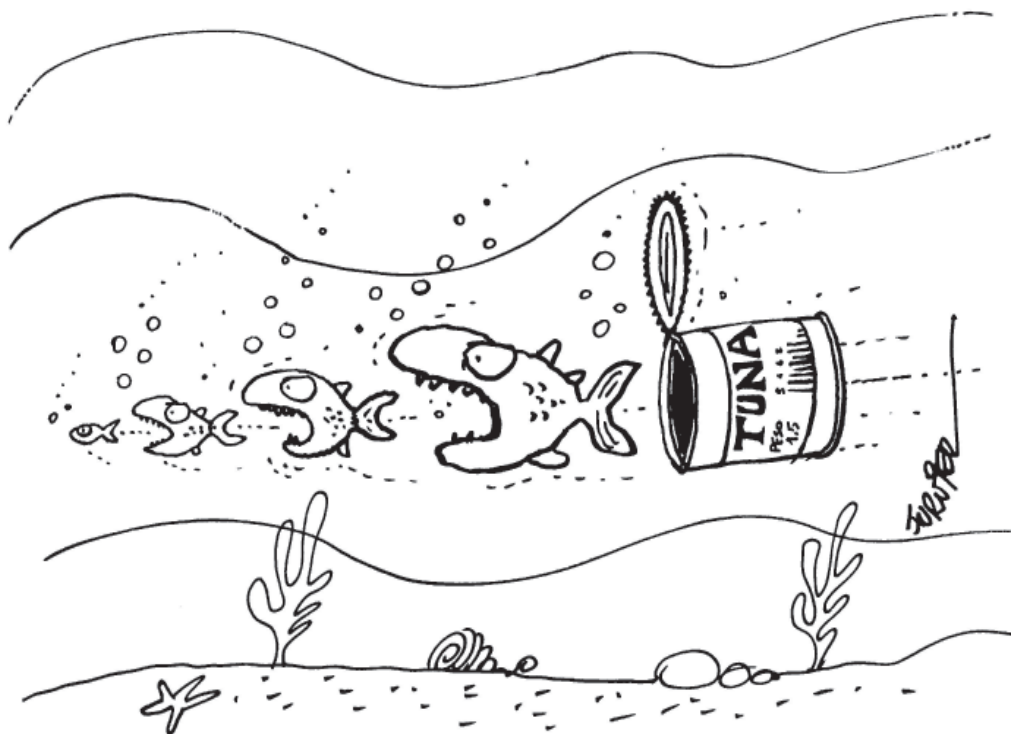


Over the Limit



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Eating too much high-mercury fish

Prepared by Edward Groth, PhD
for the

**Mercury
Policy Project**

October 2008

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Over the Limit

Eating Too Much High-Mercury Fish

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Over the Limit: Eating too much high-mercury fish

Executive Summary

This report describes and analyzes 22 cases involving 24 individual patients who got methylmercury poisoning from eating fish. The cases include 20 adults and 4 children; 21 patients ate commercially-caught fish, while three were sport anglers who ate lake fish they caught. All the patients had two things in common that set them apart from most Americans: First, they ate a great deal of fish, and second, the fish they repeatedly chose were varieties that contain moderately high to very high levels of methylmercury.

The patients' symptoms closely match the classic symptoms of this environmental disease, observed in mass-poisoning incidents in Japan and Iraq. Each case was diagnosed as methylmercury poisoning by a doctor, based on both the symptoms and an elevated mercury level in blood or hair. When patients stopped eating high-mercury fish, their blood mercury level went down and symptoms largely or completely disappeared. Although other diseases or toxic agents are known to produce similar symptoms and might theoretically be considered as possible causes of these patients' illnesses, alternative causes were generally ruled out by the examining physicians. The known facts strongly support the conclusion that these patients got methylmercury poisoning from the fish they ate.



The 21 patients who ate commercially caught fish got their mercury doses from just six popular fish varieties: Tuna, swordfish, sea bass, halibut, yellowtail, and king mackerel. The prevalence of tuna as a source of methylmercury poisoning in these cases is striking: 18 cases (86 percent) regularly ate one or more forms of tuna (tuna steaks, canned tuna, sushi). In 9 cases (43 percent), tuna was the only known source of mercury exposure. Swordfish was a source in 8 cases (38 percent), halibut and sea bass in 3 cases (14 percent) each, yellowtail in 2 cases, and king mackerel in one case. (The total exceeds 100 percent because most patients ate more than one variety of fish.) The contributions of tuna and halibut, which typically contain from 0.2 to 0.5 ppm of methylmercury, not an extremely high level, to these toxic exposures highlight the importance of the amounts of fish eaten, as well as the mercury levels in the fish, as primary risk factors.

The blood mercury levels associated with symptoms of poisoning in several cases reviewed here were between 7 and 50 parts per billion (ppb), below the level historically regarded as safe. This observation (and other evidence reviewed in the report) suggests that sensitive individuals may experience some adverse effects from methylmercury exposure at dose levels previously regarded as without risk.



