MERCURY HEALTH TOOLKIT

Information to Identify, Reduce, and Prevent Mercury Toxicity in the Human Body

California Indian Environmental Alliance
Mercury Tribal Health Program
2013

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California Indian Environmental Alliance
526 Grand Ave.
Oakland, CA 94610

PO Box 2128
Berkeley, CA 94702
(510) 848-2043
www.cieaweb.org
info@cieaweb.org

California Indian CIEA
Environmental Alliance
PO BOX 2128, BERKELEY, CA. 94702 • (510) 848-2043 • www.cieaweb.org • info@cieaweb.org

March 5 2013,

Dear Health Care Provider,

We are happy to bring you the latest edition of our Mercury Health Toolkit.

This Toolkit, the accompanying "Eating Fish Safely" brochure and training were designed to assist you in identifying patients that may be at risk of exposure to methylmercury and to provide these patients with advice on how to continue to eat fish, while avoiding mercury toxins. Our hope is that the enclosed information will assist you in navigating the often contradictory studies and fish consumption guidelines, and provide resources for further study.

The California Indian Environmental Alliance (CIEA) was formed in 2006 to address mining contaminants in the state of California left over from the Gold Rush. This neurotoxin threatens the physical, cultural and spiritual health of California Indian communities. Native Americans have been identified as a high-risk group from toxins in fish, and because pregnant women, developing fetuses, and children are most affected by mercury in the body it is essential that we reach out to these community members. Our materials were created with these patients in mind.

CIEA staff are community health advocates and we have been providing tribal leaders, community members, and Indian health centers with information about mercury contamination since 2003. We are dedicated to providing this information to California families and to the health care providers that serve them.

To assist your medical staff we also now offer the "Eating Fish Safely" training for Continuing Medical Education. We also designed this toolkit to be updated and will forward you related studies as new information emerges.

Thank you for your interest and dedication to the health of our community members.

Sincerely,

Sherri Norris
Executive Director
California Indian Environmental Alliance

We wish to thank the following for their time, expertise and support:

Sonoma County Indian Health, Fresno Native American Health Center, Shingle Springs Tribal Health Program, Tuolumne Miwuk Indian Health Center, Gotmercury.org, Health Care Without Harm, the Hesperian Foundation, Indian People Organizing for Change, National Indian Justice Center, Physicians for Social Responsibility, Dr. David Berry, Dr. Linda Berry, Dr. Margy Gassel, Wanda Quitiquit, Dr. Jane Hightower, Raquelle Meyers J.D., Meyo Marrufo, Sarah Ryan, Dr. Ted Schettler, Alyce Ujihara, and Andria Ventura.

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We could not have completed the Mercury Health Toolkit without your generosity, devotion, review and encouragement.

Thank you!

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Introduction: Mercury

Mercury is a wide-spread persistent global toxicant, traveling across international borders through air and water. In the environment it is found in several forms including elemental mercury (Hg) and in various organic compounds and complexes. Of these, methylmercury (MeHg) easily enters the food chain in aquatic systems and can be found in high levels in predatory fish (Alpers, Hunerlach, May, and Hothem 2005). Because of its prevalence in the food chain, this toolkit focuses on methylmercury only. For a discussion of other organomercury forms, please see *American Academy of Pediatrics – Technical Report: Mercury in the Environment: Implications for Pediatricians* in the Appendix. If consumed by humans, the methylmercury from these fish can result in adverse health effects, especially to at-risk subsistence fishing communities like California Indian Tribes.

According to the National Health and Nutrition Examination Survey, Asians, Pacific Islanders and Native Americans had the highest prevalence of elevated blood mercury of all other racial/ethnic participants in the survey (Hightower, O'Hare, and Hernandez 2006). The most sensitive sub-populations are pregnant women, nursing women, women of child-bearing age, children and developing fetuses. Of these, the most sensitive population is the developing fetus who, with a harmful dose, can develop permanent neurodevelopmental disabilities. Fish are not only an important dietary staple to California Indian Peoples, they also constitute an important physical, cultural and spiritual connection through native practices. Thus, mercury poses a threat to the continuation and growth of the physical and cultural health of California Indian communities.

In the United States, mercury contamination can be found at some level in almost all freshwater or ocean fish (Brigham 2003), and is found even in the most pristine waterbodies through atmospheric deposition (Heyvaert, Goldman, Reuter and Slotton 2000). Industrial emissions in Asia are a major source of mercury in rainwater that falls along the California coast (University of California 2003). However, California's mercury concentration is unique because our primary source is from historic gold mining left over from the California Gold Rush (Alpers et al. 2005).

Gold Rush History: California Indigenous Peoples Perspective

Prior to the start of the Gold Rush in 1849, over 150,000 Native Americans lived in California. Within 20 years disease, forced relocations and massacres had reduced the Native population to an estimated 31,000. A planned and state sponsored public genocide, complete with vigilante groups, killed whole communities of Indians. In 1851, California Governor McDougall's first address to the legislature promised, "a war of extermination will continue to be waged between the races until the Indian race becomes extinct....…" (Castillo 1998).

United States and California State law denied Indians state citizenship, voting rights, and the right to testify or effectively seek redress in court (1850). California entered the union as a free state in 1850. However, the California legislature rapidly enacted a series of laws legalizing "Indian slavery" (Castillo 1998), including Assembly Bill No. 129. Indian individuals were sold at prices ranging from $30 to $150 (Johnston-Dodds 2002). This law resulted in the killing of Indian parents in order to kidnap and indenture children. It was not repealed until four years after President Lincoln's emancipation proclamation in 1863 (Castillo 1998).

Considering the history of the Gold Rush Indian families and tribes is important when addressing patients about mining toxins such as mercury. Gold Rush history remains an emotional issue for many tribal members today because of the environmental consequences and the impact on the physical and cultural well being of tribal members.

Mercury: Toxic Legacy of the Gold Rush

During the California Gold Rush, mining companies and free-lance gold miners dug up 12 billion tons of earth, 26 million pounds of which contained mercury that was used to extract gold from the ore. It has been estimated that 10-30 percent of the mercury was lost into the environment during standard operations, therefore estimated the total amount of mercury lost to the environment is 11 million pounds or more (Alpers et al. 2005). The amount of mercury required to violate today's federal health standards is equivalent to one gram deposited each year into a small 20 acre lake, (Interstate Mercury Education and Reduction Clearinghouse 2004).

Many abandoned gold and mercury mines were never adequately cleaned up and continue to produce toxic runoff today. Although there are areas that are more toxic than others, all areas of the state are impacted. The coastal Ranges of California contain the mercury mines themselves, as can be seen in Figure 1 below.

