reported that methylmercury present in fish is bound to cysteine, not chlorine (Harris et al., 2003). It was theorized that methylmercury does not bind to chlorine until it reaches the human stomach, where acidic conditions provide for many free Cl- ions. MeHgCl has very low water solubility compared to other forms of organic and inorganic mercury (NRC., 2000),

allowing it to cross membranes, such as the blood-brain and placental barriers, more rapidly .

Mercury is distributed throughout the world, and cycles naturally through the earth's crust, atmosphere, oceans, and life forms, with trace amounts in fish, plants, and animals. It can be found in natural deposits, such as the mercury bed under the Mediterranean Sea, which holds some of the richest reserves of mercury in the world (Bacci, 1989). The main ore of mercury is the red sulphide cinnabar (HgS), which has been mined throughout the world in places such as: Spain, Italy, Yugoslavia, Russia, China, Japan, Mexico, California, and British Columbia (Hunter, 1975). Mercury is naturally emitted into the air as a result of off-gassing from the earth's surface and from volcanoes. Mercuric vapor can remain in the atmosphere for significant amounts of time and travel long distances before it cycles back to the earth in rainwater.

Human activity increases the amount of mercury emitted into water, air, and soil, through coal-combustion (used to power utility plants); mining; waste disposal; preparation of fungicide seed dressings in agriculture; and chlor/alkali plants (BNS., 1999; WHO., 2000). Mercury is used in products such as batteries, vapor discharge lamps, fluorescent bulbs, switches, and thermometers. Many of these products end up in landfills or incinerators. Dental amalgams also contain mercury and are the major source of human exposure to elemental mercury (NRC., 2000). Although mercury and mercury compounds are hazardous air pollutants according to the Clean Air Act, mercury continues to be a valuable compound for industry. It has several unique properties, such as the ability to: conduct electricity, form alloys with almost all other metals, act as a biocide, and measure temperature.

Mercury enters the food chain with the help of aquatic microorganisms. Released into the environment in inorganic form, mercury is methylated by bacteria in water and converted to an organic form, usually methylmercury. Organic mercury compounds are generally more hydrophobic, readily bind proteins, and are neurotoxic (Costa, 1988; NRC., 2000). Organic mercury bioaccumulates in aquatic organisms as it works its way up the trophic levels of the food chain. Although humans can come into contact with mercury through contaminated food, drink, or air, exposure to organic mercury is almost exclusively a result of consumption of fish and shellfish (Gunderson, 1995; NRC., 2000). Storelli et al. (2002) estimated that fish consumption accounts for 80-90% of the total exposure to mercury, of which 75 to 100% is methylmercury. Also, blood mercury concentrations were reported to be directly related to the amount of fish consumed (Mahaffey et al., 2004).

Mercury Poisoning Outbreaks

The health effects of mercury poisoning vary depending on the form of mercury and means of exposure; however, both organic and inorganic, acute and chronic exposure can cause severe, irreversible effects. Inorganic mercury poisoning was recorded as early as 415 B.C., in Almaden, Spain, when the Romans noticed it in slaves who worked to recover mercury from cinnabar mines (Hunter, 1975). Over centuries, its toxic properties have been observed in those whose professions involve working with mercury, such as: mirror manufacturers, felt hatters, amalgam platers, and goldsmiths. The first documented use of organic mercury in chemical research was in 1863, and there were reported incidents of illness and death within several years (Hunter, 1975).

Perhaps the most harmful mercury poisoning outbreak occurred in the 1950s along Minamata Bay on the island of Kyushu, Japan (Eto, 2000; Harada, 1995). A chemical factory in the area was producing chemical fertilizers, synthetic resins, plasticizers and industrial chemicals, and had subsequently been disposing a high volume of unregulated chemical waste into the water. Mercury was being used as a catalyst in the production of acetaldehyde and the resulting mercury waste accumulated in the local fish and shellfish population, which was heavily consumed by the people of Kyushu. Early on, people began to notice strange phenomena in the local animal populations: fish rotated continuously and floated belly-up, shellfish opened and decomposed, birds fell while in mid-flight, and a large number of cats suffered abnormal deaths. Many people living in the area also suffered from symptoms such as: dysarthria (mispronunciation of words generally as a result of nerve damage), ataxia (inability to coordinate muscle movements and staggering gait), and sensory, auditory, and visual disturbances (Harada, 1995). The epidemic became known as Minamata disease. By 1959, mercury was determined to be the cause, partly because of examinations of deceased cats and the brains of late Minamata disease patients. Mercury levels in human organs were also found to be extremely high, ranging from 2.6-24.8 ppm in the brain, 22.0-70.5 ppm in the liver, and 21.2-140.0 ppm in the kidneys. Human autopsies revealed notable damage to the central nervous system, mostly in the form of severe lesions in the cerebral cortex and in the granular cell layers of the cerebellar cortex (Eto and Takeuchi, 1978). Hair-mercury levels in victims of Minamata disease reached concentrations as high as 705 ppm, over 50 times the recommended limits of 10-20 ppm for mercury in the hair of pregnant women, women of child-bearing age and young children (Cox et al., 1989; JECFA., 2003). Marine life in the bay was reported to have mercury levels ranging from 5.61 to 35.7 ppm (Harada, 1995), well above the currently established action level of 1.0 ppm for mercury in edible portions of fish (FDA., 2000). Sludge near the plant's drainage channel was reported to have mercury concentrations reaching 2010 ppm.

A number of children born to mothers living in Kyushu were affected by Fetal Minamata disease. In most cases, those who suffered from the disease had cord blood mercury concentrations above 1 ppm (approximately 20 times the benchmark dose level determined by the EPA (EPA., 2001)), and hair-mercury levels ranged from 5.25-110 ppm (Harada, 1995). Fetuses proved to be much more sensitive to mercury exposure than adults; mothers who were slightly affected gave birth to children with severe problems (Watanabe and Satoh, 1996). In addition to the symptoms listed above for Minamata disease, the children exhibited problems with suckling and swallowing, abnormal reflexes, and, in some cases, mental retardation (Wooltorton, 2002). The chemical plant's waste disposal system remained unregulated until 1965, when a second outbreak of Minamata disease occurred in Niigata, and the plant was finally forced to install a circulatory waste water system. As of 1995, there had been 2252 reported cases of Minamata disease (Harada, 1995).

There have been 3 reported outbreaks of methylmercury poisoning in Iraq as a result of consumption of wheat seeds coated with alkylmercury fungicide. The first outbreak occurred in 1955-56, followed by another in 1959-60. The largest, however, was in 1971-72 (Bakir et al., 1980; WHO., 1990), when people used the mercury-coated seeds, meant solely for planting, to make homemade bread. Overall, there were 6530 cases and 459 deaths from organic mercury poisoning (Watanabe and Satoh, 1996).

