Welcome to the CLU-IN Internet Seminar

Capturing Mercury: The Human Body Experience

Sponsored by: University of California Davis Superfund Research Program

Delivered: February 6, 2013, 4:00 PM - 5:00 PM, EST (21:00-22:00 GMT)

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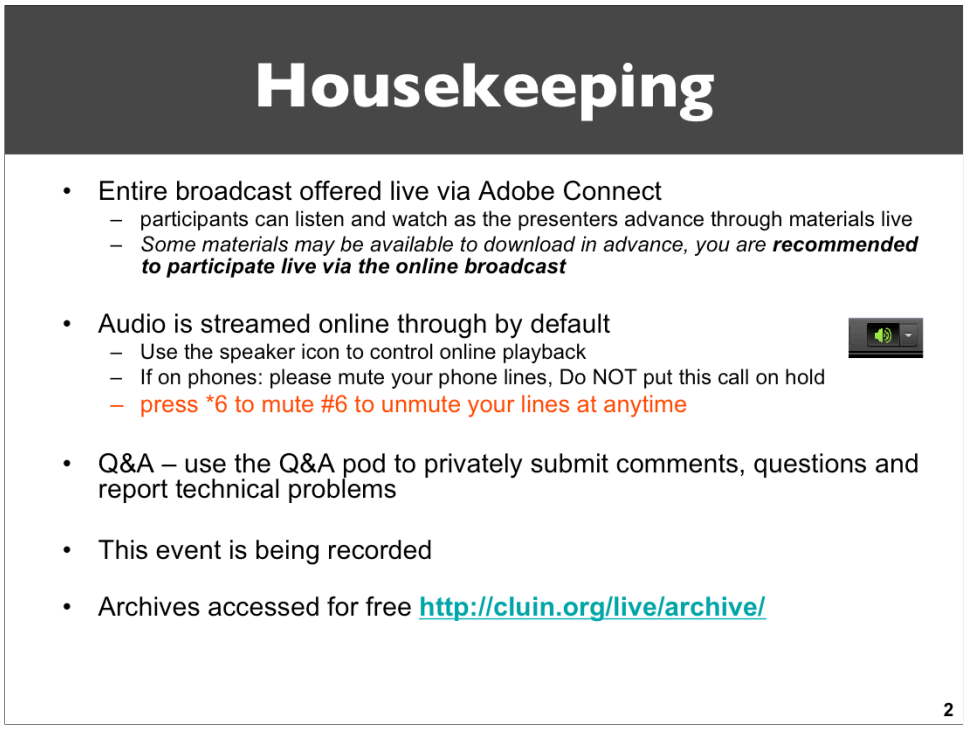
Visit the Clean Up Information Network online at www.cluin.org



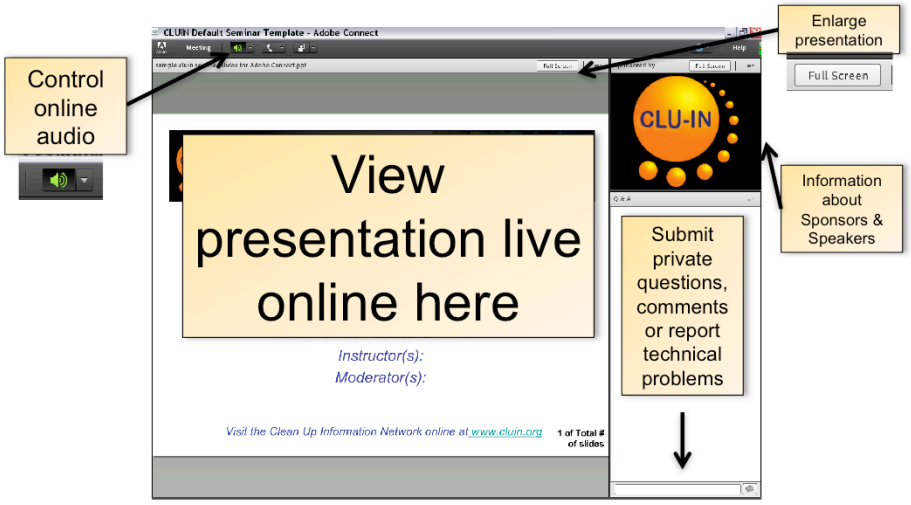
Although I'm sure that some of you have these rules memorized from previous CLU-IN events, let's run through them quickly for our new participants.

Please mute your phone lines during the seminar to minimize disruption and background noise. If you do not have a mute button, press *6 to mute #6 to unmute your lines at anytime. Also, please do NOT put this call on hold as this may bring delightful, but unwanted background music over the lines and interupt the seminar.

You should note that throughout the seminar, we will ask for your feedback. You do not need to wait for Q&A breaks to ask questions or provide comments. To submit comments/questions and report technical problems, please use the ? Icon at the top of your screen. You can move forward/ backward in the slides by using the single arrow buttons (left moves back 1 slide, right moves advances 1 slide). The double arrowed buttons will take you to 1st and last slides respectively. You may also advance to any slide using the numbered links that appear on the left side of your screen. The button with a house icon will take you back to main seminar page which displays our agenda, speaker information, links to the slides and additional resources. Lastly, the button with a computer disc can be used to download and save today's presentation materials.

With that, please move to slide 3.

New online broadcast screenshot



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Capturing Mercury
The Human Body Experience

Jane M. Hightower, MD
California Pacific Medical Center
San Francisco, CA

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Diagnostic Nightmare of the human blood mercury safety level 2000

- Laboratory: *Normal* is less than 13 mcg/l at the end of a workweek.
- Cecil's Textbook of Medicine 1996: *Normal* is less than 50 mcg/l.
- EPA: Less than 5.0 mcg/l.
- NRC: Less than 5.0 mcg/l
- Finnish men cardiac study <8.0 mcg/l
- FDA: Undeclared? 200 mcg/l? 400?

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Why Methylmercury is a Menace to Human Health

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.
6. Binds thiol groups

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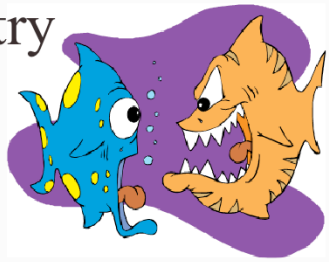
Fishing Industry Mantra

There has never been a case of mercury poisoning from normal consumption of ocean-going fish in this country



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Poison

- Middle English 13th century
- A substance that through its chemical action usually kills, injures, or impairs an organism
- Something destructive or harmful
- A substance that inhibits the activity of another substance or the course of a reaction or process