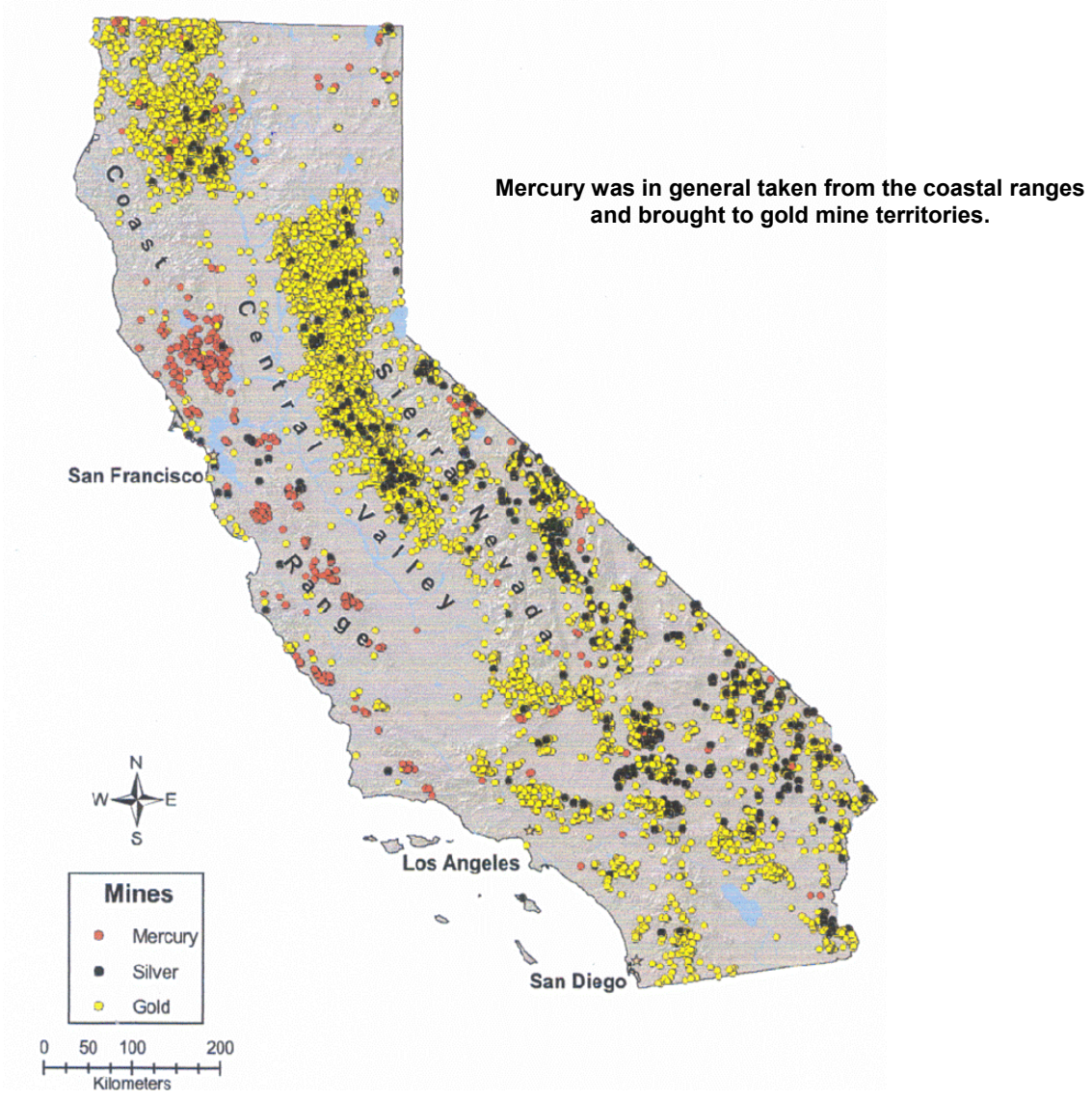


Figure 1: Locations of historic gold and mercury mines in California. (Wiener and Suchanek 2008)

There are currently warnings against eating fish from 47 California water bodies due to mercury contamination. Note that not all waterbodies have been tested for mercury. To date there is not a site with advice on which locations are safe. To access these advisories visit: http://www.oehha.ca.gov/fish/so_cal/index.html (OEHHA 2009).

In aquatic systems, mercury can mix with decaying plant matter and methylate. This methylmercury enters the food chain through microorganisms and increases in concentration as it is eaten by larger and larger organisms and fish . Because of this bioaccumulation, methylmercury levels of fish in California's rivers, lakes, streams and reservoirs can be "one million times higher than the surrounding waters" (US Environmental Protection Agency 1992). Figure 2 below shows a simplified version of the chemical composition, fate, and transport of mercury in the environment.

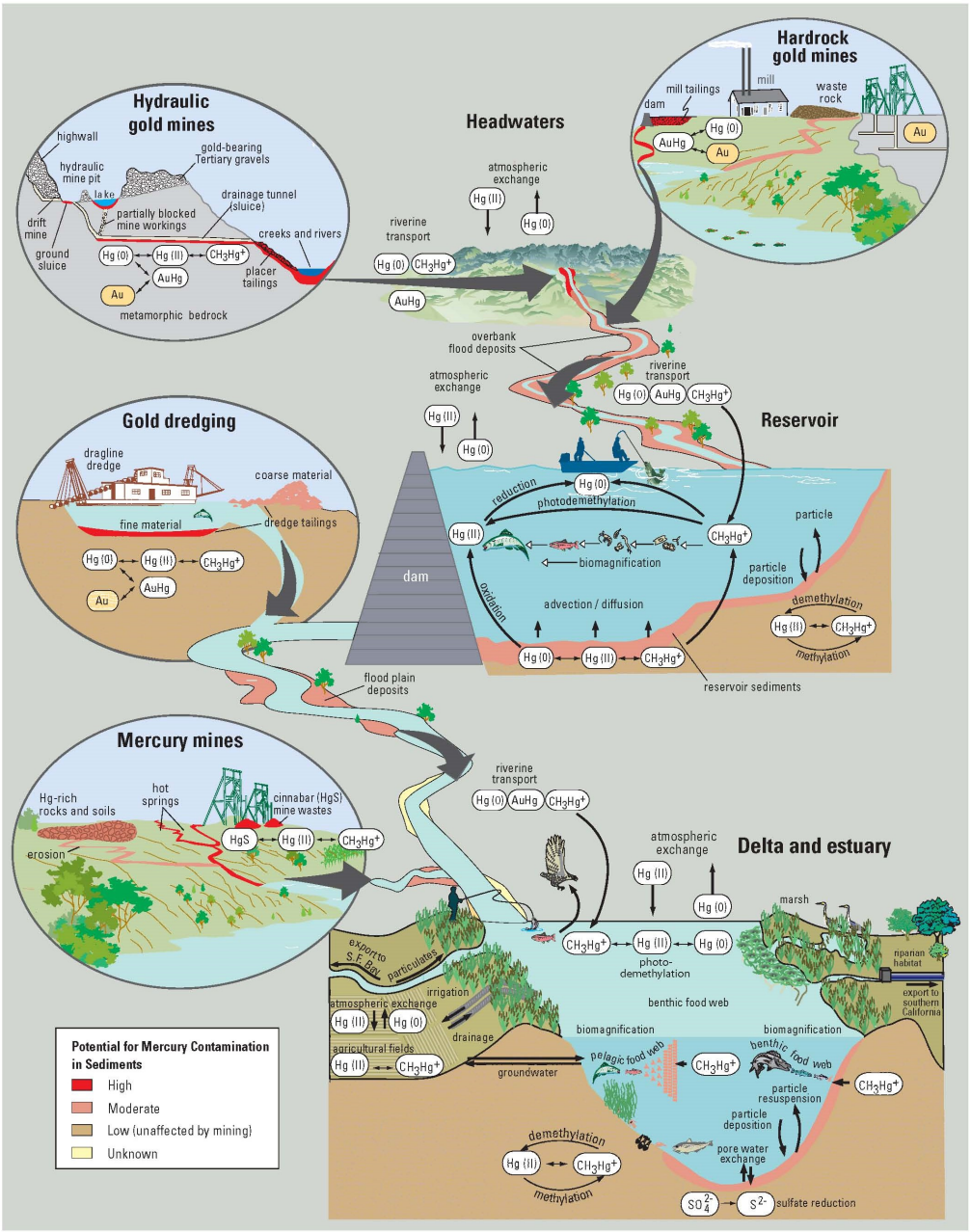


Figure 2: Source, transport, fate and potential sediments schematic diagram. A simplified mercury cycle is shown of overall methylation reactions and bioaccumulation. Actual cycling is more complex (Alpers et al. 2005).

There are approximately 39,000 historic and inactive mine sites in the state, with an estimated 128,000 mining features (Newton, Reynolds, Newton-Reed, Tuffly, Miller, Reeves, Mistchenko, and Bailey 2000). One such mercury mine is the Sulfur Bank Mine located within the E'lem Pomo Colony land, adjacent to Clear Lake. It is estimated that this lake alone contains 100 tons of mercury (Richerson, P. and S. Richerson 2001).