Epidemiology Studies and Risk Assessment

Although there is strong evidence that high concentrations of mercury are toxic, there is debate about the neurological effects of chronic exposure to low levels. This concern is especially true for pregnant women, the fetus and young children exposed to organic mercury. Since the most common form of human exposure to organic mercury is from fish consumption (Gunderson, 1995), numerous studies have been conducted to: (a) measure the mercury levels in women of child-bearing age and research health effects experienced by children born to women with elevated mercury levels and/or high-fish diets, (b) establish safe limits for consumption of fish with medium to high levels of mercury, and (c) determine the mercury content of different types of fish in various parts of the world.

Epidemiology Studies

Several epidemiology studies on the effects of chronic, low-level methylmercury intake through fish consumption on pregnant women and women of childbearing age have been published. The most notable are the Faroe Islands study, the Seychelles Child Development Study, a New Zealand study, a study from the Brazilian Amazon Basin, and the 1999-2000 National Health and Nutrition Examination Survey (NHANES) in the United States. Most epidemiology studies assess mercury exposure by measuring hair and/or blood mercury concentration. According to the World Health Organization (WHO), harmful effects could occur when mercury blood levels are over 200 μg/L in adults, or over 40-50 μg/L in pregnant women (WHO., 2000). The safety limit for mercury in hair is approximately 10 to 14 ppm (Cox et al., 1989; JECFA., 2003).

The Faroe Islands and Seychelles Islands studies have frequently been compared, because, although they were similar they reported conflicting results. The studies were both conducted in the 1990s in populations consuming high amounts of fish or marine mammals, but brain function studies on children born to women with high mercury levels showed adverse effects in the Faroese (Grandjean et al., 1997) and no significant effect among the Seychellois (Davidson et al., 1998; Myers et al., 1997).

The Faroe Islands are located between the Norwegian Sea and the North Atlantic Ocean. The Faroese, descendents of Viking settlers, consume significant amounts of fish and pilot whale meat, which can be very high in mercury (up to 150 ppm in edible tissues) (Juhlshamn et al., 1987) and other contaminants. In the study, Grandjean and colleagues evaluated 917 seven-year-olds in 20 different domain-specific intellectual tests and compared test scores with concentrations of mercury in the umbilical cords of test subjects (Grandjean et al., 1997). Hair-mercury levels of the mothers during pregnancy were also recorded, but the researchers relied primarily on cord mercury concentration. Fifteen percent of mothers had hair-mercury concentrations above 10 ppm and cord blood levels of mercury averaged 22.9 μg/L. Women who drank occasionally while pregnant had slightly lower cord blood concentrations of mercury. Children with higher cord levels of mercury scored lower on 8 of the 20 tests. Some of the areas in which they showed poorer performance were vocabulary, learning, and memory. Researchers found cord-blood samples to be much better risk predictors than hair-mercury samples taken from children at ages 1 and 7. A follow-up study on 878 of the children at age 14 showed that the children with higher mercury concentrations

experienced irreversible delays in transmission of electrical signals in the auditory brainstem (Murata et al., 2004) and slight problems controlling blood pressure (Grandjean et al., 2004).

The Republic of Seychelles is an archipelago in the Indian Ocean whose inhabitants, a mix of French, Africans, Indians, Chinese, and Arabians, consume, on average, 12 servings of fish/wk (Myers et al., 2003). In the Seychelles Child Development study, the researchers performed neuropsychological evaluations on over 700 infants at 6.5, 19, and 29 months, and then again at 5.5 years of age (Myers et al., 1997). They studied the relationship between the subjects' performances on global tests for general intelligence and the levels of total mercury in hair of the mothers during pregnancy. The range of total mercury concentration in maternal hair was 0.5-26.7 ppm, with a mean of 6.8 ppm and a median of 5.8 ppm (Myers et al., 1997). The mean total mercury concentration in the hair of the children at 5.5 years of age was 6.5 ppm, with a range of 0.9 – 25.8 ppm. Although some children born to mothers with high mercury levels did do poorly on several tests, statistical tests ruled out the ability to state any relationships between exposure to mercury and neurological damage. As an additional part of the study, 350 samples of various species of fish typically caught and consumed in the Seychelles were tested for total mercury (Davidson, et al., 1998). These fish had total mercury concentrations in the range of 0.004 to 0.75 ppm, with most of the medians ranging from 0.05 to 0.25 ppm. The researchers theorized that the differences in the results of the Seychelles study and the Faroe Islands study were due, in part, to the source of mercury exposure -- the Seychellois eat ocean fish with low to medium levels of mercury, and a major part of the Faroese diet is pilot whale meat, shown to be heavily contaminated with mercury. Differences in study design, biomarkers, neuropsychological tests and prenatal exposure to PCBs may also have contributed to the differences between the two studies.

In 1998 the National Academy of Sciences (NAS) held a peer review panel to determine the reasons for the conflicting results of the Seychelles and Faroe Island studies (Jacobson, 2001). The main differences between the studies were: the Faroese study used the umbilical cord to test for mercury concentration while the Seychellois survey used maternal hair; the Faroese study used domain-specific tests and the Seychellois study used globally-accepted tests, which may have been too global and not sensitive enough to the region; the Faroese children were evaluated at age 7 and the Seychellois at age 5.5 (a less sensitive age for neuropsychological tests). Also, the Faroese eat whale meat, which can significantly raise the concentration of mercury in the body in a short amount of time. This could be more shocking to the fetus than chronic consumption of fish with lower levels of mercury. Additionally, due to atmospheric and oceanic currents, the Faroese are heavily exposed to polychlorinated biphenyls (PCBs) while the Seychellois experience minimal exposure. Taking this into consideration, some of the NAS workshop members theorized that prenatal exposure to PCBs could increase the neurotoxic effect of methylmercury; however statistical analyses indicated otherwise (Rice et al., 2003). After taking the above differences into account, NAS determined that the study from the Faroe Islands fulfilled the most criteria for use of an epidemiology study in risk assessment (Jacobson, 2001).

In a similar study from New Zealand, researchers compared mercury levels in prenatal maternal hair samples to scholastic and psychological test performances of 237

children ages 6-7 (Crump et al., 1998). The original findings did not show significant correlations. However, when one outlier was omitted whose mother's hair mercury level was 86 ppm (over 8 times the recommended safety threshold), there was a significant association between lower test scores and higher mercury intakes in 6 of 26 administered tests. Children whose mothers had hair-mercury concentrations above 6 ppm had a higher tendency for abnormal test results.

Another study took place in several towns downstream from informal gold mining operations in the Brazilian Amazon Basin (Grandjean et al., 1999). Informal gold mining in the Amazon Basin involves the use of elemental mercury to capture gold particles as amalgam. As a result, mercury is released into the river and accumulates in organic form in piscivorous fish (Malm, 1998). In a study of 351 children living in towns downstream from the mining, Grandjean and colleagues (1999) examined the relationship between children's hair-mercury concentrations and performances on neuropsychological tests. The average hair-mercury concentration in the children was 11.0 ppm and the median was 12.8 ppm. The researchers found that children with higher hair-mercury concentrations did poorer on tests involving motor function, attention, and visuospatial performance.