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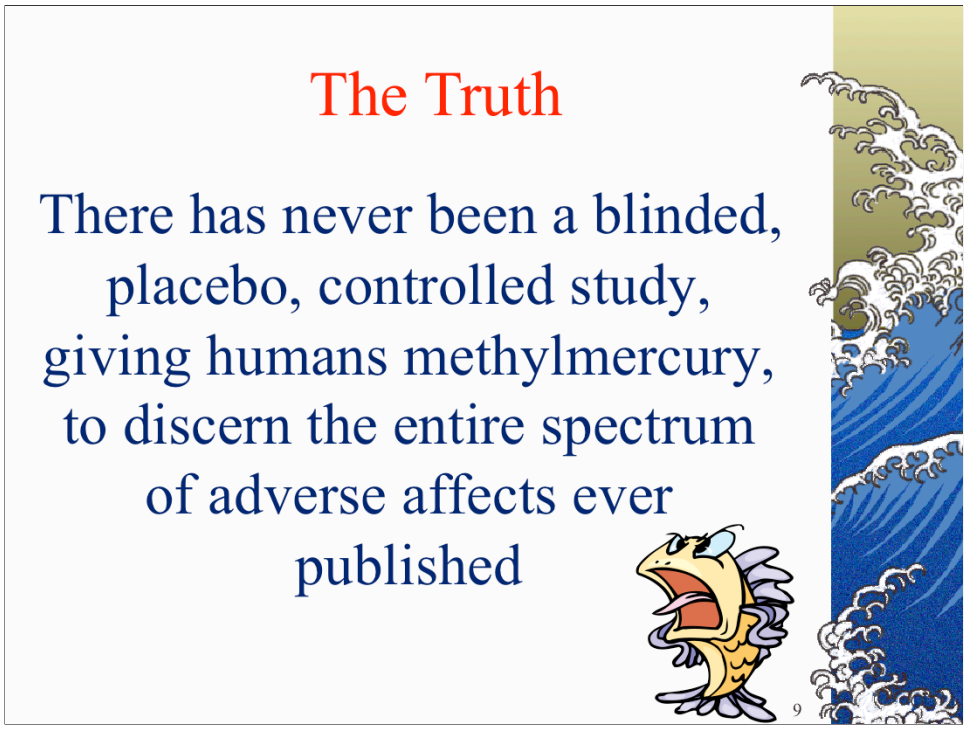
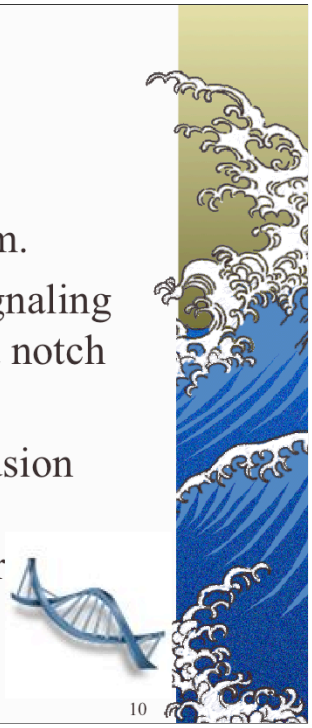


Therefore, in-vitro studies are critical

The Human Body

- ✓Hard drive: DNA encoding system.
- ✓Software included: Cell to cell signaling system programs--NF-Kappa B and notch signaling.
- ✓Special software/firewall for intrusion prevention, firewall and antivirus: Glutathione, metallothionein, bacter defense...



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Nuclear Factor Kappa B
The Master Switch

- Thiol protein complex that controls the transcription of DNA.
- Found in nearly all animal cell types.
- Involved in cellular responses to stimuli such as stress, cytokines, free radicals, ulatraviolet radiation, oxidized LDL, and bacterial or viral antigens.
- First responder to harmful cellular stimuli, where its binding to DNA affects gene expression.
- KF kappa B lays in wait in cytoplasm, therefore not active unless stimulated.
- Physiological responses: Inflammatory or immune response, a cell survival response, or cellular proliferation.
- Incorrect signaling/chronically active NF Kappa B leads to cancer, inflammation, autoimmune disease, infection, improper immune development.

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Glutathione

- It is the most abundant intracellular thiol peptide.
- It contains one amino acid residue each of glutamic acid, cysteine, and glycine.
- Plays an important role in biological oxidation-reduction processes and as a coenzyme.
- Key to breakdown/inactivation/protection against numerous toxicants to include methylmercury.
- Glutathione complexes with toxicants and escorts them from the body in feces and urine.
- The human body has to make it.

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Mercury (all forms of it) binds to glutathione through a process catalyzed by glutathione S transferase

Metallothionein

- Family of thiol proteins that have the capacity to bind both physiological (zinc,copper, selenium) and xenobiotic (mercury, cadmium, silver, arsenic) heavy metals.
- May provide protection against metal toxicity.
- In humans, large quantities are produced primarily in the kidney and liver.

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Methylmercury binds strongly to thiol compounds

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Thiol

- A thiol is a class of organic chemical compounds similar to the alcohols and phenols but containing a sulfur atom in place of the oxygen atom (sulfhydryl).
- Thiol compounds (mercaptans) form strong complexes with many metal ions.
- Many cofactors (important helper molecules) are thiols.
- The term "mercaptan" was derived in 1835 from the Latin *mercurium captans* (capturing mercury) because it forms its strongest bond with mercury.

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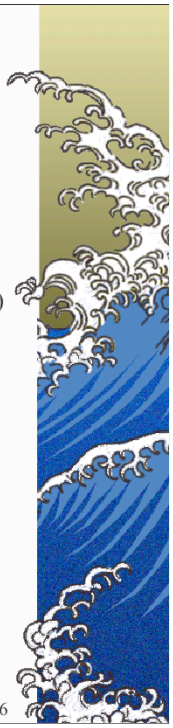
The human body depends on sulfhydryl bonded molecules to run important cellular functions.

Important Thiols

- Nuclear Factor Kappa B (NF Kappa B)
- Glutathione
- Metallothionein



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NF Kappa B and Mercury

- Mercury prevents NF Kappa B---DNA binding by mercaptide (S-H) bond formation.
- Mercury interferes with NF Kappa B's ability to bond with DNA to receive proper signaling. Even at low levels of exposure.
- Inhibition of the NF Kappa B—DNA binding by mercury modulates cytokine expression and suppresses nitric oxide synthesis.
- Enhances the sensitivity of kidney cells to apoptotic stimuli which kidney cells are otherwise resistant.

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Glutathione and Mercury

- Glutathione binds most strongly to mercury.
- Mercury is escorted from the body in urine and feces as glutathione conjugates.
- Glutathione keeps toxicants from causing cellular damage and stimulating NF Kappa B.

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Is Selenium the fishing industry's methylmercury repellant?

- Ocean fish Se content is fairly uniform amongst fish species.
- Methylmercury content can vary over 100 times between fish, even amongst the same species.
- Se is an integral part of glutathione. It gets used up as glutathione is complexed with mercury to be eliminated from the body.
- Se is tightly regulated in the human body.

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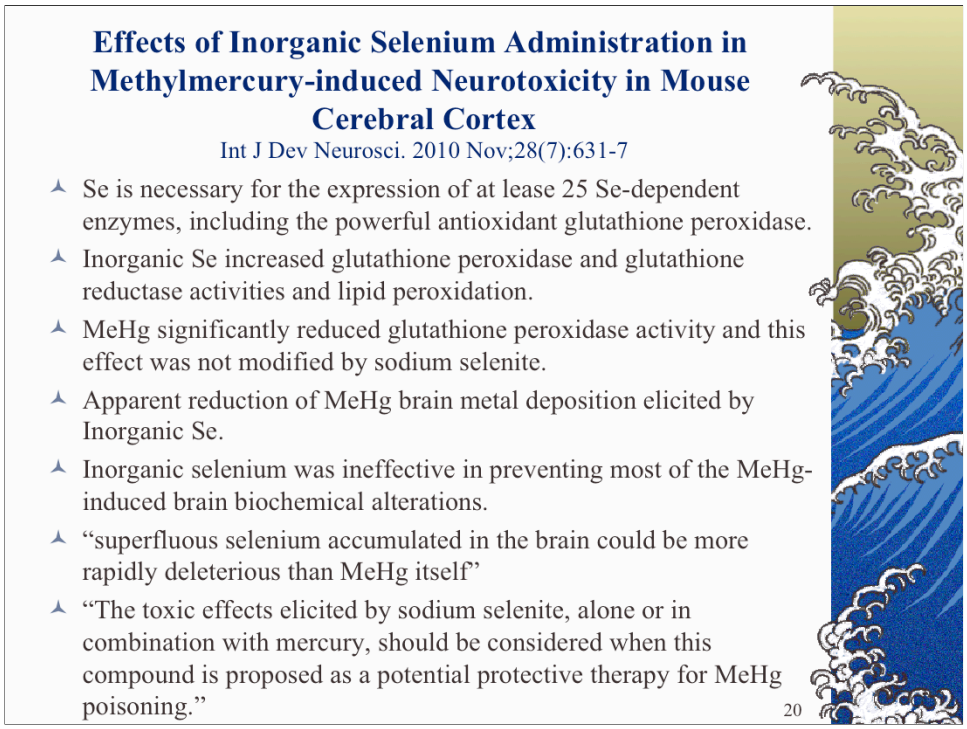


This was an investigation of the effects of chronic exposure to sodium selenite on brain energy metabolism and oxidative stress parameters in MeHg-poisoned mice.