In an attempt to characterize the extent of mercury toxicity found in California's rivers and reservoirs, the California State Water Board's Surface Water Ambient Monitoring Program (SWAMP) randomly sampled lakes and reservoirs throughout the state. Initial results estimate that 74% of California's lakes and reservoirs are likely to contain fish for which fish consumption advisories would be issued (0.07 ppm), and of these, 26% of them are estimated to contain fish unfit for human consumption for sensitive populations (greater than 0.44 ppm). The largest source of the contamination is mercury (Davis, Melwani, Bezalel, Hunt, Ichikawa, Bonnema, Heim, Crane, Swenson, Lamerdin, and Stephenson 2009).

Fish eaten from non-California waterways are also implicated in toxicant contamination. In a random sampling of United States waterways, "Mercury and PCB's [Polychlorinated biphenyls] were detected in all fish samples," and half of those sampled were at levels "which exceeded the Environmental Protection Agency's (EPA) 0.3 ppm [mcg/g] mercury fish tissue criterion" (USEPA 2009).

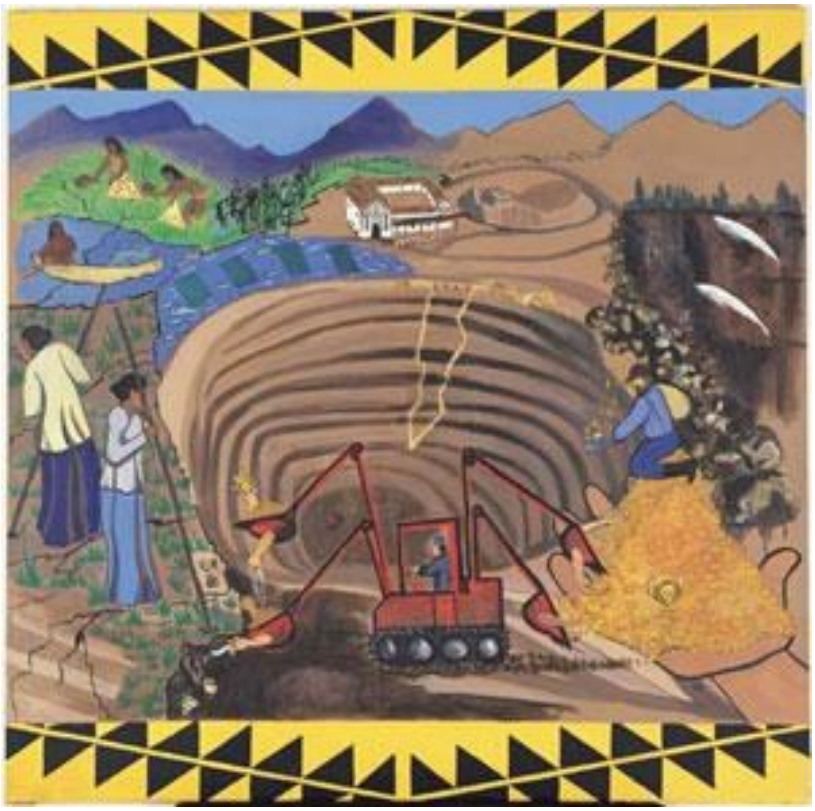


Figure 3: *Maidu Nation* from Video Cover of "Gold, Greed & Genocide." (International Indian Treaty Council. 2003.) Artist: Denise Davis 1999

Mercury in the Human Body

Prior to a mass poisoning event in the 1950s in Minamata, Japan, what we knew about mercury in the human body came from occupational exposures (Hunter, Bomford, and Russell 1940); Lundgren and Swensson 1949). What we now know about high-level (acute) poisonings comes from studies of population poisonings in Minamata, Iraq, and Canada (Hightower 2009). More recent epidemiological investigations have shed new light on the developmental neurotoxic effects of chronic low-level exposure to MeHg through fish consumption common in the United States, particularly in California and in tribal Indian populations in California.

There continues to be heated debate concerning the level of mercury concentration in the human body that causes neurotoxic effects and whether these effects are even attributable to mercury contamination. In some cases, especially in long-term low-dose scenarios, what we know is due to epidemiological evidence.

How it functions

When consumed, methylmercury is 90% to 100% absorbed into the body through the digestive system. Its half life in the human body ranges from 20 to 70 days and it is predominately excreted in feces. It takes approximately one year for mercury to leave the body. Methylmercury is lipid soluble, easily crosses the blood brain barrier and the placenta, and is found in breast milk. It accumulates in all bodily tissues, but especially the brain, kidneys, heart, and other muscle tissue, interfering with normal cell function. "In the developing brain, methylmercury is toxic to the cerebral and cerebellar cortex, causing focal necrosis of neurons and destruction of glial cells" (Goldman and Shannon 2001). Fetal blood mercury levels often exceed those of the mother by more than double and the damages sustained from the effects of MeHg exposure in utero are permanent (Budtz-Jørgensen, Grandjean, Weihe, and Keiding 2004). In 2004, an EPA study estimated that 630,000 babies born each year are at risk of developing learning disabilities and other forms of neurological damage due to mercury contamination (Mahaffey 2004).

Symptom History

In 1956, thousands of Japanese people unexpectedly developed severe neurological symptoms from MeHg poisoning after consuming fish contaminated by industrial dumping of mercury into Minamata Bay, Japan (Harada, Fujino, Oorui, Nakachi, Nou, Kizaki, Hitomi, Nakano, and Ohno 2005). The combination of symptoms they experienced became known as "Minamata Disease." The diagnostic critera for Minamata disease includes sensory impairment of the extremities in addition to two or more of the following: tunnel vision, ataxia, impaired speech and impaired hearing (Harada 1995, Harada et al. 2005, Harada 1968). This criteria only identifies extreme cases and does not account for those suffering lesser symptoms.

In 1962, researchers noted that children born of mothers who had eaten contaminated fish during pregnancy often developed severe neurological disabilities, leading to the identification of congenital Minamata Disease (Harada 1968). The most commonly observed symptoms included mental retardation, impaired reflexes, coordination disturbances, dysarthia, limb deformation, growth disorders, chorea-athetosis, and extremely high hypersalivation rates. Many of these symptoms were observed five to eight

years after birth, so mercury concentrations at birth or in utero are unknown. Because hair and blood concentrations were not measured at the time of the poisoning, data from this case cannot provide accurate projections of the minimum dose of MeHg required to produce the effects of congenital Minamata Disease (National Research Council 2000).

In Manitoba, Canada, Ojibway tribal members were continuously exposed to high levels of MeHg through fish consumption. Tribal members had not been informed of local fish advisories in place due to high levels of mercury in nearby lakes caused by emissions from chlor-alkali plants. In 1975, researchers from Japan evaluated tribal members experiencing symptoms and confirmed that they had Minamata Disease. Neurological symptoms brought on by MeHg consumption earlier in life have been shown to increase with aging. Following up in 2002, the same Japanese investigative team noted that elderly tribal members had experienced a higher rate of neurodegenerative symptoms and that as they aged, the severity of the symptoms increased. Twenty-seven years after the initial clinical evaluation, symptoms experienced included numbness in the hands and feet, pain in the joints of all limbs and hips, leg cramps, dizziness, hearing difficulty, disturbed gait, headaches, trembling, forgetfulness, stiff fingers and difficulty grasping. Of the neurological symptoms, the most prominent were sensory disturbances including glove and stocking-type neuropathy, difficulty in balance and walking, tremors, perioral sensory impairment, mental retardation, ataxia, impaired speech, disturbed ocular movements, sensory impairment of the whole body, tunnel vision, convulsions, fainting, and sensory impairment of either side of the body. Additionally, findings confirmed that chronic long-term exposure or "chronic Minamata disease," can occur in adults even when the level of mercury in hair is below the 50 ppm that is currently established as an acceptable level of exposure by the World Health Organization and Japanese standards, established from the Minamata disaster decades ago and still in use today (Harada et al. 2005; Harada et al. 2009).

