The speaker, Dr. Ned Groth III, has recently authored a major study on methyl mercury in fish. This talk will discuss cases of people who suffered from methylmercury poisoning after eating widely consumed fish. Methylmercury is very toxic to the nervous system. Some kinds of fish have much more methylmercury than others, and some people are much more sensitive to mercury than others. The talk concludes with advice on which fish are safe, which fish should be consumed in small quantities, and which fish should be eaten rarely if ever. It should be of interest to everyone who eats fish or is interested in environmental issues.

From 1979 until his retirement in 2004, Groth was a scientific expert at Consumers Union, publisher of Consumer Reports magazine. He is the author or coauthor of many books and studies, and he has also served on the Food Forum of the National Academy of Sciences and on expert committees for the World Health Organization and the UN Food and Agriculture Organization. This lecture is sponsored by UCSC Chapter of Sigma Xi (the Scientific Research Society), and by the UCSC Departments of Physics and Microbiology and Environmental Toxicology (ETOX).
Methylmercury Poisoning in High-End Fish Consumers: A Risk Communication Challenge

Edward Groth III, PhD
Groth Consulting Services
Pelham, NY 10803  USA
April, 2009
Topics to be covered:

- Background & context
- Mercury in US fish and seafood
- Summary of 24 case histories
- Is it really methylmercury poisoning?
- Dose-response issues
- Fish involved in these cases
- How prevalent a problem?
- Research needs
- Risk communication aspects
Americans are eating more fish, which benefits public health significantly, overall. But it also increases the likelihood of exposure to methylmercury, from eating fish. Risk is greater for people who eat a lot of fish. The type(s) of fish consumed also matter. Methylmercury exposure in general and extreme high-end exposure are each likely to increase if more Americans eat more fish.
Conventional Hg Wisdom:

- Critical effect = developmental neurotoxicity
- Populations at risk = fetuses (i.e. women of childbearing age) and young children
- No appreciable risk to other populations
- Benefits (lower risks of CHD & stroke) far outweigh Hg risks for general population

This perspective is reflected as recently as in the 2006 NAS/IOM report on benefits and risks of fish & seafood consumption
Basis for C.W.:

- Epidemiology from incidents in Japan and Iraq, most studies 30-40 years ago
- Found clear-cut neurotoxic effects in adults only at high doses (blood Hg > ~200 ppb)
- Some effects in children @ > 50 ppb
- Amounts of MeHg from fish in “normal diet” believed to be below the level of concern, except for potential for fetal exposure
Key questions:

- Do we need to revisit and update this risk assessment?
- If so, how might we approach that task?
- What about “abnormal” (high-fish) diets?
- On what issues do we need better data?
- Given what we know and don’t know, what advice should we give consumers?
A Few Basic Principles of Environmental Health
Risk is a Continuum

- **Very high doses**: Clearly harmful dose
  - Dose with measured adverse effect in studied population
- **Higher doses**: Threshold of observable harm
  - Below threshold of observable harm
  - Margin of uncertainty: Neither clearly harmful nor clearly safe doses
- **High doses**: "Virtually safe dose"
  - Reasonably certain to cause no harm in humans
- **Range of typical dietary exposure**
- **NOAEL**
- **LOAEL**
- **Benchmark Dose**
- **Low doses**: "Virtually safe dose"
  - Reasonably certain to cause no harm in humans
- **USEPA RfD**
- **JECFA PTWI**
- **Lower doses**: Even safer doses
- **Very low doses**
Sensitivity to toxic effects varies along a distribution.
Sensitive subpopulation

Number affected

Dose
Fish consumption and methylmercury exposure
Fish consumption

- Long-term trend of increasing per capita consumption in US
- Recent years at/near all-time high
- Patterns of consumption also changing
- More fresh and frozen steaks and fillets
- More (mostly imported) shrimp
- Less canned and breaded/processed fish
US Per capita fish consumption, pounds/year, 1990-2006 (NMFS)
Consumption of selected items, pounds/person/year, 1990-2006
Per capita consumption, canned fish, pounds/year, 1990-2006
# Top 10 Seafoods, 2005-2007

US consumption in pounds per capita per year (NFI)