Inorganic Se is toxic and should not be used for the purpose of countering mercury.

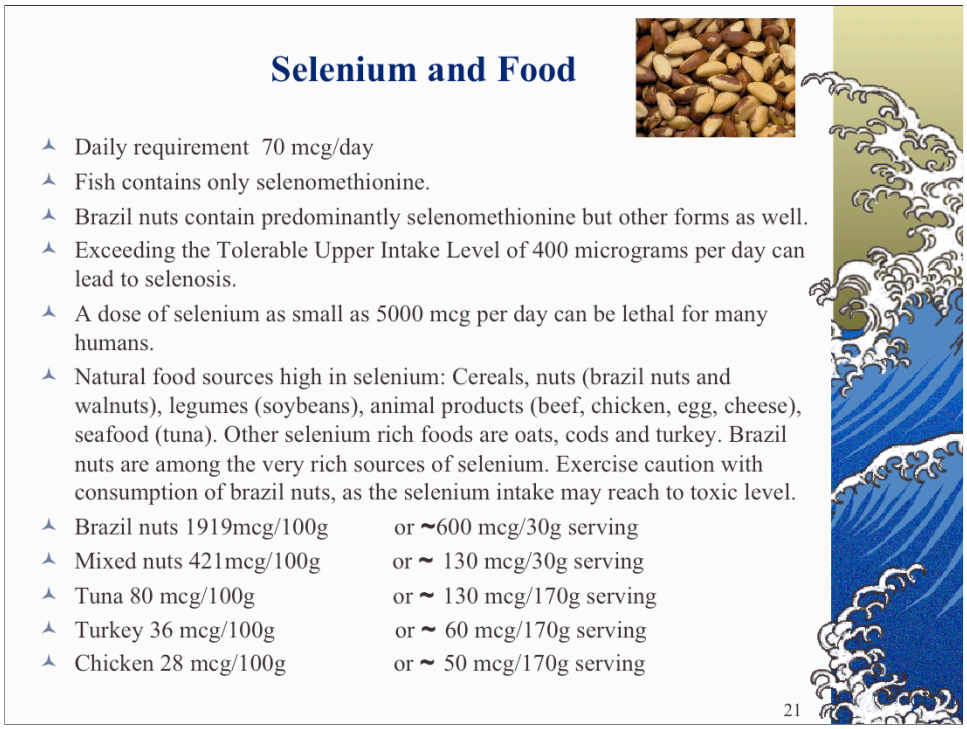
Se inhibited mitochondrial complex enzyme activities and induced oxidative stress.

MeHg-induced brain toxicity is also associated with impairment of mitochondrial function.

Na2SeO3 metabolism involves the transformation to hydrogen selenide (H2Se), the central metabolite in the assimilatory and excretory pathways of selenium via selenoglutathione with the participation of thiols. The interaction between selenium and mercury depends on the glutathione-mediated H_2Se formation.

Another study showed that selenium administration to MeHg poisoned rodents increased the brain concentrations of mercury as a HgSe salt. Little is known about the long term fate of this insoluble compound.

Wouldn't you want dietary Se to be available for glutathione production?



Selenium is a trace mineral that is essential to good health but required only in small amounts. Selenium is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. The antioxidant properties of selenoproteins help prevent cellular damage from free radicals. Free radicals are natural by-products of oxygen metabolism that may contribute to the development of chronic diseases such as cancer and heart disease. Other selenoproteins help regulate thyroid function and play a role in the immune system.

Acute oral exposure to selenium compounds results in pulmonary edema and lesions of the lung; cardiovascular effects such as tachycardia; gastrointestinal effects including nausea, vomiting, diarrhea, and abdominal pain; effects on the liver; and neurological effects such as headaches, irritability, chills, and tremors.

Chronic (long-term) exposure to high levels of selenium in food and water results in discoloration of the skin, deformation and loss of nails, reversible loss of hair (baldness), excessive tooth decay and discoloration, a garlic odor to the breath, weakness, lack of mental alertness, and listlessness.

Brazil nuts. 8 nuts=30 g.

Bottom Line

- Don't waste your limited supply of the selenium/ glutathione detox system on unnecessary toxicants such as MeHg.
- MeHg depletes glutathione.
- MeHg can also directly bind to organic and inorganic Se and therefore make Se unavailable for glutathione production.
- Depletion of glutathione leaves the body more susceptible to further toxicant exposure and to exposure to other toxicants that also go through the glutathione pathway.
- In all chronic disease, low or deficient glutathione levels are found. This can be organ specific.
- Too much mercury can then lead to NK Kappa B stimulation.
- Most diseases are found to be a result of NF Kappa B mis-signaling.

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Longevity Game

- Quiescent but appropriately responsive NF Kappa B.
- Plenty of glutathione.
- Appropriate DNA for the environment you live in.

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Living Organisms Must Balance Oxidant/Antioxidant Status

A Pro inflammatory and anti inflammatory state is constantly oscillating in the human body

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Humans are Not Created Equal

- Glutathione polymorphisms
- NF Kappa B polymorphisms
- Metallothionein polymorphisms
- Vitamin D Polymorphisms

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Pharmacology science: Metabolism highly variable between individuals.

Polymorphism

- Multiple/variable alleles of a gene within a population, usually expressing different phenotypes.
- Allows for the human population to survive as a whole in many environments.
- Some polymorphisms allow protection, and some increase susceptibility to a cell insult.
- Determines the expression of toxicity or disease.

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"Functional differences between these alleles and their uneven distribution in the wild suggest that different genotypes could be favored in different environments, perhaps environments that vary in their levels of peroxides or thiol-reactive compounds." **Two alleles of NK Kappa b in the sea anemone Nematosella vectensis are widely dispersed in nature and encode proteins with distinct activities. PloS One. 2009 oct 6;4(10):e7311**

Glutathione-S-Transferase polymorphism, metallothionein expression, and mercury levels among students in Australia

Sci Total Environ. 2007.Oct 15;385(1-2):37-47.

- GST T1 and GST M1 deletion polymorphisms
- Hair mercury concentrations are significantly increased in persons with the double deleted genotype (GSTT1-/- and GSTM1-/-) compared to persons with the intact genotype (GST1+/+ and GSTM1+/+)

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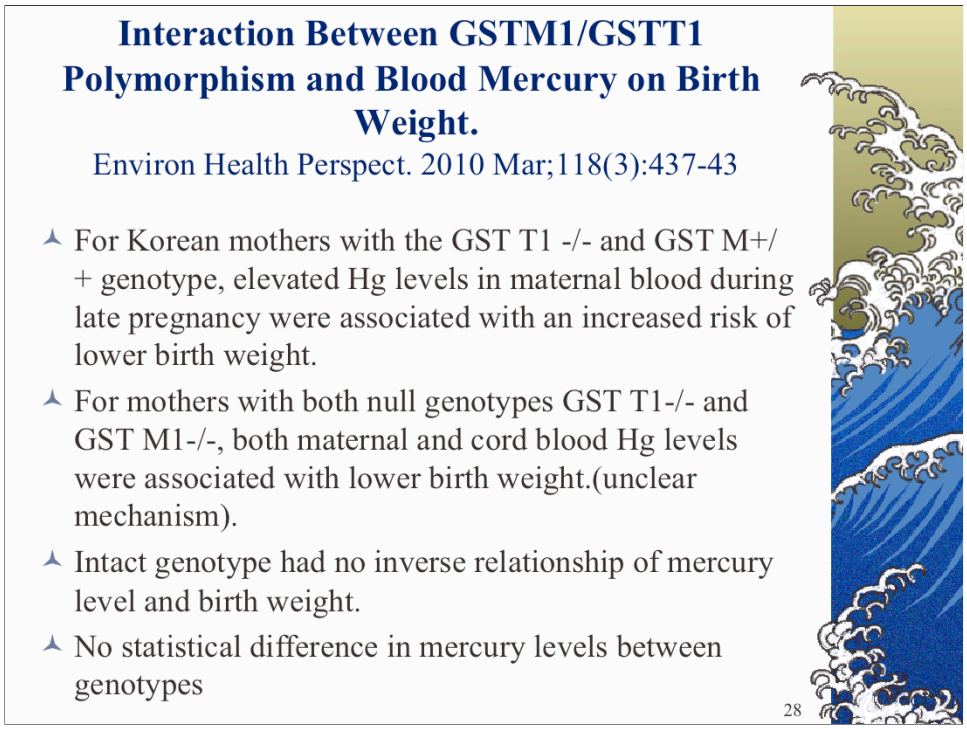
GST's conjugate glutathione to a variety of electrophilic compounds and are involved in the detoxification of mercury.