Since the discovery of Minamata disease, there have been many attempts to determine useful dose-response relationships in order to confirm a "no adverse affect level" for methylmercury. This has proven to be extremely difficult since symptoms related to mercury are vast and inconsistent. Patients may have various combinations of subjective, objective and non-typical symptoms in varying degrees ranging from mild to serious, and these symptoms do not correspond to the mercury blood levels found in patients (Hightower 2009; Harada et al. 2005). In order to predict clinical symptoms over the long run, researchers like M. Harada, MD, believe it is more important to know the long-term effects of methylmercury than to know at what level the toxin is safe (Harada et al. 2005). While it is clear the fetus could be at risk even when the mercury level in the hair of a pregnant woman is below the WHO threshold and possibly that of the EPA 5.8mg/L in maternal blood or 1.2 ppm in hair (Chander et al. 2011; Grandjean, Weihe, White, Debes, Araki, Murata, Sørensen, Dahl, Yokoyama, and Jørgensen 1997), adults may also be at risk from mercury exposure at such levels (Yokoo et al. 2003).

Possible Health Effects

The list of possible symptoms and resulting illnesses caused by mercury exposure is extensive, so the following discussion of evidence and conclusions are grouped by effects and organ systems.

Carcinogenicity

On the basis of available human and animal data, the International Agency for Research on Cancer (IARC) and the U.S. Environmental Protection Agency (EPA) have classified MeHg as class C, a possible human carcinogen due to a link with renal cancer(EPA 2000). While overall cancer rates have not been linked with methylmercury or mercuryexposure, studies have shown an association

with certain types of cancer , such as leukemia, liver cancer and non-Hodgkin's Lymphoma (Kinjo, Akiba, Yamaguchi, Mizuno, Watanabe, Wakamiya, Futatsuka, and Kato 1996); Janicki, Dobrowlski, and Krasnicki 1987).

Cardiovascular Effects

Studies as far back as 1953 have linked exposure to mercury to a multitude of cardiovascular problems in both children and adults (Warkany and Hubbard 1953). Symptoms include tachycardia, hypotension, and hypertension (Hallee 1969; Soni, Singhania, Bansal, and Rathai1992; Bluhm, Bobbitt, Welch, Wood, Bonfiglio, Sarzen, Heath, and Branch 1992). Thermometer plant workers exposed to mercury on a daily basis over a long period of time were shown to have much higher rates of hypertension than the surrounding population (Vroom and Greer 1972). Exposure can also lead to an increased risk of myocardial infarction and heart disease (Salonen, J., Seppänen, Nyyssönen, Korpela, Kauhanen, Kantola, Tuomilehto, Esterbauer, Tatzber, and Salonen R. 1995). "Prenatal exposure to MeHg has been shown to alter blood-pressure regulation and heart-rate variability in children. Those adverse effects were observed at very low cord-blood Hg concentrations (less than 10 μg/L)" that have not been associated with other developmental effects (Sørensen, Murata, Budtz-Jørgensen, Weihe, Grandjean 1999).

Cellular Effects - Genotoxicity

Evidence that human exposure to mercury causes genetic damage is inconclusive, although "several investigators have reported higher rates of chromosomal aberrations among workers exposed to elemental or inorganic forms of Hg" (Popescue, Negru, and Lancranjan 1979; Verschaeve, Kirsch-Volders, Susanne, Groetenbriel, Haustermans, Lecomte, and Roossels 1976; Barregard, Hogstedt, Schutz, Karlsson, Sallsten, and Thiringer 1991). Studies show a significant increase in the percentage of micronuclei, chromosomal aberrations in lymphocytes, and incidence of sister chromatid exchange in humans from eating contaminated fish and seal meat. Unfortunately these studies did not control for smokers or workers exposed to other heavy metals (Queiroz, Bincoletto, Quadros, and De Capitani 1999); (Skerfving, Hansson, Mangs, Lindsten, and Ryman 1974); (Wulf, Kromann, Kousgaard, Hansen, Niebuhr, and Alboge 1986).

Central Nervous System Toxicity

As the number of neurological symptoms associated with mercury is very high, discussion of them occurs throughout this toolkit. The neurodevelopmental effects of methylmercury following high-dose mercury exposure is well documented, and there are a number of studies on chronic low-dose methylmercury exposure. New research has focused on sensitive and subtle types of neurological endpoints observed in children exposed in-utero. "Of the three major prospective long-term studies, the Faroes study reported associations between low-dose prenatal MeHg exposure and children's performance on standardized neurobehavioral tests, particularly in the domains of attention, fine-motor function, confrontational naming, visual-spatial abilities, and verbal memory, but the Seychelles study did not report such associations. The smaller New Zealand study also observed associations, as did a large pilot study conducted in the Seychelles" (National Academy of Sciences 2000). Unfortunately, few studies have focused on these same subtle endpoints for adults, and there is controversy over what minimum dose of MeHg is required to produce these subtle effects in either adults or children.

A study "examining association of material fish intake during pregnancy and … and infant cognition" suggests that higher maternal fish intake was associated with higher infant cognition… For each additional weekly fish serving, offspring visual recognition memory scores were 4.0 higher, … but

higher mercury levels were associated with lower cognition (Oken 2005).

Mercury exposure has also been associated with Alzheimer's Disease (AD). Alzheimer's patients have been shown to have higher levels of mercury in cerebrospinal fluid samples than similar patients without AD symptoms (Gerhardsson, Lundh, Minthon, and Londos 2008). Exposure to methylmercury can in certain instances contribute to brain inflammation which can lead to senile plaques that Alzheimer's patients often develop (Boschat, Corbaz, Honegger, Monnet-Tschudi, and Zurich 2006). CIEA believes that more research exploring the association between Alzheimer's disease and lifetime mercury exposure is vital to protecting the future health of our constituents.

Endocrine Effects

"Laboratory studies suggest that exposure to methylmercury at a level similar to those found in fish may induce pancreatic islet β-cell dysfunction. Few, if any, human studies have examined the association between mercury exposure and diabetes incidence… Our results are consistent with findings from laboratory studies and provide longitudinal human data, suggesting that people with high mercury exposure in young adulthood may have elevated risk of diabetes later in life." (He 2013).

Immune Effects

What we know about the effects of MeHg on the human immune system is from studies of occupational exposures, *in vitro,* and animal studies. MeHg has long-term effects on the developing immune system in rats following exposure during the pre and perinatal (nursing exposure) periods (Ilbäck, Sundberg, and Oskarsson 1991; Wild, Ortega, Lopez, and Salvaggio 1997). A study evaluating the urine mercury levels of workers in a Brazilian mercury plant found a correlation between increased urine Hg levels and decreased B and T lymphocyte populations (Dantas and Queiroz 1997). This correlation between urine Hg levels and T lymphocyte reduction was also demonstrated by Moszcynski, Slowninski, Rutkowski, Bem, and Jakus-Stoga (1995). In animal studies, MeHg has been shown to inhibit normal lymphocyte proliferation and increase susceptibility to viral infections (Ortega, Lopez, Takaki, Huang, Arimura, and Salvaggio 1997). Therefore, "exposure to MeHg could increase human susceptibility to infectious diseases and autoimmune disorders by damaging the immune system" (National Academy of Sciences 2000).

Renal toxicity

The kidneys are known to be one the areas of the body most susceptible to damage from mercury exposure (Samuels, Heick, McLaine, and Farant 1982). Renal impairment including altered function, renal hypertrophy, and nephron damage has been observed in patients already experiencing neurological symptoms from mercury toxicity (National Academy of Sciences 2000).

Reproductive Effects

The effect of methylmercury on human fertility has not yet been extensively studied (Salonen et al. 1995). However, it is important to note that after the seed grain poisoning in Iraq, investigators found a very low rate of successful pregnancies among exposed women (Bakir, Damluji, Amin-Zaki, Murtadha, Khalidi, Al-Rawi, Tikriti, Dhahir, Clarkson, Smith, and Doherty 1973). Additionally, occupational exposure studies have noted an increased incidence of spontaneous abortion among the wives of a group of men exposed to Hg. "Preconception paternal urinary Hg concentrations above 50 mcg/L were associated with a doubling of the spontaneous abortion risk" (Cordier, Deplan, Mandereau, and Hemonet 1991). Occupational studies of women exposed to mercury while pregnant do show a higher incidence of congenital anomalies, but no significant difference in spontaneous

abortion rates (Elghany et al. 1997) Animal studies, including work in nonhuman primates, indicate that MeHg causes functional reproductive effects including low abnormal sperm count, abortion, still births, low conception rate, decreased litter size, and fetal malformations (Mohamed et al. 1987, Burbacher et al. 1988, Khera 1973a, Lee and Han 1995, Hughes and Annau 1976, Fuyuta et al. 1978, Fuyata et al. 1979, Hirano et al. 1986, Mitsumoria et al. 1990, Inouye and Kajiwara 1988).