<table>
<thead>
<tr>
<th>Rank</th>
<th>2005</th>
<th>Species</th>
<th>Lbs</th>
<th>2006</th>
<th>Species</th>
<th>Lbs</th>
<th>2007</th>
<th>Species</th>
<th>Lbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>Shrimp</td>
<td>4.10</td>
<td></td>
<td>Shrimp</td>
<td>4.40</td>
<td></td>
<td>Shrimp</td>
<td>4.10</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Tuna, can</td>
<td>3.10</td>
<td></td>
<td>Tuna, can</td>
<td>2.90</td>
<td></td>
<td>Tuna, can</td>
<td>2.70</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Salmon</td>
<td>2.43</td>
<td></td>
<td>Salmon</td>
<td>2.03</td>
<td></td>
<td>Salmon</td>
<td>2.36</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Pollock</td>
<td>1.47</td>
<td></td>
<td>Pollock</td>
<td>1.64</td>
<td></td>
<td>Pollock</td>
<td>1.73</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>Catfish</td>
<td>1.03</td>
<td></td>
<td>Tilapia</td>
<td>1.00</td>
<td></td>
<td>Tilapia</td>
<td>1.14</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Tilapia</td>
<td>0.85</td>
<td></td>
<td>Catfish</td>
<td>0.97</td>
<td></td>
<td>Catfish</td>
<td>0.88</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Crab</td>
<td>0.64</td>
<td></td>
<td>Crab</td>
<td>0.66</td>
<td></td>
<td>Crab</td>
<td>0.68</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>Cod</td>
<td>0.57</td>
<td></td>
<td>Cod</td>
<td>0.51</td>
<td></td>
<td>Cod</td>
<td>0.47</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>Clams</td>
<td>0.44</td>
<td></td>
<td>Clams</td>
<td>0.44</td>
<td></td>
<td>Clams</td>
<td>0.45</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>Flatfish</td>
<td>0.37</td>
<td></td>
<td>Scallops</td>
<td>0.31</td>
<td></td>
<td>Flatfish</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Where’s the mercury?

- Among popular fish and seafood choices, how much does each variety contribute to potential methylmercury exposure?
- Which fish are likely to contribute most to methylmercury intake, among people who eat a great deal of fish?
Methylmercury Exposure: Source Strengths

- Contributions of different fish and seafood items to total amount of mercury in the US fish/seafood supply, calculated using:
  
  A: 2006 US market data from NMFS
  
  B: Mercury content from FDA database

\[ \text{Hg Input} = (\% \text{ of market}) \times (\text{Hg ppm}) \]
Relative Hg Contributions

- Hg inputs calculated for 51 types of fish and shellfish for which there are both NMFS market data and FDA Hg data
- Results are not precise indicators of exposure, but provide relative comparisons
- Results can be ranked and compared various ways (e.g., percent of total Hg)
A Key Fact:

- The weighted average methylmercury concentration in the US seafood supply is 0.086 ppm.
Color-coding fish for methylmercury content

- **GREEN** = very low = \( \leq 0.043 \) ppm
- **BLUE** = below average = 0.044 - 0.086 ppm
- **BLACK** = above average = 0.087 - 0.172 ppm
- **ORANGE** = moderately high = 0.173 - 0.344 ppm
- **RED** = high = 0.345 - 0.688 ppm
- **VIOLET** = very high = > 0.688 ppm

Note: Different breakpoints than FDA has used
# Top 10 Seafoods, 2005-2007
US consumption in pounds per capita per year (NFI)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Species</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shrimp</td>
<td>4.10</td>
<td>4.40</td>
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</tr>
<tr>
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<td>2.43</td>
<td>2.03</td>
<td>2.36</td>
</tr>
<tr>
<td>4</td>
<td>Pollock</td>
<td>1.47</td>
<td>1.64</td>
<td>1.73</td>
</tr>
<tr>
<td>5</td>
<td>Catfish</td>
<td>1.03</td>
<td>1.00</td>
<td>1.14</td>
</tr>
<tr>
<td>6</td>
<td>Tilapia</td>
<td>0.85</td>
<td>0.97</td>
<td>0.88</td>
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<td>Cod</td>
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<td>0.51</td>
<td>0.47</td>
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<td>Clams</td>
<td>0.44</td>
<td>0.44</td>
<td>0.45</td>
</tr>
<tr>
<td>10</td>
<td>Flatfish</td>
<td>0.37</td>
<td>0.31</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Total, Top 10: 15.0, 14.9, 14.8
## Top 10 Hg Sources

<table>
<thead>
<tr>
<th>Fish</th>
<th>Market Share (%)</th>
<th>ppm Hg</th>
<th>Percent Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuna, all types</strong></td>
<td>16.44</td>
<td>next slide</td>
<td>37.37</td>
</tr>
<tr>
<td><strong>Haddock &amp; Hake</strong></td>
<td>4.86</td>
<td>0.170</td>
<td>9.73</td>
</tr>
<tr>
<td><strong>Swordfish</strong></td>
<td>0.44</td>
<td>0.976</td>
<td>5.06</td>
</tr>
<tr>
<td><strong>Catfish</strong></td>
<td>5.71</td>
<td>0.068</td>
<td>4.66</td>
</tr>
<tr>
<td><strong>Cod</strong></td>
<td>3.36</td>
<td>0.115</td>
<td>4.55</td>
</tr>
<tr>
<td><strong>American lobster</strong></td>
<td>1.22</td>
<td>0.310</td>
<td>4.46</td>
</tr>
<tr>
<td><strong>Pollock</strong></td>
<td>7.32</td>
<td>0.049</td>
<td>4.23</td>
</tr>
<tr>
<td><strong>Shrimp</strong></td>
<td>22.21</td>
<td>0.012</td>
<td>3.14</td>
</tr>
<tr>
<td><strong>Salmon</strong></td>
<td>6.83</td>
<td>0.028</td>
<td>2.25</td>
</tr>
<tr>
<td><strong>Sea Bass</strong></td>
<td>0.51</td>
<td>0.301</td>
<td>1.81</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>77.26</td>
</tr>
</tbody>
</table>
## Tuna, by type