GST T1 and GST M1 null polymorphisms cause loss of functionality.

These null genotypes are associated with increased oxidative stress.



Paper was done in Korea on women.

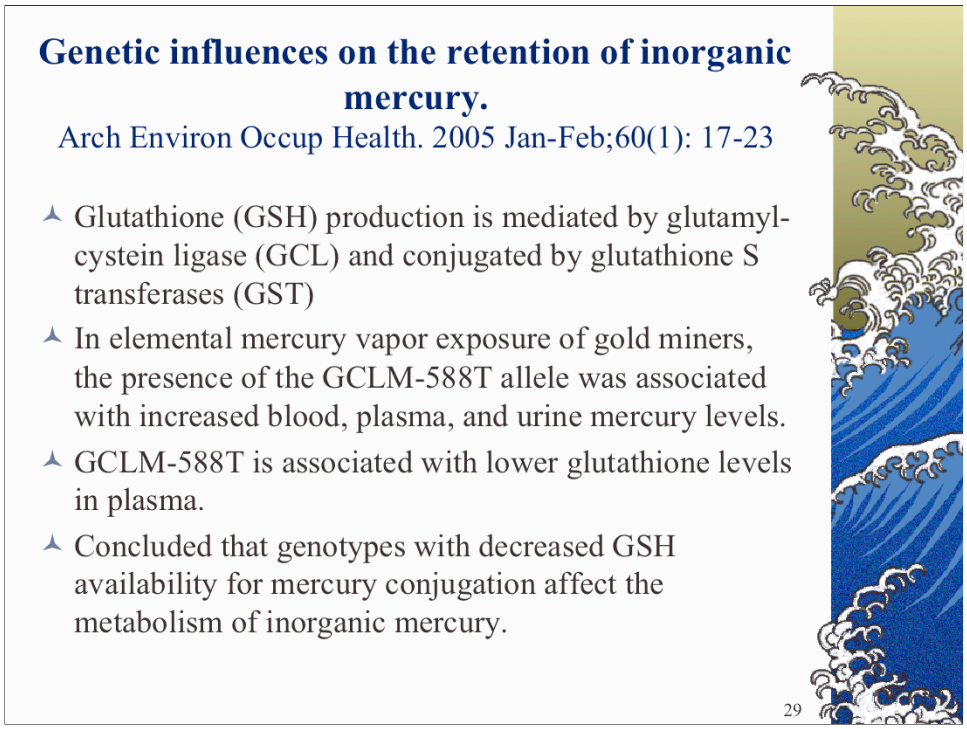
Double null was most obvious.

"This implies that an effect of *GSTM1*/*GSTT1* on the association between Hg and birth weight might be mediated by genetic modification on the oxidative stress level induced by Hg rather than an effect of *GSTM1*/*GSTT1* on the metabolism of Hg."

In other words, they did not have an explanation. ? NF Kappa B?

Mean maternal blood in late pregnancy 3.3 mcg/l, mean cord blood 5.53 mcg/l

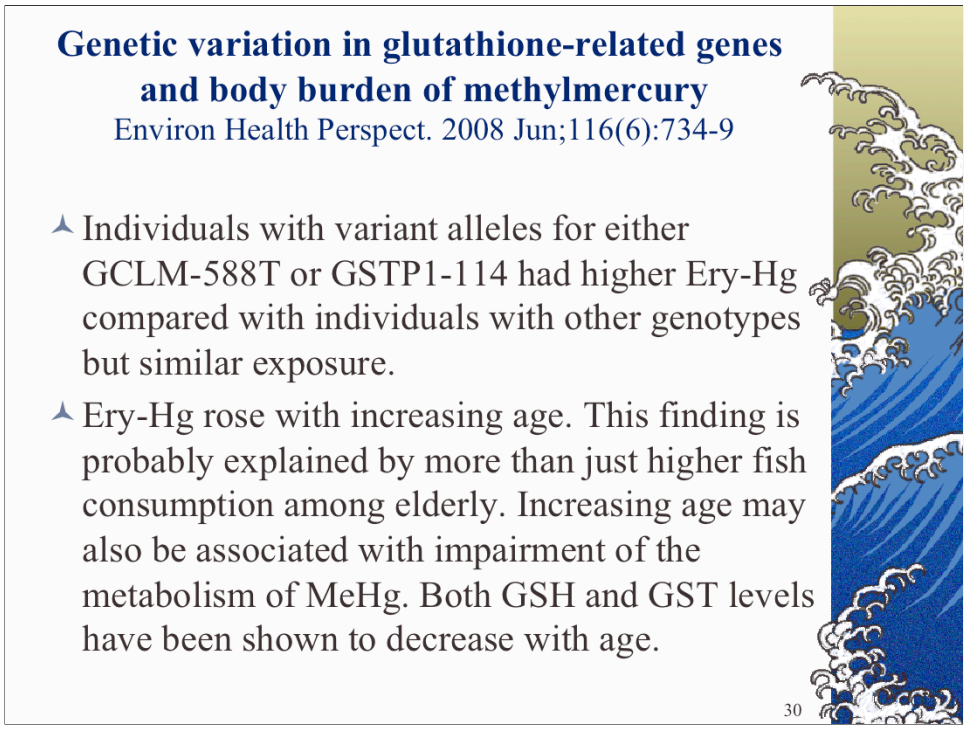
Low birth weight can be associated with adverse fetal/ infant outcomes.



Tuan's comment on "don't humans just make more glutathione?"

Alcohol flush reaction (colloquially referred to as Asian Flush, Asian Red or Asian Glow) is a condition in which the face and/or body experiences flushes or blotches, due to an accumulation of acetaldehyde. The acetaldehyde accumulation can be caused by a missense polymorphism that encodes the enzyme, acetaldehyde dehydrogenase (ALDH2), normally responsible for breaking down acetaldehyde, a product of the metabolism of alcohol.

Research has shown that a history of facial flushing when drinking is indicative of ALDH2 deficiency, and that an ALDH2-deficient drinker who drinks 2 beers per day has 6 to 10 times the risk of developing esophageal cancer as a drinker not deficient in the enzyme.