EPA Mercury Reference Dose

"EPA defines an RfD as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime (EPA 1997)."

The current reference dose (RfD) used by the U.S. EPA is 0.1mcg/kg-day. This is based on a measurement of mercury in fetal cord blood using an uncertainty factor of 10, "to account for sensitivity among individuals, fish mercury levels, and unforeseen factors." It is expected to keep those who consume fish from raising their blood mercury over 4-5 mcg/L (NAS 2000.) The creation of this benchmark dose included several decisions, for which there was limited or non-absolute information available, including the 1) no-observable-adverse-effect level (NOAEL), the 2) lowest-observed-adverse-effect level (LOAL), and 3) derived uncertainty factors (UFs) based on a review of the entire toxicity database (Dourson et al. 2001), including comparisons of fetal blood mercury concentrations and that of their mothers through measuring cord blood (NRC 2000; U.S. EPA 2001)

In 2000, after reviewing the standard, the National Academy of Sciences (NAS) and supported the EPA's RfD of 0.1 mcg/kg body weight/day. However, they and subsequent reviewers have highlighted the following areas which may require additional attention:

- Dose estimations from either peak concentrations or more continuing chronic low-level exposure to methylmercury in the Faroe Islands (exposures of several times a week), creating differing body burdens.
- The possibility that cardiovascular or immunological effects could be detected at lower doses than neurological effects.
- Exposures to mercury in conjunction with additional chemicals a largely unknown. (Dourson et al. 2001).

Of particular concern are recent findings of neurological effects in children born of exposed mothers at lower levels. The current RfD of 0.1mg/kg-day of mercury is associated with fetal blood mercury concentrations of 5.8 μg/L (NRC 2000; U.S. EPA 2001). However, as is articulated well in the 2009 National Nutrition Examination Survey (NHANES), "differences have been found between maternal and cord blood concentrations due to bioconcentration of MeHg across the placenta (Butler Walker et al. 2004; Mahaffey et al. 2004; Mergler et al. 2007; Morrissette et al. 2004; NRC 2006; Stern and Smith 2003). As a result, maternal BHg [blood mercury level] concentrations as low as approximately 3.5 μg/L may be a concern. (Mahaffey 2009)."

> "The RfD is an important risk characterization tool that is broadly used as a measure of the "acceptability" of population exposure levels. It is used to guide risk-management decisions and regulatory policies ranging from fish-consumption advisories to air-emissions permits."

National Academy of Sciences and the National Research Council."Toxicological Effects of Methylmercury." 2000.

Fish Consumption Advice

"Higher fish consumption in pregnancy was associated with better infant cognition, but higher mercury levels were associated with lower cognition. **Women should continue to eat fish during pregnancy but choose varieties with lower mercury contamination"** (Oken 2005).

Previous to the above study, in March 2004 the EPA and FDA issued the following advisory for fish consumption for women who might become pregnant, women who are pregnant, nursing mothers and young children:

EPA and FDA Consumer Advisory on Methylmercury in Fish, 2004

1. Do not eat Shark, Swordfish, King Mackerel, or Tilefish because they contain high levels of mercury.
2. Eat up to 12 ounces (2 average meals) a week of a variety of fish and shellfish that are lower in mercury.
   - Five of the most commonly eaten fish that are low in mercury are shrimp, canned light tuna, salmon, pollock, and catfish.
   - Another commonly eaten fish, albacore ("white") tuna has more mercury than canned light tuna. So, when choosing your two meals of fish and shellfish, you may eat up to 6 ounces (one average meal) of albacore tuna or tuna steaks per week.
3. Check local advisories about the safety of fish caught by family and friends in your local lakes, rivers, and coastal areas. If no advice is available, eat up to 6 ounces (one average meal) per week of fish you catch from local waters, but don't consume any other fish during that week.

Follow these same recommendations when feeding fish and shellfish to your young child, but serve smaller portions.

US Food and Drug Administration, "FDA and EPA Announce the Revised Consumer Advisory on Methylmercury in Fish," News Release, March 2004, http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108267.htm

Other than the above joint advisory, the FDA does not provide fish consumption advice. The EPA Fish consumption advice and local OEHHA advisories are more protective than the FDA action level.

Consumer Fish Advisories

The FDA's advice for consumption of commercial fish is based on an acceptable level of mercury consumption of 0.5 mcg/kg/d (microgram per kg of body weight per day), and their action level in fish is 1 mcg/g or 1 ppm per serving of fish. The U.S. Food and Drug Administration (FDA) concludes that we can, therefore, safely eat about 12 ounces of fish or about two servings per week to get the benefits of Omega-3 fatty acids and proteins (FDA). However, this advice cannot be safely applied to all fish, and following this advice would put many individuals over the FDA's own acceptable limits (US FDA 1995, Hightower 2009).

The FDA's action level for commercial fish is 1 mcg/g or 1 ppm per serving of fish, which corresponds to an acceptable level of blood mercury of 0.5 mcg/kg/d in the body (microgram per kg of body weight per day). The U.S. Food and Drug Administration (FDA) therefore, concludes that we can safely eat about 12 ounces of fish or about two servings per week to get the benefits of Omega -3 fatty acids and proteins (FDA). FDA action levels offer 5 times less protections than EPA fish consumption advice. Also, FDA advice cannot be safely applied to all fish as following this advice would put many individuals over the FDA's own acceptable limits, even for species not listed explicitly in the 2004 EPA and FDA Consumer Advisory on Methylmercury in Fish (US FDA 1995, US EPA/FDA 2004, Hightower 2009).

In 2009, the U.S. Food and Drug Administration reviewed its recommendations and issued a 270-page FDA draft report, which concludes that the health benefits of eating fish appear to outweigh the potential dangerous effects of mercury. Fish contain essential omega-3 fatty acids, protein and minerals (FDA 2009). As a result, the FDA has considered lessening or choosing not to distribute fish consumption advisories. Although the benefits of eating non-toxic fish are clear, eating those laden in toxins can be dangerous. In response, the Environmental Protection Agency released a memo to the White House calling the FDA's study "scientifically flawed and inadequate" and an "oversimplification" (EPA 2009).

The Mercury Policy Project, CIEA and other non-governmental organizations also responded to the FDA's Assessment Report. This response stated overall that that the FDA draft report was "scientifically unsound and should not be the basis for any overall policy change by FDA to the joint FDA/EPA federal fish consumption advisory for mercury" (Mercury Policy Project 2009).

The EPA's fish consumption advice is based on an RfD of 0.1 mcg/kgbw/d. This level corresponds to a blood mercury level of 4-5 mcg/L. An individual with blood mercury levels below this value is considered to be without appreciable risk by the EPA. The U.S. EPA uses a risk-based fish consumption limit which relates the number of fish meals that can be eaten per month with the fish tissue concentration of methylmercury. Meal sizes are assumed to be 8 oz. uncooked and 6 oz. cooked fish. Inputs used are 70 kg, average body weight of adult males and females combined, and the reference dose is 1x10(-4) mg/kg/d (US EPA 2004).