Assessment of Safe Exposures to Methylmercury in Fish

Estimating safe levels of methylmercury intake from eating fish is highly controversial. This is because some population groups are much more sensitive to methylmercury than others; the types, amounts, and frequency of seafood consumed vary widely; mercury concentration of species differs greatly; and there is disagreement about the reliability, variability, and interpretations of existing data. Further, the methods used to establish a level of safety or risk of adverse effects differ among groups charged with estimating risk. All agree, however, that pregnant women and young children are the most sensitive groups, methylmercury is neurotoxic, and seafood is the primary dietary source. Moreover, all recognize the many health benefits associated with seafood consumption, especially during pregnancy and early life.

Although trace amounts of organic mercury may be obtained from antiseptics, fungicides and antibacterial agents, fish consumption is the primary source of exposure (Storelli et al., 2002). Exposure increases with the frequency and amount of fish consumed, as well as the concentration of methylmercury in the species. Therefore, the FDA advises limits on the amount, frequency, and species of fish consumed by pregnant women and young children.

US Environmental Protection Agency (EPA) Approach: The EPA established a reference dose (RfD) level for methylmercury exposure, mainly from food, that is related to a "benchmark" concentration of mercury in cord blood deemed without appreciable risk. EPA determined its benchmark as "the lower 95% confidence interval on an estimated dose that doubles the prevalence of children with test scores deemed subnormal" (Mahaffey et al., 2004). The value was statistically determined from the findings in the Faroe Islands study, one of three large epidemiological studies reporting neurodevelopmental outcomes in relation to methylmercury exposure. This benchmark concentration was 58 ppb. To this value EPA applied an uncertainty factor of 10 for a final benchmark blood concentration of 5.8 ppb. The uncertainty factor was designed to

account for individual variation, uncertainty associated with food recall methodology, variability of methylmercury concentration within and between species, and other sources of uncertainty. EPA's approach, and the uncertainty factor it used, was endorsed by the National Academy of Sciences (NAS) (NRC., 2000).

For practical purposes, one needs to know how much methylmercury can safely be consumed so that blood levels do not exceed the benchmark level. EPA defined the RfD as the daily exposure to the human population that is likely to be without appreciable risk of deleterious effects during a lifetime (EPA., 2002). The principle of an RfD for establishing safe exposures to hazardous substances is well accepted in toxicology. EPA calculated the reference dose for methylmercury to be 0.1 μg/kg body wt/day.

More recently, EPA suggested adding additional safety factors to the RfD based on the differences in the concentration of methylmercury in cord and maternal blood. Stern estimated a ratio of cord to maternal blood mercury of 1.7:1.0 (Stern and Smith, 2003), whereas EPA's RfD was based on a ratio of 1:1 (Rice et al., 2003). If differences in blood hemoglobin between maternal and cord blood are also included, the estimate for the benchmark blood concentration falls from 5.8 ppb to about 3.5 ppb. With more stringent assumptions EPA's estimate of the percent of women potentially at risk of exceeding the RfD increases from 7.8% to 15.7%, based on values from the 1999-2000 NHANES data.

Some have criticized EPA's reference dose as unjustifiably conservative, while others hailed it for its caution. Critics have pointed to the use of only one study, the Faroe Islands study, with no consideration given to the lack of statistically significant detrimental effects from the Seychelles study. The latter study reported no association between methylmercury exposure and developmental outcomes from an average consumption of 12 fish meals/week. It was excluded because one cannot estimate a benchmark dose where there are no adverse outcomes. However, such reasoning does not negate the findings from the Seychelles. Another criticism is the selection of the lower 95% confidence level as the mark below which psychological test responses were considered adverse. This is not standard for tests of learning or intelligence. Doubling the percentage of children with abnormal scores was defined as indicative of an adverse effect. The high uncertainty factor of 10 used by EPA is substantially greater than uncertainty factors used by other organizations. For example, WHO used a safety factor of 6.4 to its estimate of a steady-state exposure to methylmercury deemed without adverse effect (JECFA., 2003).

On the other hand, Grandjean suggested that EPA's benchmark dose overestimates the amount of methylmercury that poses a neurodevelopmental risk to developing infants (Grandjean, 2004). Based on reassessment of the imprecision associated with assessing methylmercury exposure, Grandjean testified that the benchmark dose used by EPA may be overestimated by a factor of two. Further, the conversion of hair mercury content to blood levels may be more accurately estimated using a factor of 360 instead of 250 (Budtz-Jorgensen et al., 2004). If taken into consideration, these adjustments could possibly reduce the RfD to the point where high numbers of women would be considered to have risky blood mercury levels.

EPA has used its BMDL and the NHANES data to estimate the number of infants who may have been at increased risk of adverse neurodevelopmental effects from

exposure to methylmercury *in utero* (Mahaffey et al., 2004). Currently, the EPA suggests that over 600,000 may have may have exceeded its recommended reference dose (Grandjean, 2004). These numbers are derived from the 1999-2000 NHANES blood mercury and food consumption data in which blood mercury levels were attributed to consumption of fish and shellfish, and 7.8% or 81 women aged 16-49 yr had blood methylmercury levels of 5.8 μg/L or higher. However, of these 81 women, dietary records revealed that 38% did not eat fish in the past 30 days and another 38% ate fish or shellfish 1-5 times in the same period. Only 8 reported consuming fish 10 or more times in the previous 30 days (an average of 2.3 times/wk). Additionally, although mercury has a half-life in the blood of about 44 days (Wooltorton, 2002), the study did not account for dietary fish intake beyond a 30 day time period. These observations cast considerable doubt on the likelihood that fish consumption was the main reason for the blood mercury levels reported in the NHANES data.

US Food and Drug Administration: FDA is concerned about potentially hazardous levels of methylmercury in seafood consumed in the U.S., and advises the most vulnerable groups to limit their intake of the more contaminated species. FDA uses risk assessment tools to prepare consumer advisories about mercury in fish applicable throughout the country. It specifically targets women who might become pregnant, those who are pregnant, nursing mothers, and young children. In developing its consumer advisories, FDA considered the patterns of seafood intake in the U.S., the top species consumed, and the frequency of fish consumption. Based on seafood consumption data from 1999-2000 NHANES survey and blood and hair mercury levels, FDA used a probabilistic approach to estimate the quantities of fish of high, medium, or low methylmercury content that could safely be consumed by 99% of women without exceeding EPA's reference level of 0.1 μg/kg/day. It advised pregnant and nursing women and young children to avoid eating the four leading fish species having average mercury levels close to or exceeding 1.0 ppm in the tissue (swordfish, shark, king mackerel, and tilefish) (Table 1). The final advisory, issued jointly with EPA in 2004, recommended eating up to 12 oz/week of fish low in mercury, and restricting consumption of albacore tuna (*Thunnus alalunga*) to 6 ounces as part of the 12 total ounces of fish permitted per week (FDA., 2004a).