The 24 patients described here represent only a tiny fraction of the US population that eats a great deal of fish and often chooses high- or moderately-high-mercury varieties. We used several methods, none of them satisfactorily precise, to estimate the size of the population at risk, and got numbers ranging from a few thousand to a few hundred thousand. Research is clearly needed to reduce this uncertainty.

The cases reviewed here document the need to expand government advisories on fish consumption (which currently focus on women of childbearing age), to include advice for people who eat a lot of fish. Similarly, point-of-sale information programs about methylmercury in fish need to be expanded and improved, so that people who eat a lot of fish know the mercury content of the fish people eat a lot of.



Introduction

Mercury is a metallic element that enters the environment from natural and human-made sources, generally as inorganic compounds. In aquatic environments, inorganic mercury is converted by bacteria to an organic form, methylmercury, which is taken up in aquatic food chains. Some fish, especially large, predatory species like tuna, pike, swordfish and shark, can accumulate high levels, and people who eat those fish regularly can be exposed to large doses of methylmercury.

The claim has often been made that “No one in the United States has ever been harmed by mercury from eating fish.” But that’s just another fish story. Americans can get methylmercury poisoning, just like people in Japan, New Zealand, the Faroe Islands, and other places where epidemiological studies have linked fish consumption and associated mercury exposure with adverse health effects.¹ All a person—in any country—has to do is eat too much fish with too much mercury in it. The truth is, very few studies in the U.S. have looked for methylmercury poisoning from fish consumption. But when researchers have made the effort to seek it, they’ve generally found it.

Most research on methylmercury hazards has looked at the effects of a mother’s fish consumption during pregnancy on her baby’s developing brain. An ongoing study in Boston has found that when mothers-to-be ate fish it had both beneficial effects (from fish nutrients) and harmful effects from mercury.² Children born to mothers who ate two or more fish



meals per week did better on several tests of cognitive development, at ages 6 months and 3 years, than children whose mothers ate less fish. But children whose mothers had the highest mercury exposure scored

lower on those same tests than children whose mothers had lower mercury exposure. Eating fish during pregnancy thus both benefitted and harmed babies’ developing brains. The two effects were roughly equal in magnitude.

Although these results still need to be confirmed, they suggest that the mercury in as little as two fish meals per week can measurably affect cognitive development. This is a much lower level of mercury exposure than was previously found to be harmful (in the Faroe Islands study³), but the findings are consistent with research on other environmental nerve poisons. Lead, for example, has been shown to damage the brain at progressively lower and lower doses over the years, as research methods have improved, and a similar trend has been reported for methylmercury (see discussion in **Appendix D**).

While possible damage to the developing brain has been the primary research focus, methylmercury exposure from eating fish can also cause nervous system damage in adults and older children. This was first observed in mercury pollution incidents in Minamata and Niigata, Japan, several decades ago. In those incidents, mercury levels in fish were very high, and the adverse health effects were often devastating. But environmental health experts know that less severe, often subtle effects can occur at exposures much lower than those that

cause the most obvious harm. In fact, similar cases of methylmercury poisoning have been seen in people who eat a lot of fish here in the United States. Some cases involve anglers (and their families) who ate sport-caught fish; others ate too much of one or more relatively high-mercury commercially caught fish. This report reviews and analyzes 22 such cases.



The cases described here meet these criteria:

- (1) The patient experienced symptoms of toxic effects consistent with those known to be caused by methylmercury.
- (2) The patient regularly ate one or more varieties of fish known to contain significant mercury levels.
- (3) The patient was tested by a physician for mercury exposure, and had a high blood or hair mercury level.
- (4) A physician diagnosed their illness as methylmercury poisoning, based on their symptoms, their fish consumption and their elevated mercury level.
- (5) When they stopped eating mercury-containing fish, their blood mercury level dropped and their symptoms lessened or disappeared.

Some of these cases have been published in peer-reviewed scientific journals, but unfortunately, most doctors rarely take the time to

write up a case history and submit it for publication. The cases that come from non-scientific publications contain sufficient detail to determine that most of them meet most of the criteria listed above.

Overview of the Cases: A Mysterious Illness Strikes Healthy People

This report tells the stories of 24 people, most of them otherwise healthy and quite health-conscious individuals, who were poisoned by methylmercury in the fish they ate.

Many people like to eat fish, and Americans are being widely encouraged to eat more of it, because a fish-rich diet has proven nutritional benefits, reducing the risk of death from heart attack and stroke and providing essential fatty acids for early brain development. Americans are eating more fish; U.S. per capita consumption of fish and seafood has steadily increased over the past 20 years. But the people described in this report ate far more fish than the average American does. In addition, each had a preference for fish varieties that accumulate significant levels of mercury. (Many other popular fish and shellfish choices, in contrast, are very low in mercury; see **Appendix F**.)