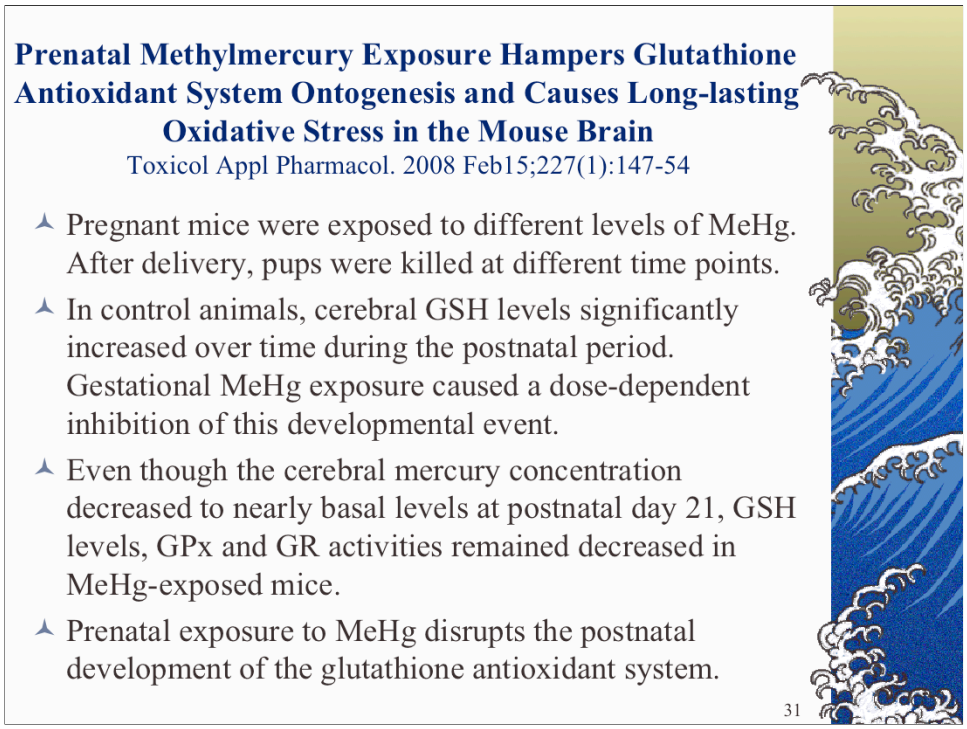


Same authors as 2005 Arch Environ Occup Health paper.

The Role of Intracellular Glutathione in Inorganic Mercury-induced Toxicity in Neuroblastoma cells

Neurochem Res. 2009 Sept;34(9):1677-84

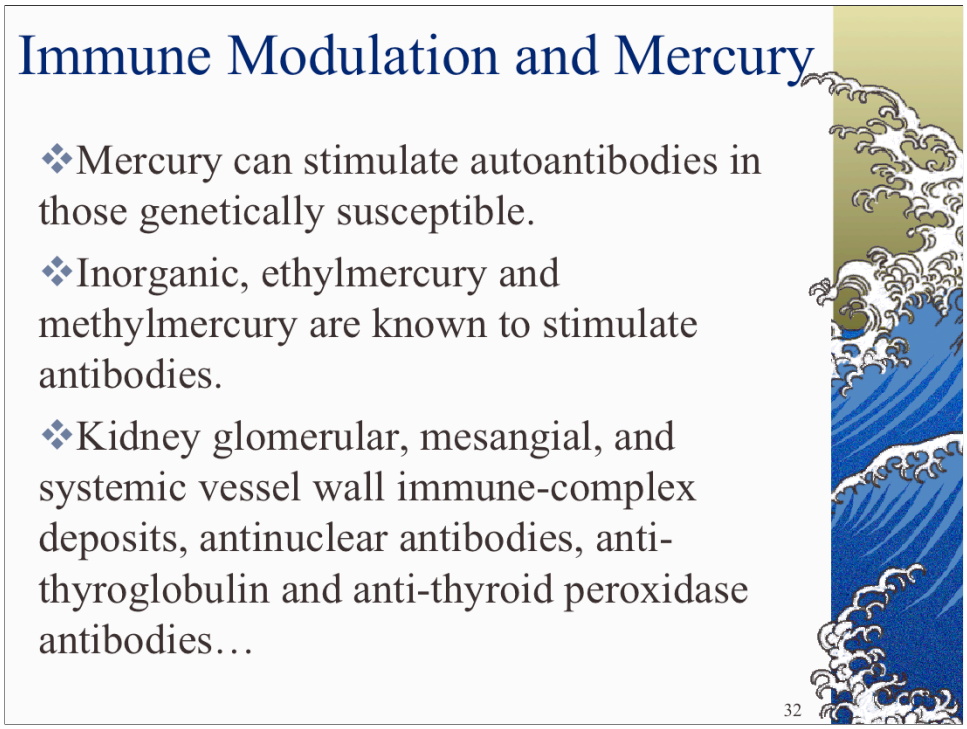
"The availability of GSH to the cells may not be sufficient to provide protection against mercury toxicity and the de novo synthesis of intracellular GSH is required to prevent the damaging effects of mercury."



GPx= glutathione peroxidase

GR= glutathione reductase

Methylmercury is thought to trigger cell death via a primary depletion of glutathione but in the absence of ROS overproduction.

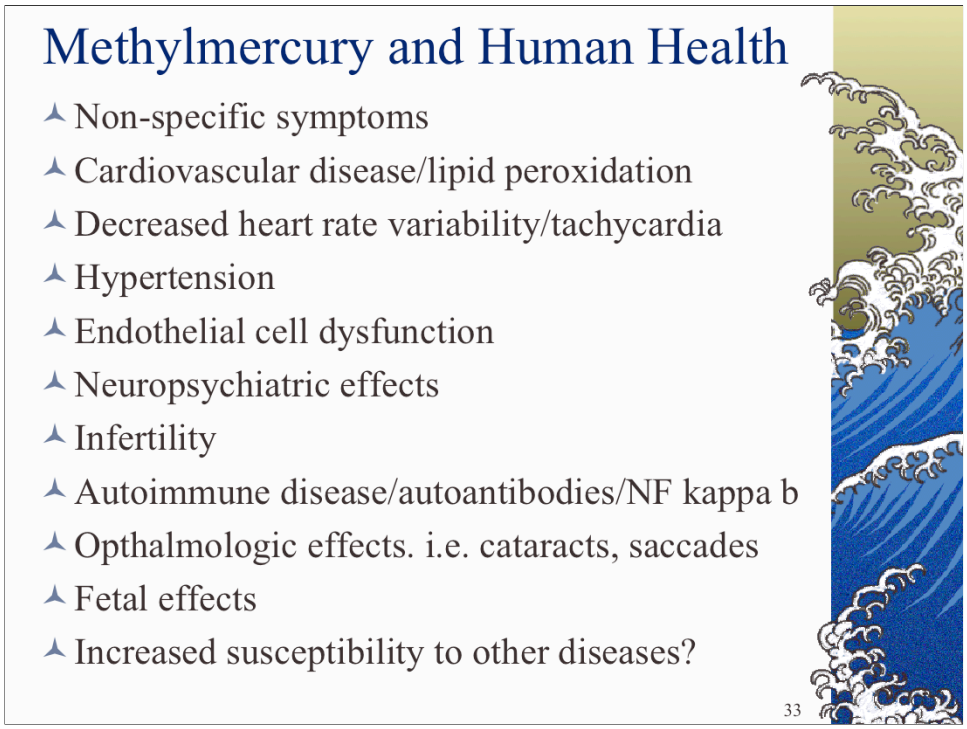


Anti TPO and anti TG Ab study and hypersensitivity (lymphocyte proliferation test) and amalgam.

Compared to Ab levels at the beginning of the study, only patients with mercury hypersensitivity who underwent amalgam replacement showed significant decrease in the levels of both anti-tpo and anti-tg antibodies

Melisa and USA

Levels of autoantibodies in patients with or without mercury hypersensitivity who did not replace amalgam did not change.



Does MeHg allow for other chemicals to be toxic at lower exposures?
Hg plus Pb---LD50--100 times more lethal than either agent alone.

Many countries involved in MeHg effects.

USA, Brazil, Bolivia, Spain, Sweden, Denmark, Japan, Korea, China, India, Germany, Canada

Majority of papers I pulled were published in the last two years.

Two papers out of Japan's Tohoku University and Okayama University in 2010. Positive correlation to HTN, and increased HR

One showed that increased HR (sympathodominant state) occurred at the WHO's Provisional Tolerable Weekly Intake.