Table 1. Mercury levels in commercial fish according to the FDA (FDA., 2004b). For a more thorough listing of mercury levels in fish, see http://www.cfsan.fda.gov/~frf/sea-mehg.html.

High range (ppm Hg)	Mid-range (ppm Hg)	Low-Range (ppm Hg)
King Mackerel (0.73)	Snapper (0.19)	Salmon (Fresh/Frozen) (0.01)
Swordfish (0.97)	Halibut (0.26)	Trout (Freshwater) (0.03)
Shark (0.99)	Bass (Saltwater) (0.27)	Anchovies (0.04)
Tilefish (Gulf of Mexico) (1.45)	Lobster (Northern/American) (0.31)	Atlantic Mackerel (0.05)
	Tuna (Canned Albacore) (0.35)	Hake (0.1)

Tuna (Fresh/Frozen) (0.38)	Cod (0.11)
Grouper (0.55)	Tuna (Canned, Light) (0.12)

FDA's approach has been criticized for being too lenient, especially in regard to tuna, for putting an upper limit on the consumption of seafood species low in methylmercury, and for mentioning only a few species. FDA established an action level for methylmercury in commercial fish of 1.0 ppm (FDA., 2000). Fish having mercury concentrations higher than this may not be sold in the U.S. This level is twice that established by WHO and the Canadian Food Inspection Agency (CFIA) (0.5 ppm), although the latter allow exemptions for large pelagic fish, which are the ones likely to exceed 0.5 ppm (CFIA., 2002). Exemptions permit trade in these species and occasional but infrequent consumption.

Agency for Toxic Substances and Disease Registry (ATSDR): ATSDR evaluated the same scientific literature used by EPA and estimated a minimum risk level (MRL) for methylmercury of 0.3 µg/kg body wt/day (ASTDR., 1999). The MRL is the level considered "safe" for all potentially exposed populations for a specified duration; it is not a threshold for adverse effects. MRLs are useful for public health screening for potential overexposure. Note that the agency's MRL is three times EPA's reference dose. Although the definitions of MRL and RfD differ, they are similar in concept.

World Health Organization: In 2003, WHO revised its recommendation on methylmercury based on the report of its expert committee on food additives (JECFA). JECFA recommended that the Provisional Tolerable Weekly Intake for methylmercury be reduced from 3.3 to 1.6 µg/kg body weight/wk in order to sufficiently protect the developing fetus (JECFA., 2003). Expressed on a daily basis, this is equivalent to 0.2 µg/kg body wt, or twice the level recommended by EPA.

JECFA used the average of the Seychelles and Faroe Is. studies to estimate maternal hair concentrations associated with no observed effect level/benchmark dose level (NOEL/BMDL) for neurotoxicity associated with *in utero* exposure (15.3 and 12 ppm maternal hair, respectively). They arrived at a composite of 14 ppm maternal hair as a level that would be without appreciable adverse effects.

To estimate the steady state ingestion of MeHg from maternal hair concentration requires conversion of concentrations in hair to blood and blood to diet. JECFA used a hair:blood ratio of 250 (range 140-370) and arrived at a blood level of 0.056 mg/L (14/250). They calculated a steady-state daily intake of 1.5 µg/kg body wt/day that would yield this blood level of NOEL.

JECFA used an adjustment factor of 2 to account for the inter-individual variability in the ratio of hair:blood MeHg (range 1.5-2.3). To adjust for inter-individual pharmacokinetic variability, they used a combined uncertainty factor of 3.2 when converting maternal blood concentration to dietary intake. Thus, a total factor of 6.4 [1.5 x (2x3.2)] was applied to the NOEL level to derive the Provisional Total Weekly Intake of 1.6 µg/kg body wt/wk (1.5/6.4 x 7days=1.64) or 0.2 µg/kg body wt/day.

The JECFA approach started with an exposure level associated with no observed effect derived from both the Faroe Islands and Seychelles studies, in contrast to the

benchmark dose selected by EPA from the Faroe Islands study. They also used a more modest uncertainty factor than EPA, 6.4 compared with 10. As a result, these experts estimated a consumption level for methylmercury about half the level previously suggested, yet considerably less restricted than that of EPA.

Canada: In 1998, Canada's health agency lowered its maximum daily exposure for methylmercury by 57% from 0.47 to 0.2 µg/kg body weight/day (Dabeka et al., 2004; Health Protection Branch, Bureau of Chemical Safety, Canada. 1998. Review of the Tolerable Daily Intake for Methylmercury. Ottawa: Health Canada.). The revised level is described as 95% below the level that may cause health effects (Jones, 1999). This is the same level set by WHO and it was derived using data from both the Faroe Islands and Seychelles studies. As of 2002, the CFIA's limit for total mercury in fish was 0.5 ppm (CFIA., 2002). The CFIA advises no more than one meal per week of swordfish, shark, or fresh/frozen tuna and no more than one meal per month for young children and women of child-bearing age.

Germany: The German Commission on Human Biomonitoring developed reference values for concentrations of methylmercury in blood and hair that amount to safe upper limits (Kommission, 1999)(Kommission "Human-Biomonitoring" des Umweltbundesamtes. 1999. Stoffmonographie Quecksilber--Referenz-und-Human-Biomonitoring-Werte (HBM). Berlin: Kommission "Human-Biomonitoring" des Umweltbundesamtes.). The commission considered findings from both the Seychelles and Faroe Islands studies. Maternal blood mercury levels $\geq$ 15 µg/L or hair mercury of 4-5 ppm are considered indicative of a child's risk of adverse events. They are considered grounds for additional investigation and intervention. Maternal blood mercury levels in excess of 5 µg/L or hair levels of 1.5 ppm are basis for determining whether the woman consumes fish known to have high mercury concentrations or uses medicines containing organic mercury.

United Kingdom: The Food Standards Agency's (FSA) Scientific Advisory Committee on Nutrition recently revised its recommendations for the intake of methylmercury for pregnant women or those who might become pregnant within a year to 1.6 µg/kg body wt/week, which is equivalent to a daily intake of 0.2 µg/kg body wt. For nursing women, however, the committee considered that its previous guideline of 3.3 µg/kg body wt/week (0.5 µg/kg body wt/day) remained appropriate because intakes reaching the breast-fed infant would not exceed 0.2 µg/kg body wt/day (FSA., 2004). These values are consistent with those set by WHO and Canada. In 2004, FSA recommended that pregnant and nursing women should limit their consumption of tuna to no more than 4 medium-sized cans (drained weight around 140 g/can) or two fresh tuna steaks per week (FSA., 2004). Additionally, the agency recommended that pregnant and nursing women, along with young children, avoid eating shark, swordfish, and marlin due to their high mercury levels.

