Fish Mercury
Medical Literature Review
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How much methylmercury (MeHg) is “safe?”

- Define “safe”
- Human reference dose (RfD): 0.1 mcg/kg body weight/day
- This corresponds to a blood level of about 4-5 mcg/l or hair of 1.0 mcg/g.
- Original Safety factor of 10?
- No exposure level has been found that does not affect the human body in some way, especially looking at the cellular level.
Most Noted Recent Mercury Sources

- Coal-burning power plants
- Mining
- Waste incinerators, hospitals, Crematoria
- Cement factories
- Thimerosal
- Chemical plants i.e. chlor-alkalai, fungicides, switches, florescent lights, gauges, etc.
- Shipwrecks, Spanish, WWII, Submarines
- Volcanoes, Earthquakes, Geothermal vents
- Latex house paint until 1991. Artists paint
- Amalgams for teeth
- Mercurochrome, vaccines, homeopathy
General Facts

1. Mercury cannot be cooked out of the fish!!
2. Methylmercury is on average 95% absorbed when consumed.
3. It is taken up by all tissues 1-2 days after a single dose.
4. It can penetrate every cell in the body, where it can disrupt cell division and molecular pathways.
5. Half-life in blood for majority of adults is about two months.
Humans are Not Created Equal

- Many genes can lead to higher tolerance or intolerance to toxicants and toxins
- Many genes influence whether we will have health or disease
Glutathione (GSH)

- It is the body’s master antioxidant and is responsible for the body’s detoxification system.
- It protects cells against damage from exposure to many external agents and oxidative stress.
- MeHg binds strongly to glutathione
- GSH complexes with toxicants and escorts them from the body in feces and urine.
- The human body makes it in the liver.
- Poor nutrition, especially poor intake of vitamin C and sulfur rich foods can reduce production of GSH
- People with certain genetic glutathione variants tolerate higher mercury exposures due to faster elimination and or better anti-oxidative glutathione-associated capacity.

(Vazquez 2014, Andreoli 2016)
Family Members are Different
Genetic Susceptibility
Glutathione and MeHg

- Glutathione S-Transferase T1 (GSTT1) and Glutathione S-Transferase M1 (GSTM1) genotype polymorphism Hg studies
  - GSTM1 null -/- 50% Asians and Caucasians. “Substantially lower prevalence in African and African Americans”
  - GSTT1 null -/- 50% Asians, 20% Caucasians.
  - Those with either or both of the GSTT1 or GSTM1 null genotypes have higher mercury levels in their blood given the same exposure.
  - This also transmits to more adverse effects to the growing fetus of those mothers who have the null genotype.

FDA-EPA Guidelines for Eating Fish that Contain Mercury

Eating fish when pregnant or breastfeeding can provide health benefits. Fish and other protein-rich foods have nutrients that can help your child’s growth and development. As part of a healthy eating pattern, eating fish may also offer heart health benefits and lower the risk of obesity.

Nutritional Value of Fish

The 2015-2020 Dietary Guidelines for Americans recommends:

• At least 8 ounces of seafood (less for young children) per week based on a 2,000 calorie diet
• Women who are pregnant or breastfeeding to consume between 8 and 12 ounces of a variety of seafood per week, from choices that are lower in mercury.

Fish are part of a healthy eating pattern and provide:

• Protein
• Healthy omega-3 fats (called DHA and EPA)
• More vitamin B₁₂ and vitamin D than any other type of food
• Iron which is important for infants, young children, and women who are pregnant or who could become pregnant
• Other minerals like selenium, zinc, and iodine.

https://www.epa.gov/mercury/guidelines-eating-fish-contain-mercury
Current FDA-EPA Fish Mercury “Advice”

![Image showing the guidelines for fish consumption](https://www.epa.gov/mercury/guidelines-eating-fish-contain-mercury)

For an adult, 1 serving = 4 ounces
Eat 2 to 3 servings a week from the “Best Choices” list (OR 1 serving from the “Good Choices” list).