<table>
<thead>
<tr>
<th>Type</th>
<th>Market %</th>
<th>ppm Hg</th>
<th>% Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canned albacore</td>
<td>3.81</td>
<td>0.353</td>
<td>15.85</td>
</tr>
<tr>
<td>Canned light</td>
<td>11.41</td>
<td>0.118</td>
<td>15.86</td>
</tr>
<tr>
<td>Fresh/Frozen</td>
<td>1.22</td>
<td>0.384</td>
<td>5.66</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>16.44</strong></td>
<td><strong>37.37</strong></td>
<td></td>
</tr>
</tbody>
</table>

(Insufficient supply data to specify contributions by tuna type to fresh/frozen category, e.g., bluefin, albacore, bigeye, etc.)
Comments on Top 10

- Swordfish is the only Violet (very high Hg) fish among the Top 10 sources.
- Two Green (very low Hg) and two Blue (below average Hg) items unlikely to be hazards; in Top 10 due to huge volume consumed.
- Two Black and two Orange items could lead to excessive exposure if eaten frequently.
- Tuna (two Red, one Black) is overwhelmingly the largest source.
- Top 10 account for more than _ of all mercury.
## Other Items of Interest

<table>
<thead>
<tr>
<th>Fish</th>
<th>Market %</th>
<th>ppm Hg</th>
<th>% Hg</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gulf Tilefish</td>
<td>0.01</td>
<td>1.450</td>
<td>0.171</td>
<td>40</td>
</tr>
<tr>
<td>Shark</td>
<td>0.07</td>
<td>0.988</td>
<td>0.815</td>
<td>21</td>
</tr>
<tr>
<td>King mackerel</td>
<td>0.05</td>
<td>0.730</td>
<td>0.430</td>
<td>29</td>
</tr>
<tr>
<td>Orange roughy</td>
<td>0.20</td>
<td>0.550</td>
<td>1.296</td>
<td>16</td>
</tr>
<tr>
<td>Marlin</td>
<td>0.02</td>
<td>0.489</td>
<td>0.115</td>
<td>42</td>
</tr>
<tr>
<td>Grouper</td>
<td>0.27</td>
<td>0.460</td>
<td>1.463</td>
<td>13</td>
</tr>
<tr>
<td>Bluefish</td>
<td>0.06</td>
<td>0.337</td>
<td>0.240</td>
<td>35</td>
</tr>
<tr>
<td>Snapper</td>
<td>0.86</td>
<td>0.137</td>
<td>1.388</td>
<td>15</td>
</tr>
<tr>
<td>Anchovies</td>
<td>3.06</td>
<td>0.050</td>
<td>1.803</td>
<td>11</td>
</tr>
<tr>
<td>Squid</td>
<td>1.92</td>
<td>0.070</td>
<td>1.583</td>
<td>12</td>
</tr>
<tr>
<td>Clams</td>
<td>2.04</td>
<td>0.023</td>
<td>0.553</td>
<td>28</td>
</tr>
<tr>
<td>Scallops</td>
<td>1.46</td>
<td>0.023</td>
<td>0.396</td>
<td>30</td>
</tr>
</tbody>
</table>
Interpreting these data:

- **Tuna** contributes 6 times as much mercury to potential US exposure as do **swordfish, shark, Gulf tilefish and king mackerel** combined.
- Americans eat 29 times as much tuna as they eat of the four highest-mercury fish combined.
- **Lobster, sea bass, cod, haddock and hake** are more important sources than many varieties with higher mercury levels, due to market share.
- Two-thirds of the market is in the **Green** and **Blue** categories, i.e., low mercury.
## Mercury Intensity of Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Weighted Mean Hg</th>
<th>% Market</th>
<th>% Hg</th>
<th>Intensity Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low</td>
<td>0.018</td>
<td>42.86</td>
<td>9.074</td>
<td>0.21</td>
</tr>
<tr>
<td>Below Avg</td>
<td>0.056</td>
<td>24.13</td>
<td>15.984</td>
<td>0.66</td>
</tr>
<tr>
<td>Above Avg</td>
<td>0.129</td>
<td>22.51</td>
<td>34.303</td>
<td>1.52</td>
</tr>
<tr>
<td>Mod. High</td>
<td>0.289</td>
<td>2.81</td>
<td>9.565</td>
<td>3.43</td>
</tr>
<tr>
<td>High</td>
<td>0.375</td>
<td>5.57</td>
<td>24.599</td>
<td>4.57</td>
</tr>
<tr>
<td>Very High</td>
<td>0.964</td>
<td>0.57</td>
<td>6.475</td>
<td>10.83</td>
</tr>
</tbody>
</table>
Mercury Intensity Indices