Environmental Working Group Body Burden Projects

EWG.org

- 10 American infants: Up to 358 chemicals were found in cord blood. 232 of them have been targets of regulatory action and government controls. One newborn had 191 individual chemicals.
- In all, EWG tested 186 individuals from cord blood, infants, children, and adults for 552 chemicals and have detected over 414.
- Because of the mercaptan reliance for detox, these will all be second in line to mercury for their elimination.

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Sensitive Individuals

- Developing brains.
- Those with polymorphisms in any of the detox or protective pathways.
- Concurrent toxicants.
- Chemotherapy patients/cancer patients
- Autoimmune patients.
- Those genetically susceptible to cancer/ autoimmune disease.
- Atherosclerosis/coronary artery disease.
- Gastrointestinal disease.
- Chronic infections/TB, MAC, HIV, Lyme.
- Transplant patients.

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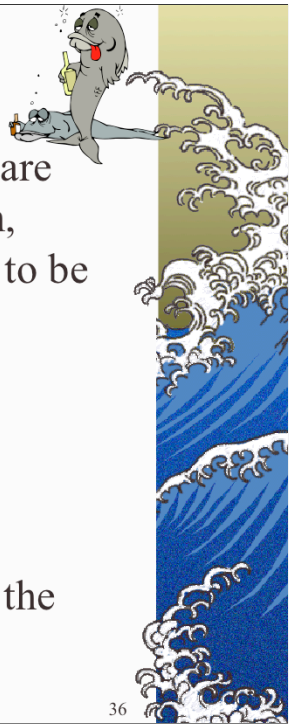
Poison



- Paracelsus (1493-1541): "All things are poison and nothing is without poison, only the dose permits something not to be poisonous."
- Do adverse effects determined at the cellular level, but not previously identified by epidemiology, still constitute a poison?
- Where do we draw the line on when the dose doesn't make the poison?

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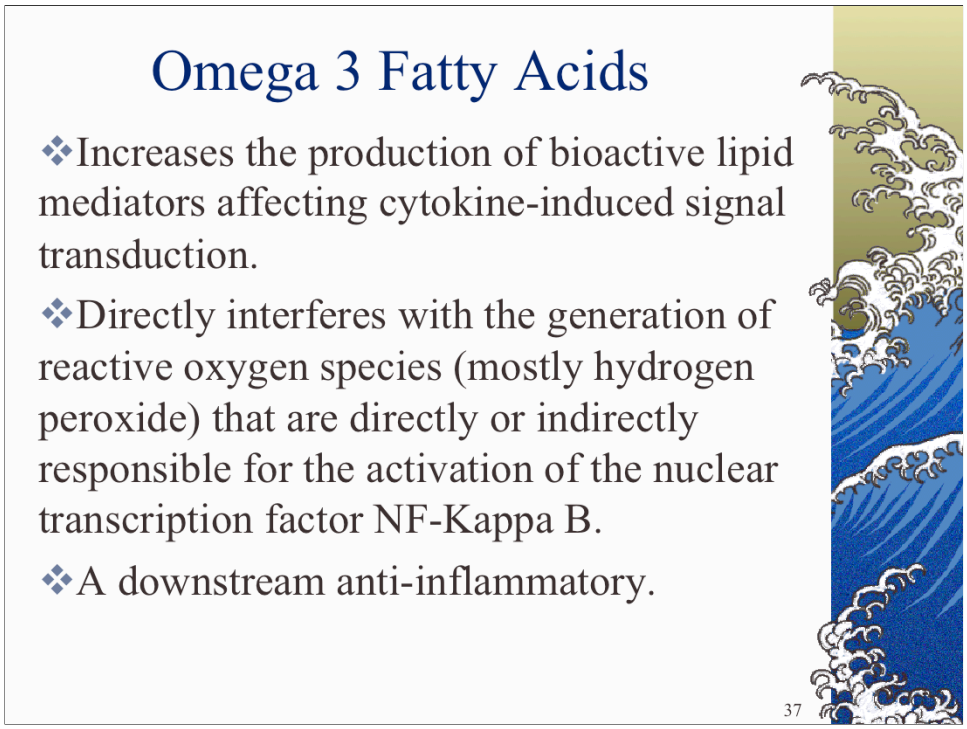
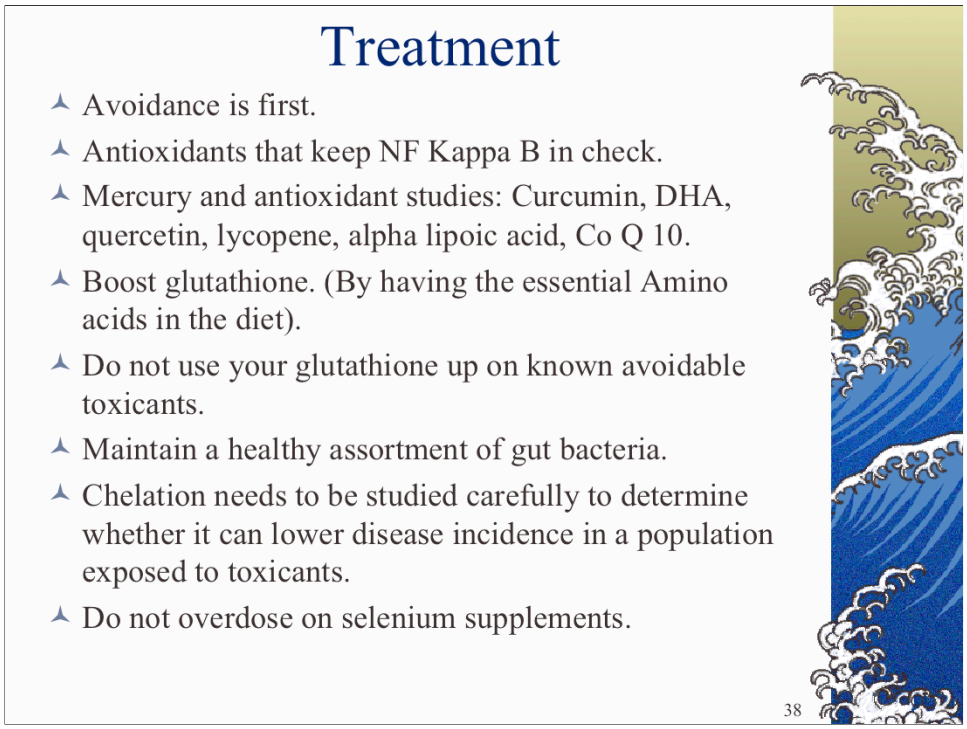


Tries to inhibit the effects on the end targets from an out of control immune system.

Said another way, Omega 3's directly or indirectly suppresses nuclear transcription factors such as NF kappa B. Which in turn will reduce the production of pro-inflammatory enzymes and cytokines, including Cyclooxygenase-2 (COX-2), TNF-alpha, IL-1beta

PCB's can also affect NF kappa B

One study from U of Kentucky showed that in vitro endothelial cells, in the presence of PCB 77, omega 3 Alpha linolenic (ALA) reduced NF kappa b and inflammatory cytokines where omega 6 Lenoleic (LA) increased them. The ratio of ALA to LA was important for the regulation of PCB induced inflammatory markers



D3

Curcumin, DHA, lycopene, quercetin (Plant genus polygala), alpha lipoic acid

Probiotic

Whey protein concentrate and antioxidant diet.

Lycopene is a bright red carotene and carotenoid pigment and phytochemical found in tomatoes and other red fruits and vegetables, such as red carrots, watermelons and papayas (but not strawberries or cherries). Although lycopene is chemically a carotene, it has no vitamin A activity.