For children, a serving is 1 ounce at age 2 and increases with age to 4 ounces by age 11.

If you eat fish caught by family or friends, check for fish advisories. If there is no advisory, eat only one serving and no other fish that week.

<table>
<thead>
<tr>
<th>Best Choices</th>
<th>Good Choices</th>
<th>Choices to Avoid</th>
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<tbody>
<tr>
<td>Anchovy</td>
<td>Herring</td>
<td>King mackerel</td>
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<tr>
<td>Atlantic croaker</td>
<td>Lobster, American</td>
<td>Shark</td>
</tr>
<tr>
<td>Atlantic mackerel</td>
<td>and spiny</td>
<td>Tilefish (Atlantic</td>
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<tr>
<td>Black sea bass</td>
<td>Mullet</td>
<td>Ocean)</td>
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<tr>
<td>Butterfish</td>
<td>Oyster</td>
<td>Tuna, albacore/white</td>
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<tr>
<td>Catfish</td>
<td>Pacific chub mackerel</td>
<td>white tuna, canned</td>
</tr>
<tr>
<td>Clam</td>
<td>Perch, freshwater</td>
<td>and fresh/frozen</td>
</tr>
<tr>
<td>Cod</td>
<td>and ocean</td>
<td>Tuna, yellowfin</td>
</tr>
<tr>
<td>Crab</td>
<td>Pickerel</td>
<td>Weakfish/seatout</td>
</tr>
<tr>
<td>Crawfish</td>
<td>Place</td>
<td>Tuna, canned light</td>
</tr>
<tr>
<td>Flounder</td>
<td>Pollock</td>
<td>(includes skipjack)</td>
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<tr>
<td>Haddock</td>
<td>Salmon</td>
<td>Whitefish</td>
</tr>
<tr>
<td>Hake</td>
<td>Sardine</td>
<td>Whiting</td>
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* Some fish caught by family and friends, such as larger carp, catfish, trout and perch, are more likely to have fish advisories due to mercury or other contaminants. State advisories will

[www.FDA.gov/fishadvice](http://www.FDA.gov/fishadvice)

[www.epa.gov/mercury](http://www.epa.gov/mercury)

[US Environmental Protection Agency](http://www.epa.gov)

[US FOOD & DRUG ADMINISTRATION](http://www.fda.gov)

https://www.epa.gov/mercury/guidelines-eating-fish-contain-mercury
Current FDA-EPA Fish Mercury “Advice”

Fish are a high quality protein source, and lower mercury fish are a good choice for everyone. This advice is specifically for women who are or might become pregnant, breastfeeding mothers, and children over 2 years but everyone can follow this advice.

Use the chart to help you choose which fish to eat each week. Eating a variety of fish is better for you and your child than eating the same type every time.

You can eat 2 to 3 servings a week of fish in the “Best Choices” category, based on a serving size of four ounces, in the context of a total healthy diet.

You can eat 1 serving a week of fish in the “Good Choices” category, but no other fish that week.

https://www.epa.gov/mercury/guidelines-eating-fish-contain-mercury
A Healthy Gut Biome is Important

Kohler, WI
Gastrointestinal and MeHg

- The intestinal barrier is a complex multilayer system consisting of an external “physical” barrier and an inner “functional” immunological barrier.

- MeHg has a toxic effect in the intestinal epithelium, which in turn increases epithelial permeability and impairment of the intestinal barrier. Also can adversely alter the gut microbiome.

- Changes in intestinal permeability and or microbiota has been associated with a number of conditions and diseases: Autoimmune disease, obesity, inflammatory bowel disease, irritable bowel, atopic diseases, allergies, asthma, Type 1 DM, Type 2 DM, CVD, celiac, neuropathology, etc.

