Ocean fish consumption does not contribute to causing mercury toxicity. It prevents it.

65th PFT Conference
February 24, 2014
Monterey, Ca

Nicholas Ralston Ph.D.
University of North Dakota
WHAT WE KNOW, WHAT WE WANT TO KNOW

- Ocean fish are rich in beneficial nutrients:
  - Omega-3 fatty acids (essential for brain and heart health)
  - Vitamin D (essential for bone, neuromuscular, and immune health)
  - Vitamin E (antioxidant functions, works together with selenium)
  - Selenium (essential for brain, endocrine, and immune health)

- However, concerns about risks associated with mercury are keeping some people from eating ocean fish.

- Here are the real questions:
  - Are mercury risks serious enough to justify these concerns?
  - Do the benefits of fish consumption outweigh those risks?
  - Are ocean fish safe and beneficial to eat?
  - Is it safe to avoid eating ocean fish during pregnancy?
Chemical plants that produced chlorine and alkali (used in paper mills) used pools of liquid mercury as electrodes.

These plants released tons of mercury were into small water bodies and the fish became highly contaminated.

Hundreds of people died from eating fish with poisonously high mercury contents.

Prenatally exposed children were far more vulnerable to the effects of mercury.

Thousands of victims were diagnosed with “Minamata Disease” before the plants stopped releasing mercury.
IRAQI MeHg POISONING INCIDENTS

Iraq (1970’s)

- Mercury-treated seed grain was baked into bread eaten by villagers.
- Months later, thousands were hospitalized with mercury poisoning.
- Hair Hg levels ranged as high as 674 ppm (normal levels are <1.4 ppm).
PRECAUTIONARY PRINCIPLE:

If an action has a risk of causing harm, proving that it is safe is the responsibility of those taking the action.

For example, when introducing a product or a process whose safety is disputed or unknown, the public does not need to prove it is dangerous before restricting it. The burden of proving that it is safe is on those that wish to provide the product.

The precautionary principle has been used as the basis for advising pregnant women to limit their ocean fish meals to no more than twice a week...
If an action has a risk of causing harm, proving that it is safe is the responsibility of those taking the action.

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The precautionary principle has been used as the basis for advising pregnant women to limit their ocean fish meals to no more than twice a week...

-at least until we know it is safe...
**MATERNAL MeHg EXPOSURE & FETAL TOXICITY - THE CONVENTIONAL HYPOTHESIS:**

Increasing maternal methylmercury exposures are associated with adverse child neurodevelopmental outcomes...

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<tr>
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Results of epidemiological studies do not support the conventional hypothesis. But the biggest, best designed, and most applicable studies actually disprove it.
The conventional hypothesis of mercury toxicity seemed valid, but the epidemiological studies have failed to support it.
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WHY?
WHY?

THE ANSWER IS ELEMENTARY...
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- Selenium-dependent enzymes are vitally important in brain tissues.
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25 distinct enzymes need selenium to perform their functions.
SELENIUM-PHYSIOLOGY BACKGROUND

- Selenium is an essential nutrient that is highly abundant in seafoods.
- Selenium-dependent enzymes are vitally important in brain tissues.
- 25 distinct enzymes need selenium to perform their functions.
- Selenoenzymes restore vitamin C and various other vital antioxidant molecules to their active forms. This enables them to protect against oxidative damage in vital-but-vulnerable tissues such as the brain.
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Selenoenzymes are expressed in highly tissue specific distributions by all forms of life that have complex brains.

Only one environmental agent is known to inhibit the activities of selenoenzymes...
MERCURY
SULFUR
MERCURIC SULFIDE

Mercury + Sulfur = Mercury Sulfide (Cinnabar)

Binding Affinity $10^{39}$
Thinking that mercury interfered with sulfur metabolism was frightening because a blood Hg of 1-2 µM is toxic, but sulfur occurs in high mM amounts.
MERCURY SELENIDNDE

Mercury + Selenium = Mercury Selenide (Tiemannite)

Binding Affinity $10^{45}$
Methylmercury has the unique ability to cross placental and blood-brain barriers. Tissue selenium is present at ~1 µM, so it is no wonder that 1-2 µM Hg is toxic.
Dietary Selenium and Growth

All animals were healthy and gained weight at normal rates.

The range of dietary Se used reflects the normal physiological range of dietary selenium intakes.
Mercury toxicity is entirely dependent on selenium status.

No toxic effects

Slight toxicity

Lethal toxicity
SELENIUM “PROTECTION” STUDY & SELENIUM THERAPY STUDY

Body Weight (g)

- 0.1 µmol Se; 50µmol MeHg/kg
- 1.0 µmol Se; 50 µmol MeHg/kg
- 10 µmol Se; 50 µmol MeHg/kg

Hg:Se Ratio:
- 5:1
- 50:1
- 500:1
Since mercury’s adverse effects are defined by mercury:selenium molar ratios, how should we assess mercury exposure risks?
• Since mercury’s adverse effects are defined by mercury:selenium molar ratios, how should we assess mercury exposure risks?

• How do mercury contamination levels and selenium contents in ocean fish compare to those in shark or whale meats?
SOME OF THE NEXT QUESTIONS:

- Since mercury’s adverse effects are defined by mercury:selenium molar ratios, how should we assess mercury exposure risks?

- How do mercury contamination levels and selenium contents in ocean fish compare to those in shark or whale meats?