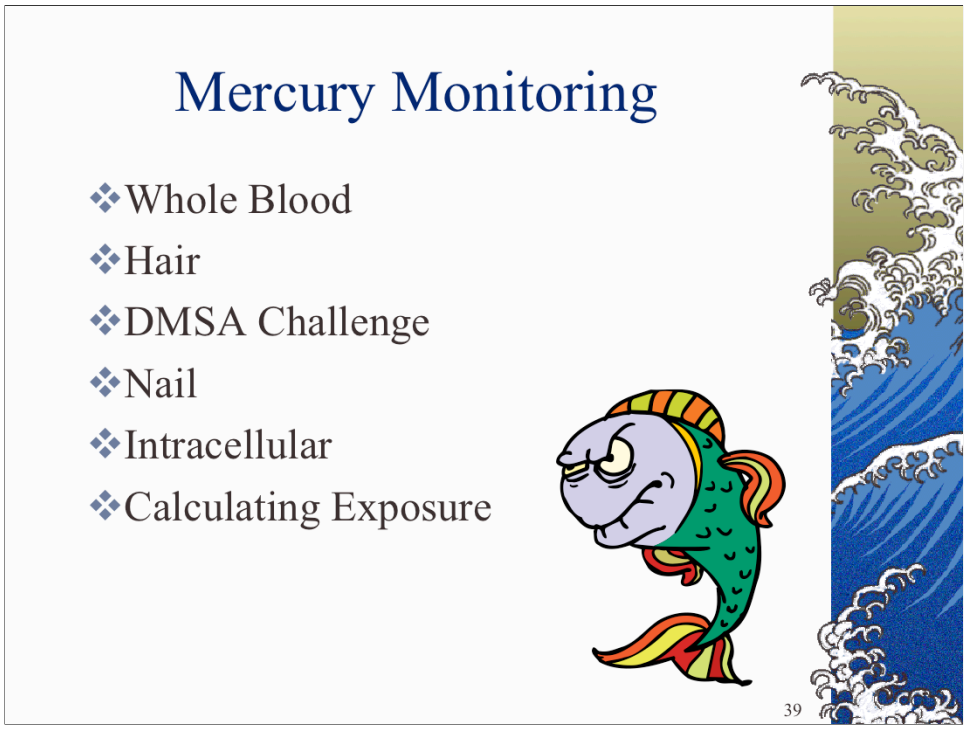
No fried food

No food cooked on high heat

No burned food

No artificial additives, preservatives

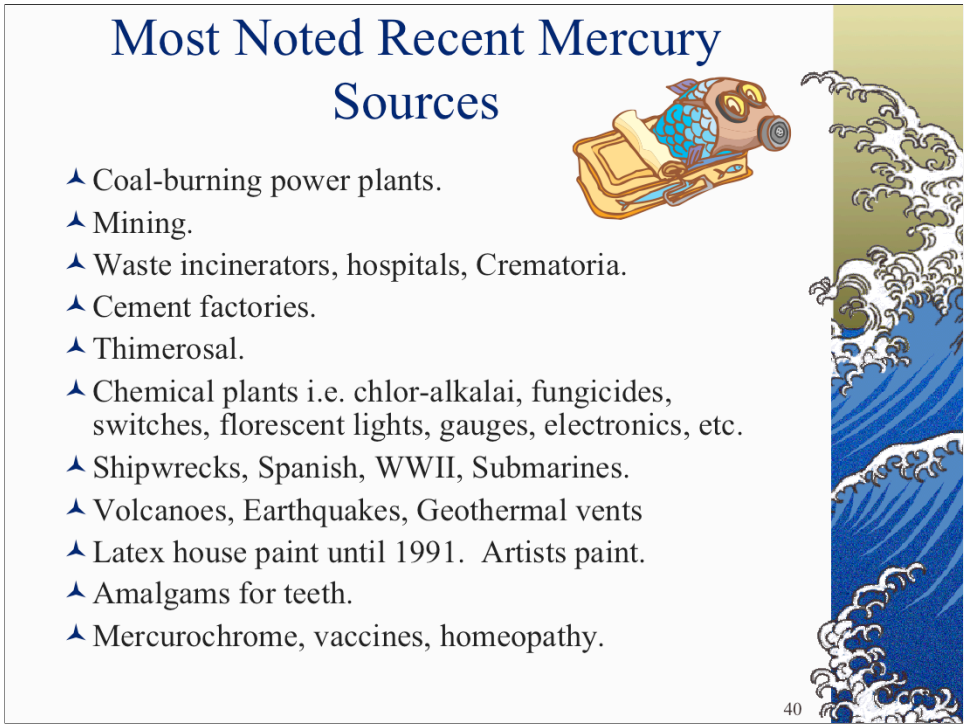
Eat real or clean food.



?threshold for MeHg causing disease.
Depends on your genetics and oxidant status.

Learning to choose low mercury fish
No amalgam
No thimerosal
>140 nations agreed to make a treaty to stop mercury pollution

Keep blood Hg <5.0
Keep load less than 0.1 mcg/kgbw/day



Pollution continues.

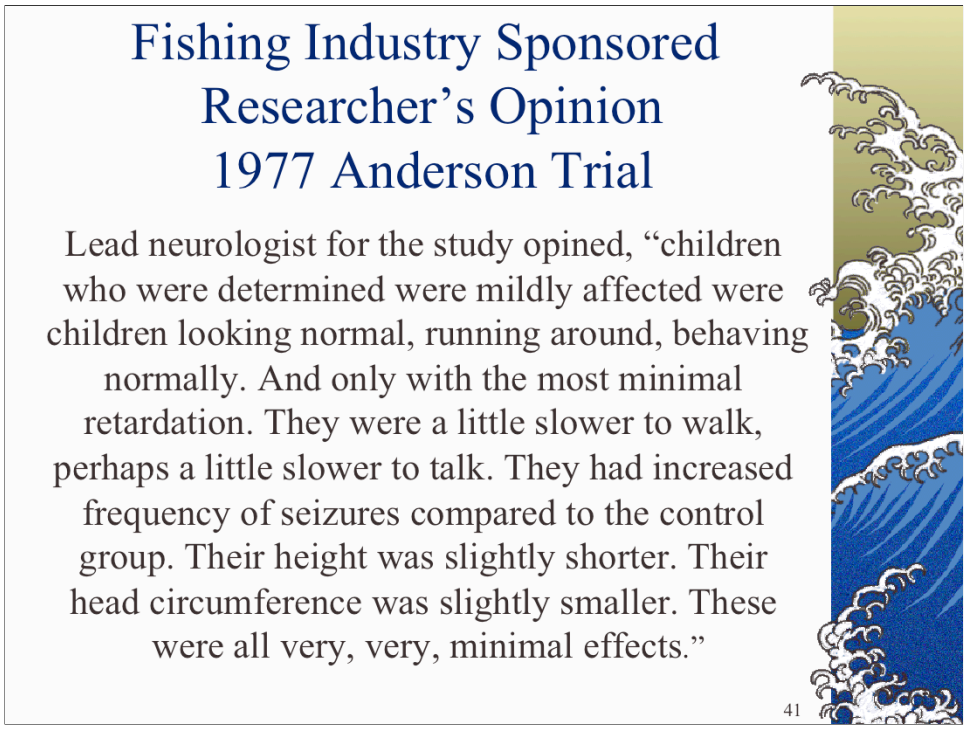
Cupertino Cement factory

Fishing industry shot themselves in the foot.

China leads in coal. Lignite emits high mercury levels.

Mining and black market mercury and contamination of water bodies

US Court of Appeals overturned Hg removal from clean air act Feb 2008.
Coal, fisheries, pharmeceutical industry, all in it together.