To date, there is no evidence of harm to infants from current seafood consumption levels in the U.S., which are notably low by world standards. A recent study from the U.K. that examined fish intakes of pregnant women and developmental outcomes in infants at one year of age in relation to mercury exposure reported improved outcomes

with maternal fish consumption of 1-3 times/week with no association with umbilical mercury levels (Daniels et al., 2004). Based on EPA's RfD, it is difficult to reconcile the lack of adverse effects in the children of mothers consuming 10-14 meals of fish/week (Seychelles study), with the hypothetical risk that a small percentage of US women, most of whom consume far less fish than this amount, may be exposing their developing infants to risky levels of methylmercury from seafood. Firm evidence that women with blood mercury concentrations above EPA's reference dose were exposed to methylmercury from consuming seafood consumption is needed before accepting the estimates of hundreds of thousands of infants at risk of unsafe exposure to methylmercury.

Omega-3 Fatty Acids in Seafood: Finally, it should be noted that pregnant women require the omega-3 fatty acid docosahexaenoic acid (DHA), found almost exclusively in seafood, for optimum infant neurodevelopment (Carlson, 2001). Current levels of seafood consumption in the U.S. appear to fall short of meeting this need. Further, some evidence indicates that long-chain omega-3 fatty acids and selenium in seafood may protect against adverse neurodevelopmental outcomes. The key may reside in emphasizing the safe consumption of fish species with generous levels of long-chain omega-3 fatty acids and low levels of mercury.

Mercury Levels in Tuna Fish

Since mercury is known to bioaccumulate in the food chain, most research on mercury levels in fish has focused on large predatory fish such as shark, swordfish, and tuna. These studies have reported wide variations of mercury concentrations in fish from different geographical locations. Many studies found that methylmercury is a high percentage of total mercury in fish muscle and that mercury content in fish increases with fish weight. As discussed in the previous section, tuna has recently been added to several advisories that warn about consumption of fish with significant amounts of mercury. This has caused some anxiety in the marketplace, as tuna is one of the most widely consumed fish in several countries, including the U.S (Johnson, 2003). Furthermore, there are several commercial species of tuna, among which mercury content varies greatly. Part of the problem in past studies is that published results did not always distinguish among tuna species when reporting mercury levels. The following is a compilation of investigations on mercury in fresh/frozen and canned tuna fish. Although this part of the review will focus on mercury in tuna, there is a considerable amount of information available regarding mercury in other fish and seafood around the world (Knowles et al., 2003; Matthews, 1983; Storelli et al., 1998; Vlieg et al., 1993).

Fresh/Frozen Tuna Fish

This section summarizes the results of published studies on mercury content in several species of fresh/frozen tuna fish, including yellowfin (*Thunnus albacares*), bluefin (*Thunnus thynnus*), bigeye (*Thunnus obesesus*), blackfin (*Thunnus atlanticus*), skipjack (*Katsuwonus pelamis*), and albacore (see also Table 2). Studies are discussed in chronological order.

A study performed in 1975 on mercury content in predatory fish in the Andaman sea (west of Thailand, Indian Ocean) reported total mercury in 16 samples of yellowfin

tuna ranging from 0.026 to 0.234 ppm, and 8 samples of bigeye tuna (0.027-0.233 ppm) (Menasveta and Siriyong, 1977). The mean concentrations of total mercury in yellowfin and bluefin were 0.142 and 0.114, respectively. The researchers found a positive correlation between weight and mercury concentration; the correlation factor (R) was near 0.92 for both yellowfin and bigeye.

In a study published in 1983, a total of 100 yellowfin and 104 bigeye tuna were caught by long-line off the coast of Hawaii and analyzed for total mercury content (Boush and Thieleke, 1983). Muscle samples were taken from the caudal peduncle area and were cleaned of skin and bones. The average total mercury concentration in yellowfin was 0.22 ppm (range 0.09 – 0.39 ppm), and in bigeye it was 0.58 ppm (range 0.30 – 0.87 ppm). Yellowfin were slightly smaller, with an average weight of 45.8 kg (range 10 - 84.4 kg) compared to 57.1 kg (range of 21.3 - 101.6 kg) for bigeye. Positive correlations between fish weight and total mercury concentration were reported for both fish. The correlation coefficients were 0.540 and 0.557 for the yellowfin and bigeye, respectively. Using the slope of the regression line for fish weight vs. mercury concentration, the authors predicted that for every 10-pound (4.5 kg) weight increase in yellowfin or bigeye, the mercury concentration would rise by 0.02 ppm.

Another study published in 1983 reported mercury levels in the 12 most commonly consumed fish in the Seychelles Islands (Matthews, 1983). Matthews analyzed 5-6 samples of each fish, and found that several of the larger predatory species exceeded the FDA action limit of 1.0 ppm. Skipjack tuna ranged from 0.191 to 0.45 ppm and yellowfin from 0.086 – 0.368 ppm mercury. The weights of yellowfin ranged from 1.6 to 50.0 kg and the weights of skipjack ranged from 2.2 to 5.7 kg. The correlation coefficients for graphs of fish weight vs. mercury concentration were 0.753 for yellowfin tuna and 0.585 for the skipjack.

As part of a comprehensive study on the nutritional data in the muscle of pelagic fish in the South Pacific, total mercury and methylmercury concentrations in 6 different species of fish were measured (Vlieg et al., 1993). The fish were caught on long lines from May to July 1990. The researchers found methylmercury ranged between 75% and 86% of the total mercury concentration. The six albacore tuna samples tested had a mean total mercury concentration of 0.49 ppm, and the only two albacore measured for length were 95 and 97 cm (weights were not reported). The average methylmercury concentration in the albacore samples was 0.38 ppm, 78 % of the average total mercury content.

In 1993-94 a survey was conducted on the total mercury and methylmercury content in edible fish and invertebrates off the coast of the Azores Islands in the Atlantic Ocean (Andersen and Depledge, 1997). Methylmercury was, on average, 80% or more of the total mercury in the samples. Forty-six samples of albacore tuna had a mean total mercury concentration of 0.370 ppm, with a range of 0.218 - 1.132 ppm, and a mean methylmercury concentration of 0.341 ppm (range 0.201 - 1.046). Methylmercury was between 85.8 to 97.2 % of the total mercury. The albacore had forklengths ranging from 87 to 117 cm, with an average of 95.6 cm. The study also reported the average total mercury concentration in 53 samples of skipjack tuna to be 0.192 ppm (range 0.089 - 0.336 ppm). The skipjack had an average forklength of 49.7 cm, ranging from 28 to 84 cm. Eight out of ten species of fish analyzed for correlations between size and mercury

content showed significant relationships. The correlation coefficient for mercury concentration vs. forklength was 0.56 for albacore and 0.34 for skipjack.

As part of a study into possible correlations between mercury and selenium concentrations in fish, 3 samples each of 24 saltwater fish, 1 freshwater fish, and 14 shellfish purchased from a wholesaler in Modena, Italy were tested for total mercury (Plessi et al., 2001). All levels of total mercury reported for the fish and shellfish were within the European Union's safety limit, and bluefin tuna was reported to have an average total mercury concentration of 0.249 ppm.