Additionally, there is evidence that adverse effects on the fetal brain may occur at less than 5 ppb maternal blood mercury levels. Therefore, in the future we may see reference doses become even more protective. This is explained in Stein, et al. 2002 as the "declining threshold of harm." *See figure 4.*

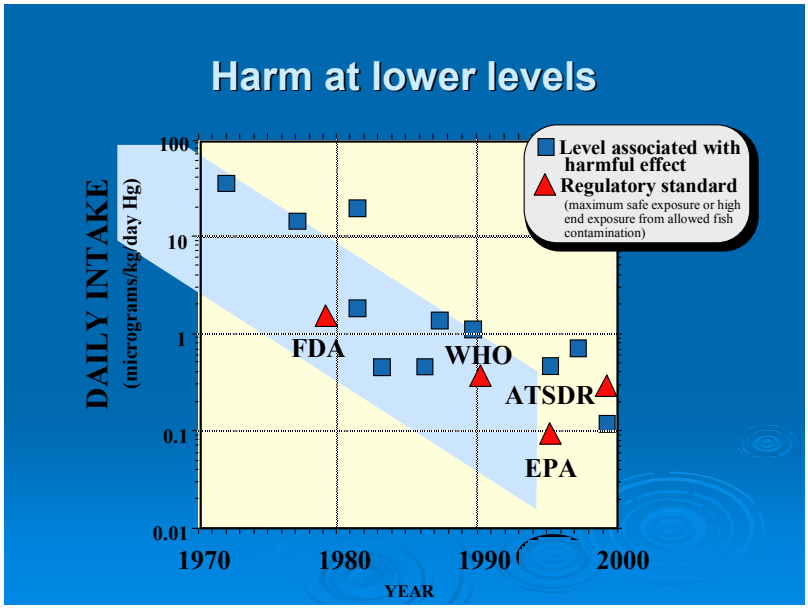


Figure 4: Stein, J., T. Shettler, D. Wallinga, M. Valenti. "In Harm's Way: Toxic Threats to Child Development." Developmental Behavior Pediatrics, Vol 12, No. 1S.

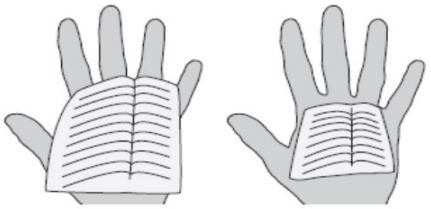
What is a Serving Size?

US Dietary Guidelines for Americans 2010

250 mg/day of EPA and DHA= minimum 8 ounces of seafood per week for adults; 8 to 12 ounces of a variety of low methylmercury seafood for women who are pregnant or breastfeeding; 4 to 6 ounces per week for young children.

CA Office of Environmental Health and Hazard Assessment

OEHHA bases advisories on an 8 ounce raw, 6 ounce cooked portion of fish. This corresponds to about the size and thickness of an adult hand. These are developed for a person weighing 70 kgs or 156 pounds.



Children should be given smaller, age appropriate servings based on their own hand size.

Source: http://www.oehha.ca.gov/fish/so_cal/index.html

Wild-Caught Fish

In California, a list of fish consumption advisories can be found at the Office of Environmental Health and Hazard Assessment (OEHHA) website:http://www.oehha.ca.gov/fish/so_cal/index.html, along with a map of advisory locations: http://www.oehha.ca.gov/fish.html. At this time, OEHHA is revising its advisories and posting them as they are complete.In March 2009, the agency issued the "2009 Update of California Sport Fish Advisories." A copy of this report can be found at: http://oehha.ca.gov/fish/pdf/DiscAdvyUpdates032309.pdf.

CIEA recommends that community members refer to the above OEHHA website and 2009 report to locate waterbodies where they fish.

It is important to note that even though a waterbody is not listed as impaired and no fish consumption advisories for it are listed on the OEHHA website, it does not mean that the waterbody has been tested and is therefore safe. CIEA and others are working with agencies to begin listing safer locations to fish, instead of merely those that contain advisories limiting fish consumption.

When there is no local advisory present, the EPA recommends limiting non-commercial fish consumption and to one meal a week. Consumers should follow one advisory at a time to avoid

exceeding exposure guidelines. This is based on the estimation that most fish caught in the United States have a mercury concentration between 0.13 ppm and 0.43 ppm (US EPA 2004). According to a recent study by the Surface Water Ambient Program (SWAMP), 76% of 152 lakes randomly sampled in California contained fish with an average methylmercury concentration above 0.07 ppm, and 26% of lakes had species with an average concentration higher than 0.44 ppm, the level unfit for human consumption (Davis et al. 2009).

Figure 5: Norgaard K. 2004. Fishing Using Sustainable Traditional Fishing Technique on the Klamath

Seafood Regulations

According to a report by the General Accounting Office (GAO), the seafood industry "offers no assurance of safety for consumers…[The] FDA's seafood program is riddled with deficiencies, woefully underfunded, and provides no assurance of safety for consumers" (U.S. General Accounting Office 2001).

The FDA only inspects seafood processors once every two years, and many are not required to register with the FDA or be inspected. The FDA does not test for a variety of well-known hazards in fish, including mercury (Center for Science and the Public Interest 2001).

Figure 7: Sushi various kinds including bluefin. Open source.

Tuna Controversy

The EPA and FDA's 2004 joint advisory lists canned or "chunk" light tuna as a fish "low in mercury," and recommends that consumers can eat up to 12 ounces (2 average meals) a week. This advisory states albacore or "white" tuna has more mercury than canned light tuna, and that a person may eat up to 6 ounces or one average meal of albacore tuna per week, as one of two meals of fish and shellfish (US EPA 2004). Unfortunately, persons following this advice of one 6 ounce meal of albacore tuna per week could be over the recommended EPA RfD (http://www.ewg.org/tunacalculator, Environmental Working Group 2004).

To test the safety of the current advisory against actual fish tissue content, the New York Times purchased sushi at 20 New York restaurants and compared laboratory results. The tuna tested was mostly bluefin. It was found that a diet of six pieces of tuna per week would cause the consumer to exceed EPA accepted levels (Burros 2008).

There is enough controversy surrounding levels of mercury in tuna to prompt the Environmental Working Group to create a Tuna Calculator, which uses in part the FDA's own advice to show that following the guidelines suggested for what one may "safely eat" of either canned light or albacore tuna would result in being over the level that even the EPA considers safe. This Tuna Calculator can be found at: http://www.ewg.org/tunacalculator (Environmental Working Group 2004). The National Resource Defense Council website http://www.nrdc.org/health/effects/mercury/tuna.asp contains a chart that shows the quantity of tuna a person can consume based on EPA guidelines (National Resource Defense Council 2009).

In 2006, Consumer Reports issued a statement that pregnant women should not eat any canned tuna, whether canned light (chunk light) or albacore. CIEA agrees with Consumer Reports and with the Environmental Working Group's recommendation that "women of childbearing age and children under 5 not eat albacore tuna at all." This is because mercury levels found in tuna vary widely; a significant portion of albacore tuna has very high mercury levels and the industry does not regulate or label this product accurately. Cans of canned light tuna are inconsistent in their levels of mercury. People eating tuna are playing roulette with mercury levels. In pregnant women and developing children this could potentially result in adverse results. There are plenty of other high omega-3 fatty acid choices that would be more beneficial to sensitive sub-populations (Environmental Working Group 2004).

Figure 6: Tuna – If regulated, unknown. Open source.

CIEA "Eating Fish Safely" Brochure

There are a variety of brochures and informational sources issued by national and state agencies for the public offering fish consumption advice. Many of these are not regularly distributed to the public or to tribal members and do not consider possible California Native exposure routes. They often downplay the actual health risks of mercury, and only provide a limited amount of the fish consumption advice available.

Fish are not only an important part of a balanced diet, they are culturally important. Eating healthy fish results in a healthy physical connection of the People to their traditional territories.

CIEA aims to distribute the most accurate, up-to-date and complete information available. Armed with information, we believe community members can make their own decisions in order to be protective of their health, the health of their family members, and of their future generations.

CIEA materials currently utilize the more protective EPA standard, and when there is controversy, we seek to err on the side of caution. We are concerned about a growing body of evidence that could result in a doubling of risk to the developing fetus (Rice et al. 2003) and may require a revision of the EPA standard. In particular, we would like to see more studies that investigate the relationship between maternal blood mercury concentrations and cord blood concentrations. We are also concerned about low-level exposure and subtle effects, since evidence has shown that the more we learn, the lower the threshold of harm actually is to the human body, and in particular to the developing fetus.