- Are ratios, % mercury / % of market
- Indicate the relative mercury dose a consumer ingests by eating an item from each category
- Span a range of over 50-fold; i.e., fish in the **Violet** category deliver over 50 times as much mercury, on average, as fish or shellfish in the **Green** category
“Trouble” Scenarios:

Ways to get excessive mercury doses:

A. Eat very high Hg fish more often than rarely

B. Eat moderately high or high Hg fish fairly often, i.e. once a week or more

C. Eating above average Hg fish very often, i.e. twice a week or more, with occasional meals from categories in A or B

There are large numbers of Americans (though a small percentage) with each of these consumption patterns.
Case Histories of methylmercury poisoning in people who eat a lot of fish
Over the Limit

Eating too much high-mercury fish

Prepared by Edward Groth, PhD for the Mercury Policy Project

October 2008
I wrote it for the Mercury Policy Project

Primary goal: To put a human face on abstract risk concepts

Sources: Published case reports, a few in scientific journals, most in other media

I readily found 24 cases of high-end fish eaters with methylmercury poisoning

Once I had these data, I subjected them to some scientific analysis
Criteria for Inclusion

- Symptoms consistent with methylmercury poisoning
- Patient often consumed high-Hg fish
- MeHg toxicity diagnosed by a physician
- Some supporting data (e.g., blood Hg)
- Patient stopped eating high-Hg fish and symptoms resolved
- Most of the cases meet all these criteria
Weaknesses in the data

- Most cases not peer-reviewed (only 4 of 24 published in scientific journals)
- Symptoms are generally subjective
- Wide range in severity of symptoms
- Exposure data (blood, hair Hg) unavailable in some cases, qualitative in some others
- Fish intake based on patient recall
- Some patients lost to follow-up
Far from ideal:

- Individual case histories are the “lowest” form of epidemiological evidence.
- Some of these cases are fairly anecdotal, limiting confidence in their reliability.
- But: Limited data are nonetheless data. What can we learn from these cases?
- Some provocative observations emerge from study of this limited data set.
Critical Questions:

- Who is at risk?
- Is it really methylmercury poisoning?
- What doses are associated with harm?
- What fish did the cases eat?
- How many other cases might there be?
- What research is needed?
- What advice should such high-end fish consumers be getting?
Who is at risk?

- Cases were generally middle-aged adults, ages 40 to 66 at diagnosis
- Four cases were children
- 20 of 24 cases ate commercially-caught fish; 4 were sport anglers
- The 16 adults in the former group were all health-conscious individuals, trying to eat a healthy diet, equally divided by gender
A minority of a minority

- Not “typical” Americans; real “fish lovers”
- Most probably are above the 99\textsuperscript{th}, some above 99.9\textsuperscript{th} percentile of fish consumers
- Within that “extreme” group, they prefer to eat higher-mercury, predatory fish: \textcolor{red}{Tuna}, \textcolor{purple}{swordfish}, \textcolor{blue}{halibut}, \textcolor{olive}{sea bass}, others
- Some may also be more sensitive than average to toxic effects
How do we know it’s methylmercury poisoning?
## Symptoms seen in cases:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognitive &amp; Behavioral</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue, loss of energy, lethargy</td>
<td>9</td>
<td>2,3,4,6,7,8,9,10,12,18,22</td>
</tr>
<tr>
<td>Memory loss</td>
<td>5</td>
<td>4,7,8,14,21,22</td>
</tr>
<tr>
<td>Inability to concentrate, confusion</td>
<td>6</td>
<td>7,8,10,11,12,19,20,22</td>
</tr>
<tr>
<td>Mood swings, irritability</td>
<td>4</td>
<td>3,9,17,18</td>
</tr>
<tr>
<td>Depression</td>
<td>2</td>
<td>10,18</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Difficulties in school (in children)</td>
<td>3</td>
<td>20,21,22</td>
</tr>
<tr>
<td><strong>Central Nervous &amp; Sensory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of balance, dizziness, fainting</td>
<td>4</td>
<td>5,8,12,15,19</td>
</tr>
<tr>
<td>Headaches</td>
<td>4</td>
<td>4,7,10,12,17,22</td>
</tr>
<tr>
<td>Impaired vision</td>
<td>2</td>
<td>10,19</td>
</tr>
<tr>
<td>Hearing loss, ringing in head &amp; ears</td>
<td>2</td>
<td>9,13</td>
</tr>
<tr>
<td>Slurred speech</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Metallic taste</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Seizures</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
### Symptoms, continued