Storelli and colleagues (2002) tested mercury and methylmercury levels in 127 albacore and 161 bluefin tuna fish in the Mediterranean Sea. The total mercury concentrations ranged from 0.84 to 1.45 ppm in albacore tuna (mean = 1.17 ppm) and 0.16-2.59 ppm in bluefin tuna (mean = 1.18 ppm). Some 78.6% of albacore and 61.1% of bluefin exceeded the European Commission Decision's maximum mercury level of 1.0 ppm for trophic fish. In both albacore and bluefin muscle, approximately 91% of the total mercury measured was present as methylmercury. The researchers also found high correlations between weight of fish and mercury content ($r = 0.77$ for albacore tuna and $r = 0.84$ for bluefin tuna).

Recently, Dabeka and colleagues (2004) published the results of their 2002 study in which they tested the total mercury concentrations in various fish purchased at Canadian retail stores. The stores were located in Halifax, Vancouver, and Toronto, but the origin of the fish was not provided. The total mercury concentrations in 13 samples of fresh/frozen tuna (unspecified) were similar to levels found by Storelli et al. (2002), ranging from 0.077 to 2.12 ppm with a mean of 0.93 ppm. Neither section of fish nor size of the fish was recorded, as only a 450 g portion of fish meat for each sample was purchased.

A study on fish imported into the United Kingdom reported an average total mercury concentration of 0.4 ppm (range 0.141 - 1.500 ppm) in 20 samples of fresh/frozen tuna (species not reported) (Knowles et al., 2003). One of the samples examined exceeded the 1.0 ppm European Commission safety threshold with a total mercury concentration of 1.5 ppm. The mercury content in canned tuna was about half of that in the fresh/frozen tuna. The 54 cans of tuna analyzed had an average total mercury concentration of 0.190 ppm and a range of 0.031 - 0.710 ppm.

A recent study reported mercury levels between 0.25 and 0.60 ppm in 20 individual albacore harvested in the Hawaiian commercial fishery (Brooks, 2004). Samples were taken from muscle tissue in the far caudal region and the fish ranged in size from 17-32 kg. Brooks (2004) reported no correlation between tuna weight and mercury concentration.

Total mercury levels were recently reported for tuna caught in Atlantic waters off Florida from Daytona Beach south to the Florida Keys (Adams, 2004). The fish were harvested between 1999 and 2002 and included blackfin tuna (*Thunnus atlanticus*) and yellowfin tuna. Samples were taken from the dorsal loin area above the lateral line and anterior to the origin of the first dorsal fin. Blackfin ($N = 37$) were reported to have a mean total mercury concentration of 0.94 ppm, with a range of 0.16 to 2.0 ppm, while yellowfin ($N = 56$) had a mean total mercury concentration of 0.25 ppm, ranging from 0.068 to 0.65 ppm. The blackfin had a mean forklength of 73.2 cm (range 45.2 – 86.0 cm), and yellowfin were slightly longer, with a mean forklength of 84.7 cm (range 60.2 –

134.0 cm). Exact weights were not reported, but through back calculations using a length-weight index the yellowfin were determined to range in weight from 3 to 50 kg, with the majority of the fish between 3 and 15 kg. Total mercury concentrations for both yellowfin and blackfin were positively correlated to size. The correlation coefficients were: 0.508 for a best fit curve between mercury concentration in yellowfin and forklength; 0.51 for a best fit curve between mercury concentration in yellowfin and weight; and 0.761 for a best fit line between the natural log of mercury concentration in blackfin and forklength. Interestingly, female yellowfin had significantly higher mercury concentrations than male yellowfin, with respective average concentrations of 0.30 ppm and 0.21 ppm; however, no significant difference was found between the sexes for blackfin.

Another study measured mercury levels in 91 samples of albacore tuna troll-caught off the US Pacific coast between Southern California and Northern Washington in the 2003 season (Morrissey et al., 2005). The average total mercury concentration in the fish muscle was relatively low, at 0.14 ppm, with a range of 0.027 – 0.26 ppm. The albacore were fairly small, ranging in weight from 3.14 to 11.62 kg, and the correlation between fish weight and total mercury concentration was $R^2 = 0.38$.

An interesting topic of debate is whether or not anthropogenic activity has caused increases in the mercury levels of fish. In a study conducted on yellowfin tuna caught off the coast of Hawaii (Kraepiel et al., 2003), researchers compared mercury levels of 105 yellowfin caught in 1998 to 100 samples caught in 1971 (Boush and Thieleke, 1983). In both studies, the samples were taken from just above the caudal peduncle. Kraepiel and colleagues proposed that the oceanic zone in which mercury is methylated would be the zone in which mercury levels rise in response to increased emissions. Taking environmental and global anthropogenic emissions of mercury into account, it was estimated that the methylmercury content in the surface waters inhabited by the yellowfin should have increased between 9 and 26% if mercury is methylated in the mixed layer or in the thermocline. However, mercury levels in the fish showed no increase over the 27-year period; the average total mercury concentration in the 1998 set was 0.21 ppm while the 1971 set had an average of 0.22 ppm (Boush and Thieleke, 1983). One possible explanation given by the authors was that mercury methylation in the oceans takes place in the deep waters or in the sediments.

Table 2. Total mercury (Hg) and methylmercury (MeHg) levels in the muscle tissue of fresh/frozen tuna including the correlation factor (R) between weight of the fish and mercury concentration.

Fresh/ Frozen Fish Sample	N	Mean of Total Hg and Range (ppm)	Mean of MeHg and Range (ppm)	R for Weight/ Total Hg	Study
Bigeye	8	0.114 0.027 – 0.223	n/a	0.920	Andaman Sea (Thailand) (Menasveta and Siriyong, 1977)

Albacore	91	0.14 0.027 – 0.26	n/a	0.38	U.S. Pacific Coast (Morrissey et al., 2005)
Yellowfin	16	0.142 0.026 – 0.234	n/a	0.927	Andaman Sea (Thailand) (Menasveta and Siriyong, 1977)
Skipjack	53	0.192 0.089 – 0.336	0.179 0.083 – 0.320	0.34 for length/Hg	Azores Islands (Andersen and Depledge, 1997)
Yellowfin	105	0.210 0.012 – 0.68	n/a	n/a	Hawaii (Kraepiel et al., 2003)
Yellowfin	100	0.22 0.09 – 0.39	n/a	0.540	Hawaii (Boush and Thieleke, 1983)
Yellowfin	5	0.231 0.086 – 0.37	0.206 n/a	0.753	Seychelles (Matthews, 1983)
Bluefin	3	0.249 n/a	n/a	n/a	Italy (Plessi et al., 2001)
Yellowfin	56	0.25 0.068 – 0.65	n/a	0.51 for curve	Florida coast (Adams, 2004)
Albacore	20	n/a 0.25 – 0.6	n/a	n/a	Hawaii (Brooks, 2004)
Albacore	46	0.379 0.218 – 1.132	0.341 0.201 – 1.046	0.56 for length/Hg	Azores Islands (Andersen and Depledge, 1997)
Unspecified Tuna	20	0.401 0.141 – 1.500	n/a	n/a	United Kingdom imported fish (Knowles et al., 2003)
Albacore	6	0.49 n/a	0.38 n/a	n/a	New Zealand (Vlieg et al., 1993)
Bigeye	104	0.58 0.3 – 0.87	n/a	0.557	Andaman Sea (Thailand) (Boush and Thieleke, 1983)
Unspecified Tuna	13	0.929 0.077 – 2.121	n/a	n/a	Canada, unknown origin (Dabeka et al., 2004)