Methylmercury is very toxic, primarily to the nervous system. The patients in these cases experienced adverse effects from their unusually high exposures. Some suffered only mild symptoms, while others were more severely affected, and a few were completely disabled. But they all got better when their problem was diagnosed and they stopped eating high-mercury fish. Details of the cases are presented in **Appendix A**. While all 22 cases (encompassing 24 individual patients) have elements in common, each person's story is unique, and worth reading in detail. Here are some examples:

Will Smith, a geophysicist, couldn't think any more. He couldn't do even simple math, and he was forced to quit work. His speech was slurred, he was losing his memory and his balance, and he couldn't even watch



TV without getting dizzy. He experienced a metallic taste, constantly. When he'd go out, he'd lose his car, or get lost himself, in a city he had lived in for decades. He had tremors in his hands, and he was always tired. Smith reported eating tuna "all the time," for lunch, for business dinners. He ate sushi often, tuna steaks, and canned tuna several days a week as a snack.



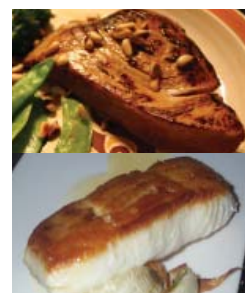
Dan Deeter, 56, of Alta Loma, CA, was very health-conscious. Beginning in 1997, he followed The Zone Diet; as part of that diet, he ate one to two cans of tuna every day for several years. Within a year of starting the regimen, he began feeling fatigued. Soon, he could no longer drive. He began having tremors, then seizures. The doctors he saw could not tell what was wrong with him. From about the end of 1998 through July of 2003, he spent most of the time in bed, suffering from spasms and pain, unable to work.



Wendy Moro, 40 a marketing consultant living near San Francisco, was active, fit and energetic; she ran every day, danced ballet, and lifted weights. She also ate fish two to five times a week, both at home and in restaurants, believing it was a healthy choice.



Her lunch was often canned tuna, and her family would regularly have fish for dinner; they favored steaks, such as ahi tuna or halibut. In the spring of 2001, Moro began feeling severe fatigue. She started having pain and weakness in her arms and legs, which got so bad she could barely stand up, and had to give up her active lifestyle.



Matthew Davis, a 10 year-old student in Berkeley, CA, was having difficulty in class. He could not focus, would labor at simple tasks, and missed assignments.



He had always been an excellent student, and his sudden loss of interest in and ability to do schoolwork came as a shock to his parents. He also began having problems with his hands. His fingers curled, he had tremors, and he could no longer catch a football or hit a baseball. Starting a year or so before he became ill, Matthew had begun eating canned albacore tuna about twice a day. His parents were delighted that he chose tuna—a reputed "brain food"—over "junk foods."



All four of these people found physicians who discovered the cause of their problems—methylmercury poisoning from the fish they were eating. They all then stopped eating the high-mercury varieties of seafood that had poisoned them, and recovered; their symptoms mostly disappeared (Smith suffered some permanent nervous system damage). In that sense, their stories generally have “happy endings.”

These individuals, and the 20 others described in **Appendix A**, are far from alone. They almost certainly represent just the tip of the proverbial iceberg. A key question is, how many Americans are at risk for methylmercury poisoning, because they eat a great deal of fish and often choose the “wrong” (i.e., relatively high-mercury) fish?

That question is difficult to answer, and is examined in detail later (See **Appendix E**). It seems clear that methylmercury poisoning among high-end fish consumers is already a significant public-health problem, and is likely to grow as more Americans heed the call to “eat more fish.” Research is needed to better define this risk, and people who eat a lot of fish need better, more detailed guidance to help them follow a fish-rich diet while choosing low-mercury fish and seafood varieties.



Subsequent sections summarize and analyze the cases presented in **Appendix A**, place this evidence in context with other scientific knowledge about methylmercury in fish and its health risks, and offer consumer guidance and policy recommendations.

Analysis of the Cases

Patient Characteristics

The 22 cases in **Appendix A** include 24 individual patients (**Case 12** has three family members). Two cases (**11** and **19**) include patients’ family members who ate the same fish but did not have symptoms of mercury poisoning; those family members are not included in the totals for this analysis. One case (**1**) describes a man who frequently ate swordfish and had a very high methylmercury level in his blood, but felt no toxic effects. (This case is included for discussion; see **Appendix D**.)

The 24 patients fall into three groups. **Group 1** (**Cases 1** through **15**) includes 17 patients, all but one of them adults (a child is part of the family in **Case 12**), who ate commercially caught fish. **Group 2** (**Cases 16** through **19**) consists of four adults who ate sport-caught fish. **Group 3** (**Cases 20** through **22**) consists of three children who were given commercially-caught fish by their parents.