#### Peripheral Nervous & Musculo-skeletal

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Count</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremors</td>
<td>6</td>
<td>2,8,9,13,14,20</td>
</tr>
<tr>
<td>Chills, tingling, numbness</td>
<td>4</td>
<td>7,10,14,15</td>
</tr>
<tr>
<td>Loss of motor coordination</td>
<td>3</td>
<td>9,16,20,22</td>
</tr>
<tr>
<td>Pain in arms and legs, joint pain</td>
<td>6</td>
<td>2,6,7,10,15,16,17</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>3</td>
<td>6,9,16</td>
</tr>
<tr>
<td>Muscle spasms, cramps, curled fingers</td>
<td>4</td>
<td>2,10,15,17</td>
</tr>
</tbody>
</table>

#### Skin and hair

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Count</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reddened skin, rash, mouth sores</td>
<td>2</td>
<td>10,13,22</td>
</tr>
<tr>
<td>Hair thinned, fell out, stopped growing</td>
<td>7</td>
<td>4,7,9,12 (3 pts), 14,21</td>
</tr>
</tbody>
</table>

#### General, non-specific

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Count</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability (could not work)</td>
<td>7</td>
<td>2,6,8,10,11,14,16</td>
</tr>
<tr>
<td>Stomach ache/nausea</td>
<td>1</td>
<td>4,7,12,22</td>
</tr>
<tr>
<td>Chronic flu-like symptoms</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1</td>
<td>16</td>
</tr>
</tbody>
</table>
Methylmercury poisoning?

- Symptoms match classic symptoms
- Diagnosed by a physician based on symptoms and elevated blood/hair Hg
- When stopped eating high-Hg fish, blood Hg dropped & symptoms resolved
- No evidence for other causes detected in often-extensive diagnostic process
- Bottom line: It is what it appears to be
How sure are we?

- Absolute proof is never possible
- See details in the 24 individual cases described in *Over The Limit*
- Some cases are a bit questionable
- But the majority are quite unequivocal: there is virtually no doubt that the person got mercury poisoning from eating large amounts of fish with elevated Hg content
Dose-response issues:

- No quantitative blood level available in 3 cases with the most severe symptoms.
- Six cases with the mildest symptoms, no blood Hg available in 4, average 8 ppb in other two.
- But: No symptoms in one patient with highest quantified blood Hg (228 ppb).
- Moderate to severe symptoms in 6 cases with blood Hg levels of 58-125 ppb.
- And: Similar moderate to severe symptoms in 8 other cases with blood Hg of 12-38 ppb.
Dose-response & gender:

24 cases: 20 adults, 4 children

- **Mild** symptoms: 6 cases, 5 males and one child, gender not specified
- **Moderate** symptoms: 14 cases
  - 5 males (3 adults, 2 children), avg bHg 68.4 ppb
  - 9 females (8 adults, 1 child), avg bHg 44.25 ppb
- **Severe** symptoms: 3 cases, all males
Interpretations:

- A small data set, but wide differences in individual sensitivity to toxic effects are still evident.
- Sensitive individuals (1/3 of cases) show symptoms at blood Hg levels long judged without appreciable risk (i.e., 12-38 ppb).
- Men seem more likely to experience either severe or mild symptoms.
- Women experienced moderate-to-severe symptoms at lower doses than men.
Low-dose effects?

- Frank neurotoxic effects associated in some cases here with far lower exposure levels than previously recognized
- Possibly hyper-sensitive individuals
- Clinical toxicity may be very rare at these doses, or perhaps just rarely diagnosed
- But adverse effects at low doses are not entirely unprecedented or unexpected
Low-dose effects

Carta et al., 2005 (Italy):

- 22 men who frequently ate tuna, had an average blood Hg level of 41.5 ppb
- 22 controls, had average bHg of 2.6 ppb
- Neurobehavioral tests of vigilance, hand tremor, psychomotor function
- Cases performed significantly worse on three functional tests (& worse on all 10)
Low-dose effects, cont’d

- **Yokoo et al., 2003** (Brazil):
- Battery of neurobehavioral and cognitive tests given to 129 Amazonian villagers
- Adults, classified by exposure based on hair Hg level (mean 4.2 ± 2.4 ppm, range 0.56 -13.6 ppm)
- Dose-related effects of Hg on fine motor speed, dexterity, concentration and some aspects of verbal learning & memory
Exposure in this group:

- Mean hair mercury of 4.2 ppm vs. mean of about 1 ppm for US adults
- Four cases in *Over The Limit* had hair Hg levels of 9, 12, 13 and 68 ppm
- I.e., tested Amazon villagers have mercury exposures not unlike Americans who eat a lot of relatively high-Hg fish
Low-dose effects, cont’d

- **Oken et al., 2005, 2008** (Boston):
  - Cognitive and neurobehavioral tests in infants & 3-yr-olds vs. maternal fish intake
  - High fish consumption correlated with improved cognitive performance
  - But: High mercury exposure correlated with decreased cognitive performance
  - I.e., antagonistic effects
Oken et al.’s subjects:

- “High fish-eaters” consumed only two fish meals per week (> twice US average)
- High mercury exposure = > 90th percentile w/in group, = hair Hg > 1.2 ppm
- 90th percentile for blood Hg in women in Northeast US (NHANES) = 5.2 ppb
- Inference: Adverse Hg effects on the fetal brain may occur @ > 5 ppb maternal bHg
Confirming Studies

- Lederman et al. (2008), New York City; mean maternal blood Hg level 2.29 ppb
- Jedrychowski et al. (2006), Krakow, Poland; mean maternal blood Hg 0.75 ppb
- Davidson et al. (2008), Seychelles; mean maternal hair Hg 5.7 ppm

(NOTE: Previous reports from Seychelles had failed to see effects; confounding by nutritional benefits of fish consumption)
Conclusions:

- We are approaching a point where our view of low-dose methylmercury effects may undergo radical revision, as occurred for lead toxicity around 1979-80.
- Sub-clinical effects measured by sensitive tests are likely to be far more widespread than overt illness.
BACK TO OUR 24 CASES...
What fish did they eat?
(commercially-caught fish, 21 cases)

- Tuna, all types (20 cases)
- Swordfish
- Halibut
- Sea Bass
- Yellowtail
- King Mackerel
Only six Fish Varieties involved in these 21 cases

- **Tuna (all types):** 18 cases, **86 %**
- **Swordfish:** 8 cases, **38 %**
- **Halibut:** 3 cases, **14 %**
- **Sea bass:** 3 cases, **14 %**
- **Yellowtail:** 2 cases, **10%**
- **King mackerel:** 1 case, **5 %**

(> 100% because many cases ate more than one type of high-mercury fish)
Noteworthy:

- Two of the “trouble scenarios” apply here
- Some patients ate swordfish, a very high Hg fish, often
- But the majority ate Tuna, sea bass, halibut and yellowtail, all fish with less extreme Hg levels
- Tuna was a source in a large majority of the cases and was the only known source in 9 cases (43%)
## Mercury Levels in Commercially Caught Fish Involved in Cases

<table>
<thead>
<tr>
<th>Fish</th>
<th># of Cases</th>
<th>ppm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuna, fresh/frozen</td>
<td>11</td>
<td>0.384</td>
</tr>
<tr>
<td>Swordfish</td>
<td>8</td>
<td>0.976</td>
</tr>
<tr>
<td>Tuna, canned, type not specified</td>
<td>4</td>
<td>0.118</td>
</tr>
<tr>
<td>Tuna, canned, albacore</td>
<td>3</td>
<td>0.353</td>
</tr>
<tr>
<td>Tuna, sushi</td>
<td>3</td>
<td>0.10-2.76</td>
</tr>
<tr>
<td>Halibut</td>
<td>3</td>
<td>0.220</td>
</tr>
<tr>
<td>Sea bass</td>
<td>2</td>
<td>0.301</td>
</tr>
<tr>
<td>Yellowtail</td>
<td>2</td>
<td>0.484</td>
</tr>
<tr>
<td>Tuna, bluefin</td>
<td>1</td>
<td>~1.0</td>
</tr>
<tr>
<td>Sea bass, Chilean</td>
<td>1</td>
<td>0.600</td>
</tr>
<tr>
<td>King mackerel</td>
<td>1</td>
<td>0.730</td>
</tr>
</tbody>
</table>

Most data from US FDA; tuna sushi, NY Times & Houston Chronicle; bluefin estimated from sushi data; Chilean sea bass, Knobelochn et al. (2005); Yellowtail, FL Fish & Wildlife Commission (2003)
Summary:

- One-third of cases (8 patients) ate a high-mercury fish (swordfish) repeatedly.
- One child case ate some king mackerel, but also ate a lot of canned tuna.
- The large majority of cases ate mostly moderately high and high mercury fish: tuna (fresh/frozen steaks, canned, and sushi), halibut, sea bass and yellowtail.
- Nine cases (43%) ate only tuna.
If there were a sign above my desk, here’s what it might say:*

* with apologies to James Carville
It’s the tuna, stupid!
How many cases might be “out there”?

Possible size of population at risk estimated by three different methods:

- Back-of-the-envelope
- Inferences from published studies
- Inferences from NHANES data
FDA estimates:

- Population **Average** Fish Consumption:
  - Women: 14.3 g/day  
  - Men: 18.6 g/day

- **99th Percentile** of Fish Consumption:
  - Women: 95 g/day  
  - Men: 134 g/day

If a typical serving is 150-180 grams (more for men), the **99th percentile** eats fish ~ 4 to 5 times per week.
Assume: Extreme fish-eaters are above the 99th percentile in fish consumption

Assume: 0.1 to 10 percent repeatedly eat high-mercury fish

3,250,000 consumers

\[ x \times (0.1 \text{ to } 10 \text{ percent}) = \]

3,250 to 325,000 possible cases
Limitations of BOTE method:

- Cases might occur below 99\textsuperscript{th} percentile; i.e., ours varied from <1 to >10 fish meals per week
- Very few data from which to estimate reliably how many people repeatedly eat higher-Hg fish; wide range of uncertainty (and perhaps >10% repeatedly eat tuna?)
- Serving size, specific type of fish also matter
- Method estimates only exposure; can’t say what fraction of people with high-end exposure might experience symptoms
Carrington & Bolger (2003)

- Maximum assumed fish intake = 18 oz per week ( = < 99th percentile)
- Estimated 99th percentile baseline bHg in women of childbearing age = 16.1 ppb, and 99.9th percentile bHg = 26.3 ppb
- I.e., 99.9th percentile consumer (1 in 1,000 people) has blood Hg in the low-mid range observed in cases in Over The Limit
Repeat consumption data:

- Carrington & Bolger also have estimated the frequency of repeat consumption from NHANES data.
- About 10 percent of women choose the same fish > 80% of the time.
- Problems: Too few data to estimate freq. of repeat eating of low-market share high mercury fish; & data are just for women.
Inferences from C&B model:

- Roughly 1 in 1,000 consumers may have blood Hg levels in the range associated with toxic symptoms in sensitive individuals among the 24 cases (i.e., > 20 ppb)
- For a lower exposure level (e.g., 15 ppb), the number possibly at risk may rises to 2 in 1000
- Far less) than 1 in 1,000 have bHg levels above, say, 50 ppb
Limitations:

- Applies to women of childbearing age
- Model lacks empirical data on those (rare) individuals who repeatedly choose higher-mercury fish
- Relied on NHANES fish consumption data; NHANES sample is nationally balanced, does not include many members of ethnic or tribal minorities with high-fish diets
Published epi studies

- Very few published epidemiological data
- Hightower & Moore (2003): 720 patients, ~100 with elevated blood Hg (> 5 ppb), ~5 had symptoms (case rate = 0.7%)
- Knobeloch et al. (2005), 2000 volunteers; 7 cases w. elevated blood Hg (0.35%); 3 with symptoms (0.15%)
- Non-representative populations in each case. Projected incidence thus < 0.1%
Inferences from NHANES

- Measured blood Hg in 5,214 women and children, 1999-2004
- No adult men, no older women, not fully balanced regionally or ethnically
- Maximum blood Hg level in the NHANES sample was 33 ppb
- What does this tell us?
Levels above 33 ppb?

- Analysis of statistical power of sample:
- Consider a high blood Hg level, defined here (arbitrarily) as > 33 ppb.
- The NHANES sample included no one with a level that high
- How many people in the US population of 325 million could have levels higher than that, and NHANES would still be unlikely to include at least one of them?
Probabilities:

- Assume for this exercise that the NHANES sample was random and representative of the US as a whole.

- If the incidence of \( bHg > 33 \) ppb were 1 in 1,000 people, the probability that NHANES would include zero is \((0.999)^{5214} = 0.0054\).

- If the incidence of \( bHg > 33 \) ppb were 1 in 10,000 people, the probability that NHANES would include zero is \((0.9999)^{5214} = 0.59\).
With 95% Confidence:

- If the incidence were 1 in 1,742 people, the probability that NHANES would not include any is 0.05.
- I.e., we can be 95% confident that there are no more than 186,567 (325,000,000 ÷ 1,742) people in the US with blood Hg > 33 ppb.
- Or, 0.06 percent of the population or less are likely to have levels above 33 ppb.
Comments:

- This conclusion is not very reassuring
- This analysis dealt with blood Hg levels above 33 ppb (max observed in NHANES sample)
- The same probabilities apply to 34 ppb, 84 ppb and 134 ppb, say, but we know the incidence decreases sharply as blood Hg level increases
- Cases suggest that symptoms may occur at 33 ppb or less in some sensitive patients
- Sub-clinical effects on cognitive processes and fine-motor coordination are also a concern
C&B model suggests 0.1 percent of US women could have bHg > 26 ppb

NHANES analysis suggests 0.06 percent could have bHg > 33 ppb

Neither predicts frequency of symptoms

Published studies suggest symptoms in 0.15 – 0.7 percent of two highly selected populations; general incidence is surely less, but can’t say how much less
None of these estimation methods is very precise or satisfactory.

But they converge around a possible incidence of about 0.06 to 0.1 percent.

I.e., from 200,000 to 300,000 Americans may have elevated blood Hg (> ~25 ppb).

Incidence of elevated blood Hg does not predict the incidence of toxic symptoms.

Actual number of cases could therefore be (much) smaller (tens of thousands?)
The need to narrow these uncertainties by focused research is urgent.

Meanwhile, however, we may wish to act as if there could be from several thousand to a few hundred thousand possible cases of methylmercury poisoning among high-end US fish consumers.
Research needs:

- More case histories need to be published in medical journals (I’d welcome referrals)
- Focused studies using sensitive outcome measures for methylmercury effects on the CNS should be done on people who eat a great deal of fish (adults & kids)
- Similar studies should be done on a large cross-section of the population, stratified by Hg exposure
More research needs:

- Better data are needed on high-Hg fish consumption: How many people eat such fish repeatedly, and how much do they eat mod-high, high and very high Hg fish?
- Better data needed on Hg levels in some fish, including low and below average Hg fish, recommended as safer choices (FDA data quite sparse in many respects)
Advice for Consumers who eat a lot of fish

- **Who**: Population needing advice is not just mothers-to-be; anyone else who eats a lot of the wrong fish (> twice a week) may be at risk too.