Blackfin	37	1.07 0.16 – 2.0	n/a	0.761 for ln Hg vs. forklength	Florida coast (Adams, 2004)
Albacore	127	1.17 0.84 – 1.45	1.06 0.80 – 1.37	0.77	Mediterranean (Storelli et al., 2002)
Bluefin	161	1.18 0.16 – 2.59	1.01 0.16 – 1.95	0.84	Mediterranean (Storelli et al., 2002)

Canned Tuna

Recently, there has been a major focus on determination of mercury in canned tuna. There are several problems inherent in these studies. For example, studies on canned tuna do not typically allow researchers to know the size of the fish nor the catch location, which can be key factors related to mercury in seafood. Although it is possible to find different species of tuna in cans, large tunas (e.g. bluefin, bigeye, and yellowfin), are typically sold as fresh steaks or sushi. Canned tuna usually contains two species: albacore or skipjack. Albacore is known as "white" tuna because albacore muscle turns a white-tan color when heat processed, while "light" tuna usually refers to skipjack, although other tunas may be included. The following are studies involving mercury content in canned tuna (see Table 3 for a summary).

A 1982 study on 26 canned samples of tuna reported the highest total mercury concentration in bluefin (max 0.55 ppm), followed by albacore (max 0.47 ppm), and yellowfin (max 0.42 ppm) (Cappon and Smith, 1982). Skipjack, which is typically the smallest in size of the tunas, averaged only 0.16 ppm total mercury (N=8). Methylmercury made up 57.4-94.7% of total mercury content in the samples. Among 8 samples of albacore, the average total mercury concentration was 0.27 ppm and methylmercury was 67.3-94.7% of total mercury. The average total mercury concentrations for bluefin (N=2) and yellowfin (N=8) were 0.50 ppm and 0.265 ppm, respectively. The researchers tested canned tuna up to 29 years old and observed no influence of sample age on mercury content. Although they found higher mercury levels in the water-packed tuna as opposed to the oil-packed, they did not have a large enough sample size for statistical analysis.

In a 1983 study, 5 varieties of canned fish sold in Port Moresby, Papua New Guinea, were examined for total mercury and methylmercury content (Kyle and Ghani, 1983). The average concentration of total mercury in 38 samples of canned tuna (unspecified) was 0.45 ppm. The canned tuna analyzed ranged in mercury concentration from 0.13 to 1.01 ppm, and 13 of the cans exceeded the WHO recommended maximum of 0.5 ppm mercury in seafood.

In 1991 the FDA undertook a study on methylmercury content in 220 samples of various types of canned tuna (Yess, 1993). None of the samples exceeded the FDA action level of 1.0 ppm. Methylmercury concentration ranged from 0.1 - 0.75 ppm, with a mean of 0.17 ppm. The highest levels of methylmercury in canned tuna were observed in chunk white (0.31 ppm), followed by solid white (0.26 ppm), and chunk light (0.11 ppm). Total mercury concentrations were not reported.

In addition to testing mercury in fresh/frozen tuna, the Dabeka et al. study mentioned in the previous section also reported total mercury concentrations in canned tuna fish (Dabeka et al., 2004). The researchers reported an overall mean total mercury concentration of 0.153 ppm (range 0.020 – 0.587 ppm) for 39 samples of canned tuna. Levels of total mercury in 7 samples of skipjack had a mean total mercury content of 0.090 ppm, ranging from 0.036 to 0.174 ppm; 11 samples of yellowfin tuna had a mean total mercury concentration of 0.085 ppm, with a range of 0.020 to 0.587 ppm; and 16 samples of albacore tuna ranged in total mercury from 0.193 to 0.384 ppm, with a mean of 0.260 ppm. Neither the origins nor the sizes of the tuna were provided, and, as mentioned in the previous section, samples were purchased from various retail stores in Halifax, Toronto, and Vancouver.

Recently, FDA compiled a summary of surveys conducted by itself and by National Marine Fisheries Services (NMFS) on mercury concentrations in fish from 1990 through 2002 and 2003 (FDA., 2004b). According to the data, the average mercury concentration of 131 samples of canned light tuna was 0.12 ppm, the average of 179 samples of canned albacore tuna was 0.35 ppm, and 131 samples of fresh/frozen unspecified tuna fillets/steaks had an average mercury concentration of 0.38 ppm. Measurements of total mercury and methylmercury were not reported separately, but rather all the results were combined.

In another study, 168 cans of tuna bought at a store in New Jersey between 1998 and 2003 were tested for mercury (Burger and Gochfeld, 2004). The researchers found that white canned tuna had an average total mercury concentration of 0.407 ppm and light canned tuna averaged 0.118 ppm total mercury. There was no difference in oil versus water packing methods.

One study (mentioned in the previous section) on the mercury levels in UK-imported fish reported that the mercury content in canned tuna was about half of that in the fresh/frozen tuna (Knowles et al., 2003). The 54 cans of tuna analyzed had an average total mercury concentration of 0.190 ppm and a range of 0.031 - 0.710 ppm. Neither origin nor species of the canned tuna was stated.

A recent survey from the Washington Department of Health tested mercury levels in 289 cans of white and light tuna purchased at retail stores throughout the state of Washington (VanDerslice et al., 2004). The researchers found that the mercury concentration in white tuna was, on average, higher than in light tuna, and tuna packed in oil had similar mercury concentrations as tuna packed in water. The mean mercury concentrations for the white and light tuna were 0.215 ppm and 0.057 ppm, respectively, and none of the samples exceeded the 1.0 ppm action level set by the FDA.

Scientists at Purdue University recently published the results of a study on the mercury content and fatty acid content in several species of canned fish (Shim et al., 2004). The canned fish were purchased in 2003 from several retail stores around Lafayette, Indiana (origin of fish was not specified). In the analysis of the fish, the contents of two cans were combined to form composite samples, which were then tested for total mercury. An overall mean total mercury concentration of 0.188 ppm was reported for 240 samples of canned tuna. Light tuna in water was lower in mercury than white/albacore tuna in water (0.054 ppm vs. 0.227 ppm, respectively). There was no significant difference between the total mercury concentrations in white/albacore tuna packed in water, spring water (0.232 ppm), or soy oil (0.220 ppm). However,

white/albacore tuna pouches packed in water had a mean total mercury concentration of 0.330 ppm. Light tuna, on the other hand, showed significant differences in total mercury concentration depending on the type of packing material used. Light tuna in vegetable oil (0.183 ppm) had much higher mercury than light tuna in water (0.054 ppm), and light tuna in soy oil had a significantly higher mercury concentration (0.340 ppm) than both samples packed in vegetable oil and in water.