Reduce Stress with Family and Friends
Hypertension (HTN) and MeHg

- US NHANES data 2003-2006, said no association of MeHg to HTN, but the mean blood mercury for the study population was 1.0 mcg/L. “Few subjects with high exposure to MeHg.” (Park 2013)

- >10 other studies, to include children, showed an association of MeHg to higher blood pressure (HTN).

- Most recent, was a study by Wells in 2017. Positive association of Hg with systolic and diastolic BP increase in African American pregnant women. Geometric mean for blood Hg 1.4 mcg/L with only 5 subjects > 5.8 mcg/L

- Mechanism proposed by Wildemann 2015: MeHg stimulated the renin-angiotensin system in rats.

Where is Everyone?
MeHg and Cardiovascular Disease (CVD) Epidemiology

- MeHg has been correlated with hypertension, coronary artery disease, myocardial infarction, stroke, increased carotid artery intimal thickness, atherosclerosis, arrhythmia, coronary dysfunction, and cardiomyopathy.

- MeHg negates the positive effects of the nutrients found in fish such as omega 3 fatty acids, minerals, vitamins B12, D, B6, Niacin.

- Two recent reviews of the literature each contain over 80 references (Houston 2014, Genchi 2017).

- Increased risk of CVD was seen in population studies as low as 2 mcg/g in hair (8 mcg/L blood).

- MeHg and Cardiac effects are the most challenged effects by the fishing industry and polluters, as they have been fighting for decades to maintain that fish is heart healthy, despite the contaminants.
Mercury and Cardiovascular Disease (CVD)

- Increased production of free radicals
- Increased reactive oxygen species (ROS)
- Increased superoxide anions
- The increment of ROS and reduction of antioxidant enzymes activity increase the risk of developing CVD
- Mercury increases LDL oxidation and destroys plasma membrane phospholipid integrity by externalization of phosphatidylserine
- Alters mitochondrial functions
- Inactivates paraoxonase, an extracellular antioxidative enzyme related to high-density lipoprotein (HDL)
- Activates phospholipase A₂ contributing to the development of several inflammatory diseases correlated with coronary artery disease, acute coronary syndrome, and cerebral plaque rupture
- Induces formation of arachidonic acid metabolites such as prostaglandins, thromboxanes, leukotriens and related compounds that are considered mediators of inflammatory response
- You can’t accumulate omega 3’s. They incorporate into cell walls. What is not used gets removed from the body. Only 2-3 times weekly for omega 3 intake needed. No added benefit having more omega 3’s.
- Other vitamins and minerals in fish are probably more important, which you need daily!
Diabetes
Find the Cure
Prevent the Cause
Diabetes

- Whether insulin or non insulin dependent, diabetes is partially genetic and partially environmental.
- Asians, North American Aboriginal people, African Americans are at greater risk (DMII)
- Highest rates by country: DMII
  - Marshall Islands 30.5% (Radiation, junk food)
  - Tuvalu 27.3% (Junk food)
  - Nauru 24.1% (Obesity)
  - New Caledonia 23.4% (Poor diet)
  - Kiribati 22.7% (Smoking, environmental, poor diet)
  - French Polynesia 22.6% (Obesity, poor diet)
  - Mauritius (22%)
  - Guam (21.5%)
  - Solomon Islands (18.7)
  - Saudi Arabia (17.7%)
  - China 11%, pre-diabetes 36% (highest # by total)
  - USA (9.4%)
  - India 7.2% (Second highest # by total)
- Highest rates by country (Top 15): DMI
  - Finland, Sweden, Saudi Arabia, Norway, UK, US, Australia, Kuwait, Denmark, Canada, Netherlands, Germany, New Zealand, Poland, Czech Republic
Diabetes USA

- Whether insulin or non-insulin dependent, diabetes is partially genetic and partially environmental.
- Rates went up drastically after 1955. The incidence began increasing after WWII (1945).
- Asians and North American Aboriginal people are at greater risk.
- Native American and Alaskan Native groups 16% prevalence DMII, highest of all ethnic/racial groups (US ≈10% rate).
- Canada First Nations 24.4%
- Arizona Pima Indians, highest DMII prevalence rates in the world at 60%.
- Obesity, poor nutrition, sedentary, are major causes. Dioxin, radiation, trans fats, other environmental causes are being discovered.
- MeHg is now questioned as a contributor.
Methylmercury and Diabetes

MeHg adversely affects islet cell development and function resulting in insulin resistance and hyperglycemia, which may lead to DM.