A fourth group is described in a sidebar in **Appendix A**. A dermatologist at Columbia University, Dr. Paul Dantzig, has published a report of 11 patients who ate commercially-caught fish and experienced a specific type of skin rash, which he diagnosed as caused by methylmercury in fish. As interesting as this report is, it has yet to be confirmed by other investigators. While two of Dr. Dantzig’s patients also had neurological symptoms such as dizziness or memory loss, most experienced just a rash. We have treated these patients separately and not included them in our analysis of methylmercury poisoning cases.

The adults in **Group 1** are evenly divided by gender, 8 men and 8 women. Where ages are available (no age was given for 6 patients), they ranged from 40 to 66 at the time of diagnosis. The four anglers in **Group 2** were all men, ages 55 to 65. The children in **Group 3** included two boys and a girl, ages 7, 10 and 5. The Child in **Case 12** was not further identified as to gender or age.

Collectively, the patients in these cases were for the most part middle-aged adults with a healthy lifestyle, trying to eat a healthful diet. All loved to eat fish, and did so from one to ten times a week. In addition, and critically, the fish varieties these patients preferred and ate again and again were quite high in methylmercury. That pattern, repeatedly eating high-mercury fish, led to their methylmercury poisoning.

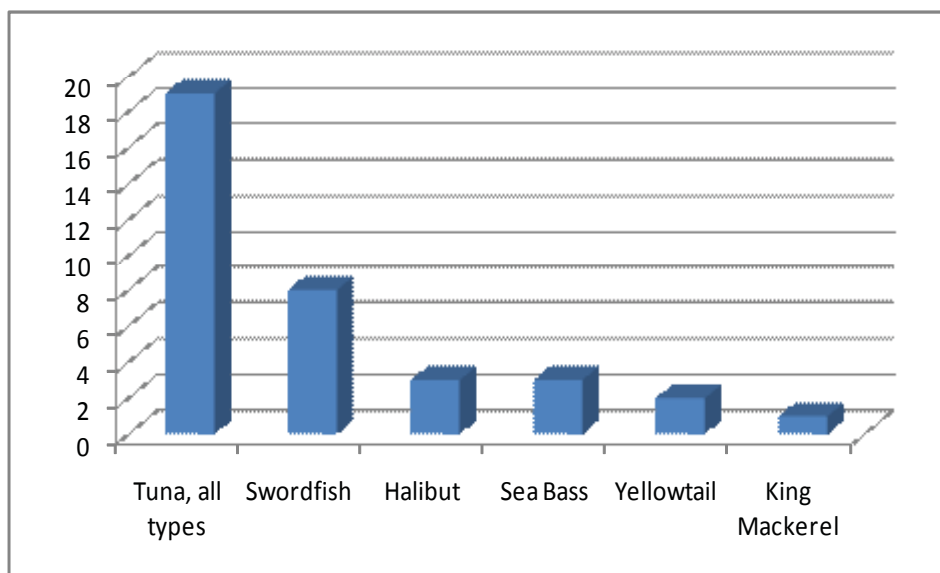
Types of Fish Involved

Each case in **Appendix A** describes the fish varieties the patients reported consuming. **Appendix B** presents a summary and analysis of fish types that contributed to mercury exposure in these cases of methylmercury poisoning.

Of the 24 patients, 20 ate commercially caught fish, and one ate sport-caught ocean fish that are also caught commercially. Those 21 individuals collectively reported eating just 6 varieties of relatively high-mercury fish (see **Figure 1**). The other three patients, all sport fishermen in Wisconsin, all ate northern pike, and each also ate various other lake fish.

Tuna fish, in one form or another, was a source of mercury exposure for 18 of the 21

Figure 1: Fish Varieties Consumed by Patients Eating Commercially Caught Fish
(Number of cases reported as eating each fish)



patients who ate commercially caught fish (86 percent), far more than any other variety of fish. In nine of those cases (43 percent), tuna was the only known source of mercury exposure. Other commercially-caught fish involved in these cases include swordfish (8 cases, 38 percent, the only source in 2 cases); halibut (3 cases, 14 percent), sea bass (3 cases, the only source in 1), yellowtail (2 cases), and king mackerel (1 case). The number of cases adds up to more than 21 (and percents to more than 100) because most patients ate more than one variety of high-mercury fish.

The prevalence of tuna as a source of methylmercury exposure in these cases is striking. In

three cases, canned tuna specifically was the only known source of the patient's mercury poisoning, and three child cases were heavy consumers of canned albacore tuna. Canned tuna is the most heavily-consumed finfish product in the US (and second overall, behind shrimp, among seafood products). Several patients ate more than one form of tuna: **Case 8**, for example, ate tuna sushi, canned tuna and tuna steaks.