- **What fish**: It’s not just very high Hg fish; high and moderately high fish also are clearly a problem if eaten often, and above average Hg fish can also contribute significantly to risk of excess exposure if eaten in large amounts.
Which fish to choose?

- Fish and shellfish in the **Green** and **Blue** categories are unlikely to lead to excess exposure no matter how much one eats.
- These two “safe” categories account for 67 percent of the market.
- So, motivated consumers can easily find low-mercury choices.
## Top 10 Seafoods, 2005-2007
US consumption in pounds per capita per year (NFI)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Species</th>
<th>2005 Lbs</th>
<th>Species</th>
<th>2006 Lbs</th>
<th>Species</th>
<th>2007 Lbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shrimp</td>
<td>4.10</td>
<td>Shrimp</td>
<td>4.40</td>
<td>Shrimp</td>
<td>4.10</td>
</tr>
<tr>
<td>2</td>
<td>Tuna, can</td>
<td>3.10</td>
<td>Tuna, can</td>
<td>2.90</td>
<td>Tuna, can</td>
<td>2.70</td>
</tr>
<tr>
<td>3</td>
<td>Salmon</td>
<td>2.43</td>
<td>Salmon</td>
<td>2.03</td>
<td>Salmon</td>
<td>2.36</td>
</tr>
<tr>
<td>4</td>
<td>Pollock</td>
<td>1.47</td>
<td>Pollock</td>
<td>1.64</td>
<td>Pollock</td>
<td>1.73</td>
</tr>
<tr>
<td>5</td>
<td>Catfish</td>
<td>1.03</td>
<td>Tilapia</td>
<td>1.00</td>
<td>Tilapia</td>
<td>1.14</td>
</tr>
<tr>
<td>6</td>
<td>Tilapia</td>
<td>0.85</td>
<td>Catfish</td>
<td>0.97</td>
<td>Catfish</td>
<td>0.88</td>
</tr>
<tr>
<td>7</td>
<td>Crab</td>
<td>0.64</td>
<td>Crab</td>
<td>0.66</td>
<td>Crab</td>
<td>0.68</td>
</tr>
<tr>
<td>8</td>
<td>Cod</td>
<td>0.57</td>
<td>Cod</td>
<td>0.51</td>
<td>Cod</td>
<td>0.47</td>
</tr>
<tr>
<td>9</td>
<td>Clams</td>
<td>0.44</td>
<td>Clams</td>
<td>0.44</td>
<td>Clams</td>
<td>0.45</td>
</tr>
<tr>
<td>10</td>
<td>Flatfish</td>
<td>0.37</td>
<td>Scallops</td>
<td>0.31</td>
<td>Flatfish</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Total, Top 10: 15.0, 14.9, 14.8
People who eat a lot of fish need more & better information about the mercury content of the fish they are likely to eat a lot of.
The ideal message (conveyed in “one voice”):

“Eat lots of low-mercury fish”
Hard to get this right:

- Conflicting messages from various expert sources and/or interested parties:
  - Not right: “Benefits outweigh risks, don’t worry about mercury.” (False trade-off)
  - Not right: “Eat lots of fish.” (Fails to make important risk-related distinctions.)
  - Not right: “To avoid mercury risk, don’t eat fish.” (Dismisses benefits.)
Communication challenges

- Americans consume a great deal of **tuna**
- Some people also eat other **moderately high**, **high**, or **very high** Hg fish repeatedly
- Need to advise those consumers as a distinct **sub-population at significant risk**
- They need more and better advice about the mercury content of all popular fish and shellfish varieties, and improved guidance to choose low-mercury items
One idea about what consumer advice might look like.
Consumer Advice

If you eat fish twice a week or less, choose fish as follows:

- **Green** or **Blue**: As often as you like
- **Black**: Up to once per week
- **Orange** or **Red**: Up to once/2 weeks
- **Violet**: Up to once per month
Consumer Advice, cont’d

If you eat fish 3-4 times a week, choose fish as follows:

**Green** or **Blue**: As often as you like

**Black**: Up to once in two weeks

**Orange/Red**: Up to once per month

**Violet**: Up to once per 3 months
If you eat fish 5 times a week or more, choose fish as follows:

- **Green**: As often as you like
- **Blue**: Up to once a week
- **Black**: Up to once a month
- **Orange/Red**: Up to once in three months
- **Violet**: Once or twice a year
Modes of Advice

- Government advisories
- NGO & private sector reports & web
- Point of sale information
- Media articles

Effort is needed to improve information through all these modes & media