- Are there risks associated with eating ocean fish?
MERCURY AND SELENIUM IN OCEAN FISH

- Pilot Whale
- Mako Shark
- Swordfish
- Thresher Shark
- Chinook Salmon
- Coho Salmon
- Albacore Tuna
- Bigeye Tuna
- Yellowfin Tuna
- Skipjack Tuna

μM concentration

- Selenium
- Mercury
SELENIUM HEALTH BENEFIT VALUES

**HBV\textsubscript{Se} = \left( \mu M \text{ Se} - \mu M \text{ MeHg} \right) \times \left( \mu M \text{ Se} + \mu M \text{ Hg} \right) / \mu M \text{ Se}**

Negative HBV\textsubscript{Se} = Harmful  
Positive HBV\textsubscript{Se} = Beneficial
FAROES vs. HAWAIIAN STUDY
CORD BLOOD Hg AND Se

\[ y = 0.4673x + 1.3741 \]
\[ \text{Adjusted } R^2 = 0.0736 \]
\[ F= 26.55; p<0.0001 \]

\[ y = 9.413x + 1.7035 \]
\[ \text{Adjusted } R^2 = 0.229 \]
\[ F= 30.44 p<0.0001 \]
SELENOENZYME INHIBITION HYPOTHESIS

MATERNAL METHYLMERCURY EXPOSURES \textit{IN EXCESS OF SELENIUM INTAKES} ARE DIRECTLY ASSOCIATED WITH ADVERSE CHILD DEVELOPMENT OUTCOMES
### SELENOENZYME INHIBITION HYPOTHESIS

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<tr>
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<td>14.4 to -123</td>
<td>√</td>
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<tr>
<td>Faroe Islands</td>
<td>Subtle harm</td>
<td>4.0 to -83</td>
<td>√</td>
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<tr>
<td>Seychelles</td>
<td>Beneficial</td>
<td>17.3</td>
<td>√</td>
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<tr>
<td>United Kingdom</td>
<td>Beneficial</td>
<td>20.2</td>
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*Results of epidemiological studies of maternal methylmercury exposures are completely consistent with the selenoenzyme inhibition hypothesis.*
Mercury exposures in excess of selenium intakes during fetal growth irreversibly inhibit and can grossly impair brain selenoenzyme activities. Therefore, developing children are at risk if their mothers eat seafoods that contain far more mercury than selenium.

Mercury:selenium molar ratios in pilot whale meats average >4:1. Pilot whale meat was the source of ~85% of total mercury exposures in the Faroe’s Study, but fish were the source of ~80% of their selenium.

Women should avoid eating meats with high Hg:Se molar ratios during pregnancy. These include pilot whale and certain types of shark meats.

Since the commonly consumed varieties of ocean fish contain far more selenium than mercury, eating them protects against mercury.
SELENIUM’S ROLE IN THE MERCURY ISSUE

- Mercury’s toxic effects directly correspond with those expected to accompany the loss of selenoenzyme activities in brain tissues.
- Mercury exposure risk evaluations have been overly simplistic.
- This is comparable to estimating bankruptcy risks by only looking at debts and ignoring debt:income ratios. Applying such unreliable methods will fail to provide reliably accurate predictions of risk.
- Eating selenium-rich ocean fish enriches the consumer’s selenium-status, protecting against mercury instead of increasing health risks.
TWISTS IN THE TALE OF THE WHALE

• Slightly smaller than their killer whale cousins, pilot whales live 45-60 years. Their meat and especially liver and kidney meats are highly contaminated with mercury, cadmium, PCP, and Dioxin, and other potential toxicants.

• Mothers that ate pilot whale muscle, liver, and kidney were highly exposed to not just mercury, but also all these other hazardous contaminants.

• Ocean fish consumption provided ~80% of their dietary selenium.

• Recent studies in the Faroes have found that the children of mothers that ate more ocean fish were much better protected against the adverse effects of mercury (and contaminants x, y, z, …) exposures.
THE PRECAUTIONARY PRINCIPLE CONFLICTS WITH THE HEALTH PROFESSIONAL’S PRIME DIRECTIVE...

• *Primum non nocere*: means "first, do no harm" in Latin. This primary concept teaches that it may be better to do nothing than to risk doing more harm than good.
  – Health professionals use this motto to remind themselves that any intervention comes with risks and intended benefits are uncertain.

• *Precautionary principle*: If an action has a risk of causing harm, the burden of proof falls on those taking the action.
  – Based on the Faroes Study, the precautionary principle was applied because mercury from eating fish might harm unborn children.
  – But they failed to consider that following this advice might cause harm...
Ideas about mercury toxicity were oversimplified…

That complicated things.

Eating ocean fish does not cause mercury toxicity…

It prevents it.

Avoiding ocean fish during doesn’t protect children…

It harms them.

Applying the precautionary principle to the seafood issue…

Violated the principle.
THE MERCURY ISSUE IN AN EGGSHELL:

This is your brain.

This is your brain without selenoenzymes…

Any questions?
THE MERCURY ISSUE IN AN EGGSHELL:

Only high mercury can impair brain selenoenzymes.

Seafood selenium keeps selenoenzyme protection intact and the brain safe...

Any questions?
The research described in this presentation was funded by:
U.S. Environmental Protection Agency: EPA STAR grant: G2009-STAR-B1 and
National Oceanic and Atmospheric Administration (NOAA): Grant NA09NMF4520172
and was performed in collaboration with EPA and NOAA research scientists.