As **Table 1** shows, tuna (except bluefin), halibut, sea bass and yellowtail, which all contributed to excess methylmercury exposure in some of these cases, generally do not have extremely high mercury levels. Current FDA/

TABLE 1. Mercury Levels in Commercially-Caught Fish Consumed in These Cases

<u>Fish Variety</u>	<u>Mercury, ppm</u>	<u>Cases</u>
Canned tuna, albacore	0.353	20,21,22
Canned tuna, general†	0.118	2,5,6,8
Tuna fillets and steaks	0.383	5,6,8,9,10,14,22
Tuna sushi*	0.10-2.76	8,10,15
Bluefin tuna*	~1.0	3,17
Other tuna, unspecified**	0.383	4,7,12
Swordfish	0.976	1,4,7,9,12,12,12,13
Sea bass, Chilean	0.386-0.60	11
Sea bass, all types	0.219	4,7
Halibut	0.252	4,6,7
Yellowtail	0.484	10,17
King Mackerel	0.730	22

Data sources: Most data are from US FDA⁴⁰; data for sushi from reports in New York Times⁴¹ and Houston Chronicle⁴²; Chilean sea bass data from Knobeloch et al.²⁰; yellowtail data from Florida Fish & Wildlife Conservation Commission⁴³. See end notes for references.

† Type of canned tuna not specified in these cases. Mercury level shown is for canned light tuna

* Tuna sushi samples with higher levels are most likely bluefin tuna; a rough average for bluefin sushi has been used to estimate the level for intact fish

** Assumed to be fresh/frozen tuna for purpose of listing mercury level

EPA advice warns against consuming four types of fish with very high mercury levels (tilefish, swordfish, shark and king mackerel), and urges women of childbearing age to limit consumption of albacore tuna to no more than 6 ounces per week.⁴ But the government has offered little advice (and none to anyone except possible mothers-to-be) about consuming fish that have moderately high methylmercury content, defined here as from 0.2 to 0.5 ppm.

In many of our 22 cases, people who ate a great deal of fish with only moderately high methylmercury levels nonetheless suffered from mercury poisoning. The association of mercury poisoning with consumption of tuna, halibut and other moderately-high-mercury fish highlights the urgent need for improved advice that focuses on the amount of fish consumed, as well as on the mercury levels in different fish, as critical risk factors.

How Do We Know It's Methylmercury Poisoning?

Many people have experienced some of the symptoms described in the cases here, and might worry that they have methylmercury poisoning. Usually, such fear is unjustified. In many cases, objective evidence, such as a blood test, can show that a person's mercury exposure is below any level that justifies concern. But each case described in **Appendix A** was diagnosed by a physician as methylmercury poisoning, based on three factors: The patient's symptoms, an elevated level of mercury in their blood or hair, and their history of eating a lot of fish of types known to contain relatively high mercury levels.

The classical description of methylmercury poisoning comes from studies of pollution incidents in Minamata and Niigata, Japan in the 1950s, and Iraq in the 1970s. Symptoms include prickling or tingling sensations in the

arms and legs; impaired vision, hearing, taste and smell; slurred speech; loss of balance and coordination; unsteadiness of gait; tremors; muscle weakness and fatigue; irritability and mood swings; memory loss; difficulty concentrating; depression; and difficulty sleeping.

Table 2 lists the classical symptoms of methylmercury poisoning and shows that the 24 patients in these cases, collectively, experienced essentially identical symptoms. **Table C-1** in **Appendix C** lists all the symptoms experienced by these patients, as described in each case report in **Appendix A**; that list includes a few additional symptoms (such as hair loss) not included in the classic syndrome, but observed in multiple cases here.

Overall, the symptoms of these 24 patients match quite closely with the clinical picture of "Minamata Disease." These American cases experienced cognitive symptoms (memory loss, confusion, irritability and mood swings, insomnia), sensory disturbances (impaired vision and hearing, slurred speech, metallic taste, dizziness, loss of balance), peripheral nervous system effects (chills, tingling, numbness, tremors), loss of fine-motor coordination, muscular weakness, pain, spasms, and a variety of other symptoms. Given these symptoms, and the patients' blood mercury levels in most cases (See **Appendix D**), their doctors' diagnoses of methylmercury poisoning in each case is entirely reasonable, and seems almost certain to be the correct diagnosis.

Can we be sure that the disease was methylmercury poisoning in each case? No; absolute certainty is usually not achievable when trying to establish the cause of health damage attributed to environmental exposures. But the argument that something else may have caused these illnesses is a weak one. That theoretical possibility cannot be ruled out, but

**Table 2. Classical Symptoms of Methylmercury Poisoning
Observed in Patients in These Cases**

<u>Classical Symptoms</u>	<u>Patients with Symptoms</u>
Fatigue, Lethargy	2,3,4,6,7,8,9,10,12,18,22
Memory Loss, Confusion	4,7,8,10,11,12,14,16,19,20,21,22
Irritability, Mood Swings	3,9,17,18
Loss of Balance, Dizziness	5,8,12,15,19
Tingling, Prickling, Numbness	10,14,15
Muscle Weakness	2,6,9,16
Loss of Coordination, Awkward Gait	2,9,14,16,20,21,22
Pain, Muscle Spasms, Curled Fingers	2,6,7,10,15,16,17,20
Tremors	2,8,9,13,14,20
Impaired Vision	10,19
Impaired Hearing	9,13
Slurred Speech	8,21,22
Metallic Taste	8
Headache	4,10,17,22
Depression	10,18
Difficulty Sleeping	11

there is no evidence in any of these cases for any cause except methylmercury exposure from fish consumption. Most of the patients were examined at length, in some cases by several doctors who initially failed to find any cause for their symptoms, until a blood test revealed elevated mercury exposure. None of the patients had either a history of or medical evidence (e.g., a blood test) of a disease or exposure to any other toxic agent that could cause the observed symptoms. In most cases, such alternative explanations were effectively ruled out as part of the diagnostic process.