Standards used in "Eating Fish Safely"

At this time the EPA's RfD is widely considered to be the safest standard used in the United States (National Research Council 2000). CIEA's "Eating Fish Safely" brochure and the mercury calculator located at www.gotmercury.org use the EPA's RfD for blood mercury level and EPA and FDA fish tissue data (updated January 2006) and found at: http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm115644.htm

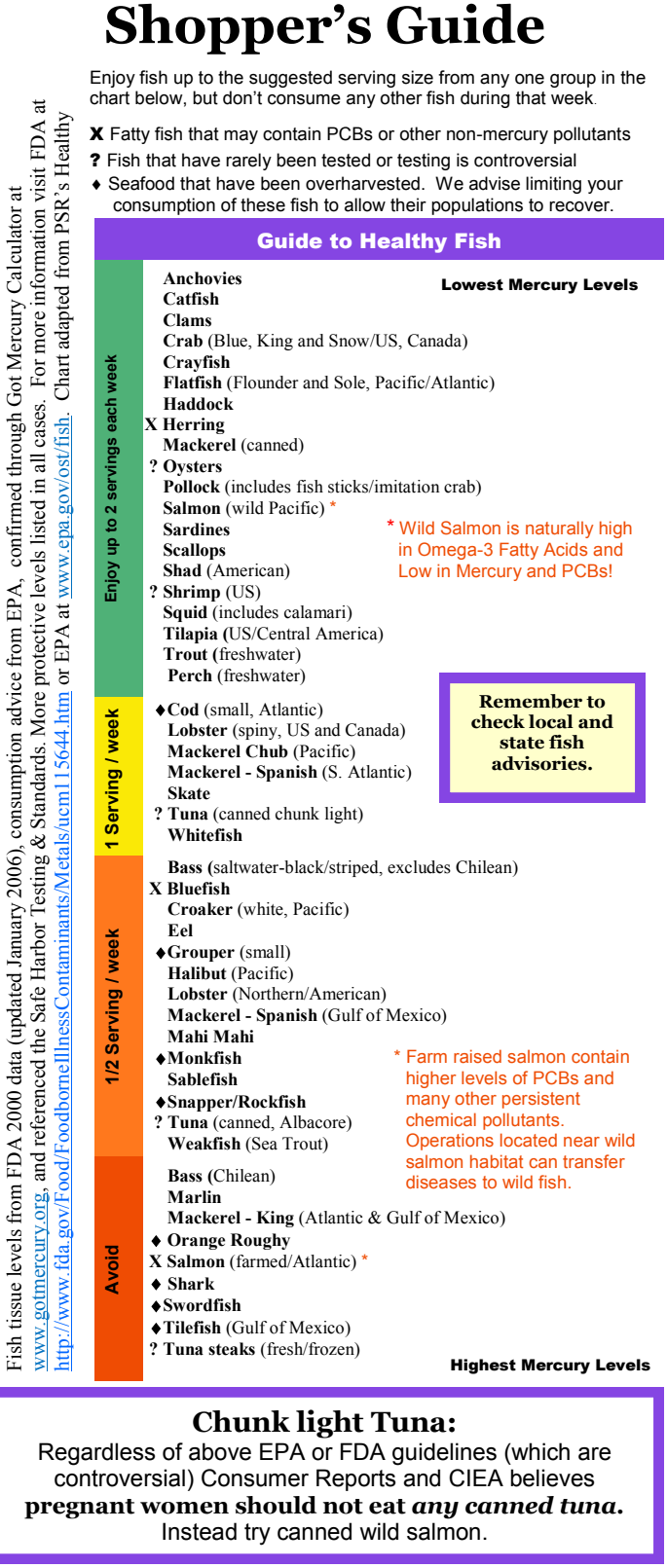


Figure 8: Excerpt from "Eating Fish Safely" brochure. (CIEA. 2009.)

Frequency of Fish Consumption

CIEA materials list advisories of what fish can be eaten per week instead of using the meals per month model that the EPA uses (EPA 2004). In our experience, regulating what is eaten in a week is more indicative of the consumption patterns of California tribal members, who eat fish regularly. Additionally, when we consider new data that correlates adverse impacts at very low levels, we want to be careful that a pregnant mother does not consume in one sitting the amount of mercury considered "safe" during an entire month. It is safer to space these meals out over four weeks.

Meal Size

CIEA materials include the cooked 6 ounce meal size since most consumers are looking at cooked portions. We recognize that 6 ounces is a smaller serving than our community members actually eat when consuming fish. However, it is the size meal that EPA and OEHHA use when developing fish advisories.

Body Weight

EPA advisories are based on a body weight of 70 kg, or 156 lbs, of adult female or male body weight (EPA 2004).

Fish Consumption Levels

In the "Shopper's Guide," CIEA compared the actual fish tissue data listed on FDA and EPA websites and utilized the EPA explanation of how it arrived at the meal-per-month and meals-per-week consumption levels for non-commercial fish. The EPA collapsed the 2-4 meal/month consumption rate into 1 meal/week (EPA 2004; Rice et al. 2003). CIEA found that in some cases when a fish was transferred into a weekly model it became clear the EPA's recommended consumption levels would lead the consumer to be over the EPA acceptable RfD. We therefore added a ½ serving per week category so the consumer could make the choice.

Fish Tissue Data and Advisory Sources

Commercial Fish:

http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm115644.htm

EPA Fish, fish consumption advice and links to national and regional advice:

www.epa.gov/waterscience/fish/advisory.html

Cal EPA/OEHHA local fish advisories, including wild-caught salmon:

www.oehha.ca.gov/fish.html and http://www.oehha.ca.gov/fish/so_cal/index.html

Recognizing Symptoms

Symptoms and summaries of the current studies that support this information are explained in more detail in this toolkit on pages five through nine.

Symptoms can be both subjective and objective. These have been proven at varying levels of certainty. Patients may have various combinations of subjective and objective symptoms, and in varying degrees ranging from mild to serious. Identifying patients by their symptoms is also complicated because specific symptoms do not directly correspond to the mercury blood levels found in patients (Harada 1995; Hightower 2009).

Physicians looking for symptoms in their patients should note that the "possibilities of the occurrence of mild and non-typical symptoms are greater than those of typical serious symptoms," especially resulting from long-term chronic exposure or low-level exposure (Harada 2002).

Sampling

The most common biomarkers used to measure mercury exposure are blood, hair, and urine. Each of these has distinct advantages and limitations, and determining which to use will depend on a number of factors.

Blood mercury levels reflect the concentration of both elemental and organic mercury present at the time of testing and are generally accepted as an accurate measurement of recent exposure. The Rfd for blood mercury is 5.8 mcg/L. This means that the blood level associated with neuropsychological impairment in maternal blood is 58 mcg/L (Chander et al. 2011). The half life for all forms of mercury in the blood falls within the range of approximately 20 to 70 days in adults (Grandjean, Weihe, and Nielson 1994; Goldman and Shannon 2001). Because of this, blood level concentrations do not necessarily represent chronic mercury exposure or past exposure that could contribute to current symptoms.

In contrast, hair mercury levels can be used to monitor exposure over a longer period of time, but are less accurate and are subject to a greater number of influencing factors. In statistical analyses conducted by Budtz-Jorgensen, Grandjean, Keiding, Weihe, and White (2003), "The total imprecision of the hair-mercury concentration was found to be almost twice that of the blood determination." Hair treatments, such as colorants or straightening, and external contamination can affect results. Additionally, results from commercial laboratories have been unreliable Results must be interpreted carefully. In the United States women, of reproductive age hair mercury level at the 90th percentile is 1.4 ppm, so an elevated result would be levels higher than this, although the Rfd is approximately 1.2 ppm (Chander et al. 2011). This means that the hair level associated with neuropsychological impairment is 12 ppm, reflective of uncertainty factor of 10. Because mercury is excreted into the hair follicle, exposure occurring less than approximately one month prior to testing will not show up in hair mercury concentration levels (Goldman and Shannon 2001).