Table 3. Total mercury (Hg) and methylmercury (MeHg) levels in canned tuna. ND stands for nondetectable.

Canned Fish Sample	Sample Size	Mean of Total Hg and Range (ppm)	Mean of MeHg and Range (ppm)	Reference
Light	n/a	0.057 n/a	n/a	(VanDerslice et al., 2004)
Chunk light	106	n/a	0.10 n/a	(Yess, 1993)
Light	45	0.118 n/a	n/a	(Burger and Gochfeld, 2004)
Light	131	0.12 ND – 0.85	n/a	(FDA., 2004b)
Skipjack	8	0.162 0.066 – 237.9	0.115 0.062 – 0.178	(Cappon and Smith, 1982)
Light	144 cans, 72 composite samples	0.145 n/a	n/a	(Shim et al., 2004)
Unspecified tuna	54	0.190 0.031 – 0.710	n/a	(Knowles et al., 2003)
White	n/a	0.215 n/a	n/a	(VanDerslice et al., 2004)
Yellowfin	8	0.265 0.098 – 0.418	0.222 0.728 – 0.364	(Cappon and Smith, 1982)
Albacore	8	0.274 0.136 – 0.475	0.240 0.110 – 0.450	(Cappon and Smith, 1982)
Solid white	71	n/a	0.26 n/a	(Yess, 1993)
White/ albacore	96	0.309 n/a	n/a	(Shim et al., 2004)
Chunk white	19	n/a	0.31 n/a	(Yess, 1993)
Albacore	179	0.35 ND – 0.85	n/a	(FDA., 2004b)
White	123	0.407 n/a	n/a	(Burger and Gochfeld, 2004)

Bluefin	2	0.500 0.454 – 0.546	0.450 0.413 – 0.487	(Cappon and Smith, 1982)

Note: canned light tuna usually refers to skipjack, but other species, e.g. yellowfin can also be used. Canned white tuna only refers to albacore. The sample identification used was that stated in the referenced papers.

Conclusions and Summary

Mercury is typically released into the environment as a result of both anthropogenic and natural activities. Once it has entered aquatic ecosystems, mercury can be converted by microorganisms into its highly toxic organic form, methylmercury. Organic mercury is known to bioaccumulate through the aquatic food chain, resulting in higher concentrations in older, larger fish. Consumption of fish is the primary means by which humans are exposed to organic mercury (Gunderson, 1995; NRC., 2000). Organic mercury is toxic to the nervous system due to its ability to cross cell membranes and the blood-brain and placental barriers readily (WHO., 2000). Methylmercury has a half-life of 70-80 days in the brain (WHO., 2000) and 44-50 days in the bloodstream (NRC., 2000; Wooltorton, 2002).

The detrimental consequences of human exposure to high levels of mercury have been observed in several large-scale outbreaks, such as those in Minamata Bay, Japan, and in Iraq. These incidents showed the irreversible damage of organic mercury to the nervous system, with effects on speech, muscular, visual, and auditory functions. The developing nervous system was shown to be more susceptible to damage, as children born to mothers with minor symptoms of the disease suffered from severe birth defects (Watanabe and Satoh, 1996).

Investigations into pre- and post-natal exposure to mercury and resulting health effects have shown conflicting results. The Faroe Islands study reported that children with higher cord blood mercury concentrations scored lower on several intelligence tests (Grandjean et al., 1997), and a 14-year follow-up showed that the same children experienced irreversible delays in neuronal communication in the auditory brainstem (Murata et al., 2004) and complications with blood pressure control (Grandjean et al., 2004). However, the Seychelles investigation reported no significant correlations between pre-natal mercury exposure and intelligence test scores in children (Myers et al., 1997). Studies out of New Zealand and the Brazilian Amazon Basin have reported some correlations between hair-mercury levels and decreased test performance.

Regulatory organizations throughout the world have used epidemiology studies to determine proper safety thresholds for mercury intake. JECFA established a Provisional Tolerable Weekly Intake of 1.6 μg MeHg/kg body wt/wk (equivalent about 0.2 μg/kg body wt/day) (JECFA., 2003). In contrast, in the U.S., the EPA has determined an RfD of 0.1 μg/kg/day (EPA., 2001). The RfD set by the EPA has received criticism both for being overly cautious and for being too lenient. The FDA set an action level of 1.0 ppm for methylmercury in fish (FDA., 2000), and based on reported levels of Hg and MeHg in fish, the FDA and EPA released a joint advisory warning pregnant women and young children against the consumption of king mackerel, shark, tilefish, swordfish, and, more recently, suggested limits on their intake of albacore tuna of no more than 6 oz. per week (FDA., 2001).

Numerous studies around the world have measured mercury levels in fish. Several reported a direct correlation between mercury content and fish weight, with methylmercury comprising the majority of total mercury in fish. Interestingly, fish of the same species have been found to have significantly different levels of mercury. For example, although the mean mercury concentration in canned albacore tuna was reported by the FDA to be 0.35 ppm, data released by other studies have shown that the mean mercury concentration in albacore can vary widely, from as low as 0.14 ppm (Morrissey et al., 2005) to as high as 1.17 ppm (Storelli et al., 2002). Such differences probably reflect diversity in age, size, and source of the fish.

The potential health risk of methylmercury exposure to pregnant women and young children is a public concern. However, there is little if any evidence that current levels of methylmercury exposure in the U.S. are hazardous or have put infants and children at increased risk. Women of child-bearing age in particular need to be aware of the species most likely to contain the highest concentrations of mercury and limit if not avoid consuming these species, especially during pregnancy. Experts generally agree that the health benefits of fish consumption within the guidelines established by FDA and EPA far outweigh the potential risks (Kris-Etherton et al., 2002). Because of the importance of long-chain omega-3 fatty acids, especially DHA, in neurodevelopment, it is important that pregnant and nursing women include fish in their diets without fearing harmful effects for their infants.

Mercury concentrations vary with the species, age, and habitat of fish, increasing in larger pelagic species such as swordfish. Fish harvested locally may differ substantially in mercury from those obtained from distant sources. Special precautionary measures to reduce potential excess methylmercury exposure may be warranted for particular groups such as natives living in the Arctic and some immigrants who consume large amounts of seafood harvested themselves. Since the mercury concentrations in fish in many areas of the world are unknown, there is need for additional data to provide consumers and government regulators with accurate information upon which to base consumption guidelines.

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