The bottom line, then, is that we can be reasonably certain, scientifically, that the illness suffered by the patients in **Appendix A** is in fact methylmercury poisoning, attributable to the mercury content of the fish they consumed in large amounts.



How Much Mercury is Too Much?

What level of mercury exposure—or more specifically, what blood mercury level—poses a significant risk of mercury poisoning in adults and children? The cases reviewed here offer valuable insights into that critical question.

Early studies of methylmercury toxicity were done mainly in cases of severe poisoning, as described above. In those studies, mostly done 30 to 40 years ago, clear signs of nerve damage in adults were generally associated with blood mercury levels above 200 parts per billion (ppb)⁵, and more subjective symptoms were observed in adults with blood levels above 50 ppb.⁶ In contrast, methylmercury toxicity occurred in cases reviewed here in adults and children with blood mercury levels from 7 to 125 ppb. Several patients with blood levels from 12 to 58 ppb had moderate to severe symptoms, quite similar to those experienced by patients with higher blood mercury (75 to 125 ppb). Most of the patients who had only milder symptoms had blood mercury levels from 7 to 29 ppb.

Such variability in the doses associated with symptoms of methylmercury poisoning is consistent with the fundamental environmental health principle that individuals vary widely in sensitivity to toxic effects. Many of the cases reported here probably represent individuals who are much more sensitive to mercury toxicity than average. On the other hand, these cases included four individuals with blood mercury levels ranging from 24 to 228 ppb who showed no symptoms of mercury poisoning. This latter group probably represents individuals who are inherently less sensitive to toxic effects of methylmercury. Determining which group is more “typical” would require more research.

Some observers might argue that these patients cannot be suffering from methylmercury

poisoning, because the doses involved are too low to cause such effects, based on historical studies. That argument goes against common experience in environmental health research, in which effects of a toxic substance are often first associated with very high doses, and then later are attributed to much lower doses. This has been the case with lead poisoning, and has also been shown with methylmercury poisoning.⁷

Studies done in Italy and Brazil, cited in **Appendix C**, have shown that methylmercury doses too low to produce symptoms of clinical illness nevertheless have adverse effects on mental processes and fine-motor coordination, as measured with sensitive tests. These studies are examples of advances in research methods that have improved our ability to detect effects and attribute them to a specific cause. This research also suggests that methylmercury poisoning can cause subtler effects than the obvious symptoms of illness that characterize most of the cases reviewed in **Appendix A**. If such “sub-clinical” effects are included in the definition of methylmercury toxicity (and they should be), the dose of methylmercury that poses a risk of adverse effects is lower, and the population at risk is correspondingly larger, than would be the case if only symptomatic poisoning were seen as the hazard to be concerned about.

There has been no concerted effort to define a dose-response relationship for neurotoxic effects of methylmercury in a “normal” population with exposure from a diet rich in fish. Several studies have looked for possible effects on cardiovascular health, but few have focused on neurotoxic effects, which in the past have not been believed to occur at the dose levels people ordinarily encounter from their diets alone. Yet the evidence of these cases suggests that the problem does occur—at least occasionally—at doses that until now have been regarded by most authorities as harmless.

How Many Other Cases Are “Out There”?

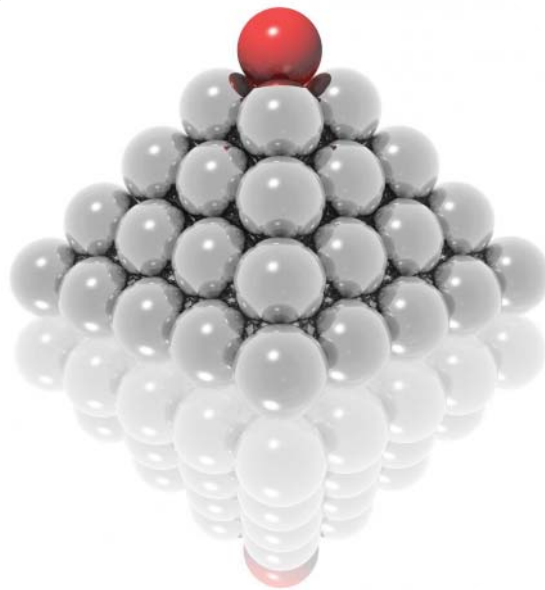
It is virtually certain that the cases reviewed here are not all the cases of methylmercury poisoning that have occurred in the United States. Instead, they probably represent the proverbial “tip of the iceberg.” They are cases that not only were properly diagnosed by a physician, but also have been described in readily accessible published sources, such as scientific journals, news reports or first-person accounts.