Faroes Study and 2 large US studies (Nurses and healthcare professionals) showed no association, corresponding average hair mercury levels 2.11-3.67 mcg/g, corresponds to about 8-15 mcg/L in blood.

Greenland Inuit study. Impaired fasting glucose and DMII prevalence increased with increasing MeHg. MeHg range (0.05-49 mcg/L).

Prospective cohort study of people of African American or Caucasian descent. 18 years followed. Toenail mercury used (corresponds to a blood level no more than 10 mcg/L). Significant linear association between decreased beta-cell function and increased toenail mercury. They concluded that this exposure of MeHg in young adulthood may elevate risk of DM later in life.

First Nations Food Nutrition Environment Study showed the risk for DM is 2 ½ times higher among First Nations people in Ontario, for those who consume fish at least once weekly as opposed to < once monthly or no fish at all. PCB’s, DDE was associated. No MeHg testing results given.

Taiwan study, RBC mercury was found to be significantly associated with insulin resistance and DMII with increasing blood mercury, and the addition of dioxins further increased risk of insulin resistance.
Mercury and Autoimmune

- Organic mercury, elemental mercury, and inorganic mercury have all been shown to increase antinuclear antibody (ANA) titers in those genetically predisposed.
- ANA formation is a sign of immune dysregulation
- ANA can pre-date clinical disease by months to years, and is age dependent. It can wax and wane over time.
- ANA associated diseases: Lupus, Sjogrens, scleroderma, polymyositis, dermatomyositis, autoimmune hepatitis, mixed connective tissue disease, juvenile idiopathic arthritis.
- Eli Lily had the first patent on ethylmercury (thimerosal) in 1928. Patented as an antiseptic. Used as and adjuvant. Replaced by other adjuvants such as aluminum, squalene (MF59), Chilean soap bark tree (ASO1B), Cytosine phosphoguanine (CpG 1018).
- CDC does not list mercury as a vaccine adjuvant on their website. It describes it as an antiseptic. Phased out of childhood vaccines beginning 1999. Only certain flu vaccines contain thimerosal.
MeHg and Autoimmune Epidemiology

- NHANES: MeHg in low levels generally considered safe, association with subclinical autoimmunity, higher ANA in reproductive age females (Somers 2015)

- Study of 9,400 proteins in the blood of individuals exposed to inorganic and or MeHg. High Hg group had elevated serum titers to 3,760 proteins compared to the low exposure group of 49 proteins. Auto Ab with highest titer in the high ANA/Hg group was Anti-glutathione S-transferase (anti GSTA 1) (Motts 2014)

- MeHg increases inflammatory cytokines. Those who had a positive ANA, MeHg increased pro-inflammatory and reduced anti-inflammatory cytokines greater (Nyland 2011)

- Omega 3’s were not able stop the inflammatory response that MeHg caused in Lupus (SLE) patients (Crowe 2018)

- Prospective study: 15,740 children. Fish consumption more than once weekly during pregnancy as well as during child’s first year, associated with Juvenile idiopathic arthritis (JIA) and ANA positivity. Al, Cd, Hg, Li correlated with the amount of fish the mothers consumed, and were higher in the children with JIA (Kindgren 2019)
Lead neurologist for the study opined, “children who were determined were mildly affected were children looking normal, running around, behaving normally. And only with the most minimal retardation. They were a little slower to walk, perhaps a little slower to talk. They had increased frequency of seizures compared to the control group. Their height was slightly shorter. Their head circumference was slightly smaller. These were all very, very, minimal effects.”