Urinary mercury levels are used to identify recent and chronic mercury exposure, but are mainly reflective of inorganic mercury excretion. Because of this, urine testing may not be the most useful method to determine methylmercury exposure. An elevated level would be considered greater than the 95th percentile of 3.33 mcg/L (Chander et al. 2011).

How to Identify At Risk Patients

Intake Questions are Key!

Screening patients using intake materials is the best way to identify a patient in need of more detailed discussion, testing, and fish consumption advice.

Because symptoms related to mercury are vast and inconsistent CIEA recommends that clinics and medical facilities revise their intake materials to include the following three questions:

- How often do you eat fish?
- Which types of fish do you eat?
- From where do you get your fish?

Common Symptoms of Possible Mercury Toxicity

Although there are many identified symptoms associated with mercury toxicity, some of the most frequently experienced include:

Fatigue	Dizziness or faintness
Headache	Chest pain or palpitations
"Foggy" thinking, trouble performing complex tasks, or reduced mental functioning	Loss of pain sensation
	Gastrointestinal upset, nausea and/or pain
Memory loss	Visual dimness
Insomnia	Staggering
Muscle stiffness, cramps, or muscle pain	Metallic taste
Muscular atrophy	Tremor
Joint pain	Hair Loss

Additional resources for health care providers on mercury exposures:

Occupational and Environmental Medicine Clinic
http://coeh.berkeley.edu/ucsfoem/clinics.html
University of California, San Francisco
2330 Post Street, Suite 460
San Francisco, CA 94115
Appointments: 415-885-7580
Fax: 415-771-4472
Contact: Linda John
Email: johnl@medsfgh.ucsf.edu

UCSF Pediatric Environmental Health Specialty Unit
http://coeh.berkeley.edu/ucpehsu/
University of California, San Francisco
2330 Post Street, Suite 460
San Francisco, CA 94115
Toll Free: 1-866-U C P E H S U (1-866-827-3478)

UC Davis Occupational and Environmental Health Clinic
University of California, Davis
Dept. of Public Health Services
One Shields Avenue, MS1C, Room 181
Davis, CA 95616-8638
Contact: Stephen McCurdy, MD, MPH
Appointments: 530-754-7635

Patient Advice

Fish and shellfish are part of a healthy diet. The general message is that seafood consumers should eat a variety of fish low in mercury and high in omega-3 fatty acids. To avoid risk and receive the benefits of fish:

- **Do Eat Fish!** Fish are an essential source of omega-3 fatty acids - primary for the development and maintenance of the brain, heart, nervous system and the cells of developing fetuses, babies, children and adults. It also has been linked to protecting the body from contracting various diseases like diabetes.
- **Eat smaller younger fish,** which generally contain less mercury. Avoid large predatory fish whether they are wild-caught or store-bought.
- **Plan Ahead.** Begin following fish consumption advice as soon as you plan on becoming pregnant. The average half life of mercury in the human body ranges from 45 to 70 days (U.S. EPA 2001)
- **Check local advisories** for locations where you or your family members fish. In California, these can be found at the Office of Environmental Hazard Assessment: http://www.oehha.ca.gov/fish/so_cal/index.html or http://www.oehha.ca.gov/. As they are currently listed, patients cannot assume the waterbody is not contaminated if there is no advisory.
- **When there is no local advisory present**, follow the 2004 EPA recommendation to limit fish consumption to one meal a week. Be aware if there ia a mine site or mine features nearby more protective advice could be assumed—avoid large predatory fish or avoid eating from that location altogether.
- **Check store-bought fish at the EPA website or a Shopper's Guide** such as the CIEA "Safely Eating Fish" brochure. You can also visit a mercury calculator website such as the one at www.gotmercury.org.
- **Eat salmon!** In California, wild river-caught salmon are low in mercury and PCBs, are high in nutrients, high in omega-3 fatty acids, and are best for the environment. Farmed salmon do not share these health benefits (they can contain mercury and PCBs) and they are a danger to the environment.
- **Choose fish low in mercury.** Mercury is stored in the entire fish. You cannot clean the heads, guts, fat and skin to get rid of it. Other chemicals, like PCBs, may be stored there, so trimming off these areas is still a good idea.
- **Adjust portions based on your body weight.** A serving of fish is considered to be 6 ounces of cooked fish if you are a 156 pound person. This can be done by estimating a serving to be the size and thickness of your hand. Children should be given smaller servings approximately the size and thickness of their own hand (OEHHA 2009).
- **Fish oil supplements are not all the same.** Choose those from fish low in mercury and PCBs like wild-caught Salmon. Under 10% of vegetarian omega-3 fatty acids (ALA) sources or supplements are converted to the same kinds of fatty acids that are found in fish (EPA and DHA). These are less efficient sources of omegas and include algal oil supplements, flax, walnuts, pumpkin seeds, soy and canola oil.
- **Do Not Vacuum Mercury!** Mercury can also enter the body by breathing in vapors caused by vacuuming. Warn patients: if elemental mercury is spilled contact local poison control.

- **Be wary of other sources.** Firewood, basketmaking materials, and foods gathered near mercury-laden sediments may contain mercury. Studies on these possible alternative sources of exposure have not yet been completed.
- **Be sensitive of patient's cultural & historical connections to fish consumption.** For many cultures, fish consumption patterns changes seasonally, as do the amount eaten. Advice for those who eat fish for subsistence or for cultural and/or spiritual purposes may should stress the benefits of eating fish while directing them towards fish lower in Mercury and other chemicals, like PCBs.
- **Nursing mothers who have mercury in their bodies may be concerned about passing mercury on to their babies.** This must be considered on a case-by-case basis. The beneficial effects of "nursing on early motor development are sufficient to compensate for any slight adverse impact that low-dose prenatal methylmercury exposure might have..." (Grandjean et al. 1995).
- **Pediatrician follow-up for exposed children.** Children who have been exposed to mercury either in utero or after birth should see their pediatrician periodically for neurological examinations.

Treatment Documentation

CIEA cannot offer advice on what treatments to give your patients. The body of information continues to grow. We look forward to further evidence and the results of ongoing studies. We encourage you to join with other physicians and nurses and begin sharing information. What we can do is share with you what other health care providers have done.

Treatment for Dr. Hightower's patients consisted of either eating no fish for 6 months or only eating lower mercury-content fish. By changing their fish consumption patterns, blood mercury levels of patients fell to less than 2 mcg/L, and their symptoms have slowly improved, although they will have to be monitored to see if there are long-term effects and if a complete recovery is possible (Hightower 2009). Hightower's patients generally had a whole blood mercury level ranging from 2.0 to 89.5 mcg/L (Hightower 2003). Her advice to patients is to "stay well within EPA guidelines so as not to accumulate mercury at all until further research is concluded." Dr. Hightower did not advise her patients to receive chelation treatments because of the lack of scientific studies to justify their use on patients with low levels of mercury exposure. (Hightower 2009).

In an article published by the American Academy of Pediatrics, doctors Goldman, Shannon and the AAP Committee on Environmental Health recommend that the "most important and most effective treatment involves identifying the mercury source and ending the exposure." It is also recommended by these authors and others, that children who have been exposed to mercury either in utero or after birth see their pediatrician periodically for neurological examinations (Goldman, Shannon 2001). and consult with your local poison control center or local environmental health clinic for next steps and course of action.(Chander et al. 2011).

Nursing mothers who have mercury in their bodies may be concerned about passing mercury on to their babies. This must be considered on a case-by-case basis, and the levels of mercury in both baby and mother must be considered. In the Faroe Island study, researchers looked at motor development milestone achievements in a 21-month birth cohort (1022 infants, 1986-1987). The researchers found an inverse association with the duration of breast feeding, suggesting that the beneficial effects of "nursing on early motor development are sufficient to compensate for any slight adverse impact that low-dose prenatal methylmercury exposure might have on the end points" (Grandjean et al. 1995).

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