Appendix E explores several methods for estimating how many such cases there may be, at any one time, in the US. None of the methods is precise, by any means, but all three approaches used suggest that less than 0.1 percent of the US population seems likely to be suffering from methylmercury poisoning (i.e., given a current US population of about 320 million people, there would be less than 320,000 cases.) That number is far too large to be reassuring. While the actual number could be much smaller than that, unfortunately, we do not have enough good data to obtain much better estimates.

A back-of-the-envelope method based on arbitrary assumptions about the number of “extreme” (high-end) fish consumers and the fraction of them that frequently choose to eat high-mercury fish produces estimates ranging from about 3,200 to 32,000 possible cases of methylmercury poisoning. This estimate is

limited by lack of data to indicate whether the assumptions used are at all realistic.

Two relatively small studies that looked for methylmercury poisoning in populations of high-end fish eaters found adverse effects in less than 1 percent of their study subjects. Since these studies focused on people with above-average fish consumption, the likely incidence of cases in the US population as a whole is probably well below the level seen in either study, i.e., probably in the range of 0.1 percent or less. Again, this method is far from precise, and is useful mainly for indicating a likely upper boundary for the possible number of cases.



A third method draws inferences from the CDC’s NHANES surveys, which tested the blood of 5,214 women and children and found none with a blood mercury level above 58 ppb, a “benchmark” of concern established by the US EPA.

While some of our cases had adverse effects of methylmercury associated with blood mercury levels below 58 ppb, it is still useful to examine the statistical power of the NHANES survey to determine how many Americans might have high blood mercury levels (> 58 ppb).

Given the NHANES data, simple probability calculations show that it is very unlikely that the incidence of blood mercury above 58 ppb could be as high as 0.1 percent (1 in 1,000 people), but that it could very well be as high as 0.01 percent (1 in 10,000), without a single

individual with a blood mercury level that high being included in the NHANES samples. A similar calculation shows that if the incidence were 1 in 1,742, the NHANES sample would have had a 95 percent probability of including at least one such person. In other words, the fact that the NHANES surveys found no one with blood mercury above 58 ppb makes us reasonably certain, statistically speaking, that there are no more than about 184,000 (320,000,000 divided by 1,742) such people in the country. This not-very-reassuring conclusion is consistent with the other methods, in that it suggests a case rate of 0.06 percent or less.

In summary, while we lack satisfactory quantitative estimates of the number of people who might get methylmercury poisoning from their high-end fish consumption, it is difficult to conclude that the number of cases is negligibly small, based on any set of reasonable assumptions. By our “triangulation” methods, the number of such cases could range from a few thousand to a few hundred thousand. This question obviously demands aggressive study and more definitive analysis.

Conclusions and Recommendations

Health authorities have recommended for many years that people should eat more fish, because of the known nutritional benefits of a high-fish diet. Americans are getting the message; per capita U.S. fish consumption has been increasing steadily for at least the past 20 years. In 2006, consumption of fresh and frozen fish, fish fillets and steaks, and shrimp reached all-time high levels.⁸ But consump-

tion of some fish also presents risks, especially from exposure to methylmercury. Many fish varieties, including most of the top-selling choices in the US market, are very low in mercury and can be safely consumed even by people who enjoy fish meals every day (See **Appendix F**).

Although the average American still eats fish only about once a week, some people do so far more frequently. Those at greatest risk of getting methylmercury poisoning are the people who really eat a lot of fish—perhaps the top 0.1 percent of the fish-consumption distribution. Within that group, people who prefer and frequently choose high-mercury varieties of fish—such as tuna, swordfish, halibut, sea bass, and a few other fish types associated with poisoning in cases reviewed here—are most at risk.

While we don’t know exactly how many such people there are, or exactly who they are, it should be feasible to inform them of the mercury levels in various fish choices and of the risks associated with eating higher-mercury varieties frequently. Federal agencies’ advice to date has focused on risks to the developing fetus, and has been aimed solely at women of childbearing age. State agencies have issued warnings to recreational anglers who eat what they catch, often focused on mercury levels in fish from specific lakes or streams. Virtually no advice has been provided for members of the general public who eat a great deal of commercially-caught fish, and who frequently choose one or more high-mercury varieties. It is past the time to end that silence.



With that in mind, the Mercury Policy Project recommends:

1. Consumers who eat fish often should continue to do so, because a diet high in fish has proven health benefits. But consumers should also be aware of the risks associated with methylmercury exposure, and should learn to choose low-mercury fish. See **Appendix F** for detailed guidance and a comprehensive listing of fish and seafood choices by mercury content.