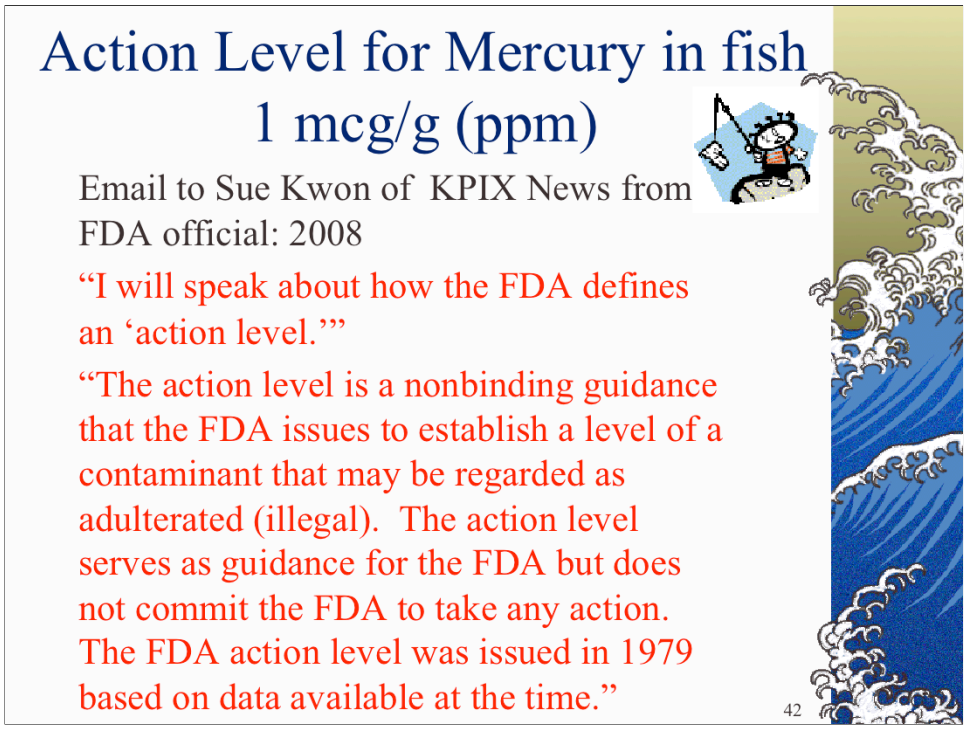


The American public deserves a second opinion.

Lesser symptoms were not investigated or included

The study did not allow for the determination of a Minimal Clinical effect Level, yet the Industry funded researchers came up with a level and said that there data showed that it was 400 mcg/l

The lead researcher, in his sealed deposition, explained that the study was a group study, whereby the more sensitive people would not be identified, and therefore an MCEL could not be determined.



Kwon---4.0, 8.9, 17.2 mcg/l After 20 days of 1 can of albacore/day.

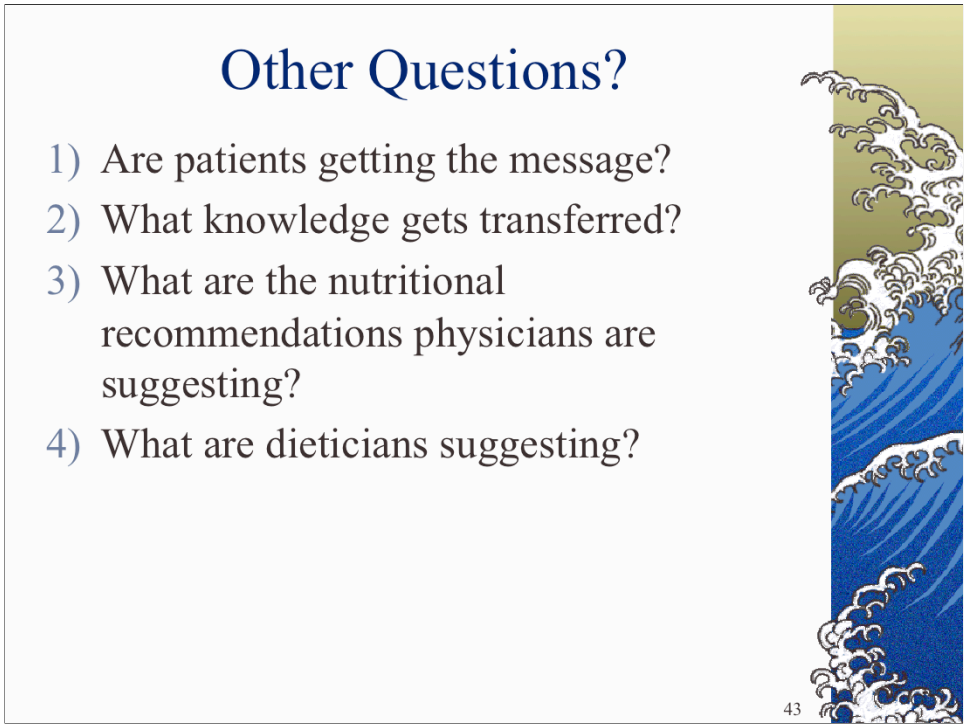
The polluters continue to pollute.

Multiple media and NGO testing shows some large predators are even over 2 or 3 mcg/g in the grocery stores. KTLA found Swordfish 4 mcg/g.

EU, Canada 0.5

Japan 0.4

USA 1.0. Was 0.5 !!!!



1. Some are, but garbled. Getting it through Dr Yahoo and Dr Google.

Nutrition, environmental contaminants, preventive med not covered by the Internal Medicine Exam.

Most physicians never ask patients what they eat, nor take any exposure history.

2. Depends on what resource the patient uses. They just want to know "how do we survive?" Give both ends of spectrum…bags of supplements, cesium, selenium, NAC, IV glutathione versus the folks who just don't care, and refuse to even consider a dietary change even if it would save their life.

3. Really? They need to look at their own diets first.

4. Have you ever seen some hospitals' food? Filled with sodas, MSG, maltdextrin, sorbitol, and other additives. Finding cost effective nutritional foods for sick patients with poor appetites is a challenge. I tell patients to get their visitors to bring them nutritious food.

5. Most people don't want to shop for food, prepare food, cook food, or even chew food. If one could just grab it off the counter and drink it on the run, they would be happy. I have people who have lived in their house for greater than 10 years and have never opened the oven door, nor used the burner for much more than cooking a hotdog or boiling water. On the other hand, I have professional chefs and foodies in my practice who love to cook and try to eat only non processed and organic…even going to the paleolithic side.

One patient stated, "I don't want to think every meal is a medical treatment."

Another, "I don't want to think of my kitchen as a laboratory."

Any More Ideas?

4000 mcg Hg/bulb on average

iStockphoto.com

http://www.npr.org/templates/story/story.php?storyId=7431198

http://www.energystar.gov/ia/partners/promotions/change_light/downloads/Fact_Sheet_Mercury.pdf

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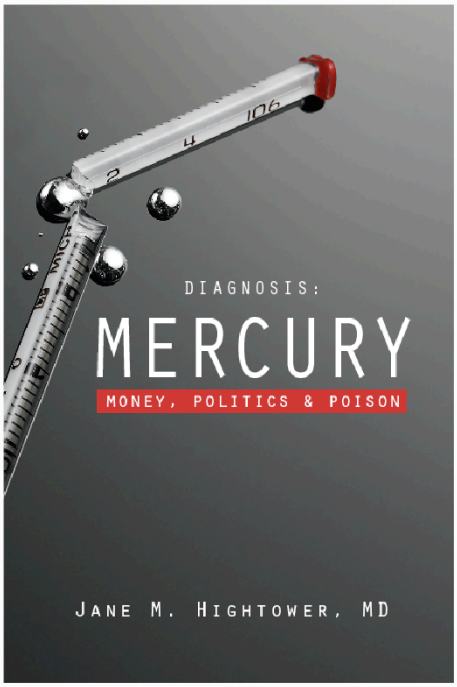
DIAGNOSIS:
MERCURY
MONEY, POLITICS & POISON
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http://www.linkedin.com/groups/Clean-Up-Information-Network-CLUIN-4405740

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- To view a complete list of resources for this seminar, please visit the **Additional Resources**
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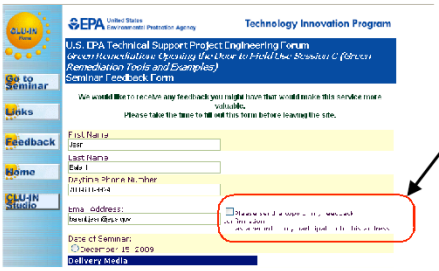

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