2. The environmental health research community should aggressively gather more and better data on the occurrence of methylmercury poisoning associated with high fish consumption, to better document risks associated with various fish and seafood choices, the nature of adverse effects at different levels of mercury exposure, and the number of people who may be at risk for these effects. The focus of research needs to expand beyond women of childbearing age and young children, and should include case-control and prospective cohort studies designed to determine the effects of mercury exposure in adults and older children who eat a great deal of fish.

3. Government agencies at the federal and state levels that manage the risks of mercury exposure should improve their consumer ad-

vice about fish consumption. At the federal level, in particular, the 2004 EPA/FDA joint advisory should be updated and expanded, to include an additional focus on high-end fish consumers. Information on mercury levels in different fish and shellfish also needs to be better presented and interpreted, with more detail and nuance, to help consumers who are trying to manage their own risk from mercury in the fish they eat. Stated simply, people who eat a lot of fish need more and better information on the mercury content of fish people eat a lot of, such as tuna, halibut and sea bass.

4. State and federal health agencies should expand their efforts to collect and integrate data on cases of methylmercury poisoning from fish consumption, and on the fish varieties and exposure levels involved in each case. The data thus collected should be made available to scientists pursuing the research questions outlined in (2) above.

5. Government agencies at all levels should acknowledge that anyone who eats too much of the “wrong” fish can get mercury poisoning. (Current information strongly suggests that no one but women of childbearing age needs to be concerned about methylmercury.) Agencies should make a greater effort to alert both physicians and consumers to this possible risk, and to guide consum-



ers to choose low-mercury fish. Agencies promoting fish consumption for its nutritional benefits should include information on methylmercury risks, and lists of low-mercury fish.

6. Physicians who encounter a patient with mercury poisoning from fish consumption should make an effort to write up the case history and publish it in a medical journal, to help alert other medical professionals to the occurrence and signs of this disease.

7. Grocery chains and non-governmental organizations developing point-of-pur-

chase mercury information programs should review their educational materials to be sure they are not unduly focused on women of childbearing age. Such materials should specifically note the possible risk of mercury poisoning in anyone who eats large amounts of a number of mercury-containing fish varieties. (See **Appendix F** for additional details.) Grocery chains not yet participating in point-of-sale information programs (roughly two-thirds of the nation's supermarkets) should join the effort to inform fish consumers about the mercury content of different varieties of fish and seafood.



APPENDIX A

Case Descriptions

The 22 individual cases described in this Appendix fall into three groups. **Group 1**, which includes 15 cases and 17 patients, consists primarily of individual adults who ate commercially-caught fish (one case is a family of two adults and a child.) **Group 2** is made up of four adult men who ate sport-caught fish, and **Group 3** consists of 3 children whose parents fed them commercially-caught fish.

Group 1: Patients Eating Commercially Caught Fish

(1) Mike Brown



Mike Brown, a 63-year-old senior executive from Claremont, CA, is a health-conscious individual. He began eating swordfish salads in the mid-1980s, and said he often ate that same meal three times a week. When he saw a news story about mercury in fish, one that specifically mentioned swordfish as high in mercury, in 2004, he had his blood tested. His mercury level was an astonishing 228 ppb (roughly 40 times the US EPA's "safe" level). Brown, however, experienced no symptoms. He stopped eating swordfish, and after several months, his blood mercury level was still above 70 ppb. He lifts weights and stays in great shape. While he feels fine, he worries about possible long-term impacts of his high mercury exposure on his health.



Source: Greene (2005)⁹

(2) Dan Deeter



Dan Deeter, 56, lived in Alta Loma, CA when he developed his health problems (he has since moved to Las Vegas). He was very health-conscious and was following a regimen called The Zone Diet; as his protein source, he began eating one to two cans of tuna per day in 1997. Within a year, he began feeling fatigued. Soon, he could no longer drive. He began having tremors, then seizures. The doctors he saw could not tell what was wrong with him. From about the end of 1998 through July of 2003, he spent most of the time in bed, suffering from spasms and pain, unable to work. His wife eventually suggested that something might be poisoning him, and he got his blood tested. The test revealed a "dangerously high" mercury level. He stopped eating fish, and two years later (in March 2005), reported he was feeling "85 percent better, nearly well. It's like night and day."



Source: Greene (2005)¹⁰

(3) Joe DiMauro



Joe DiMauro owns a fish market in Mount Kisco, NY. They sell a lot of raw and rare tuna, and his daily routine included going down to the Fulton Fish Market to select a 300- to 400-pound tuna, cutting a bite out, and tasting it, to make sure it was fresh. DiMauro began feeling lethargic, and was experiencing wild, unprovoked mood swings. Concerned about his nutrition, he had a hair sample analyzed for trace elements. The results showed a mercury level that was “off the charts,” and the analyst asked if he ate a lot of fish. A light went on in his mind. He stopped eating fish for six months, until his blood mercury level returned to near normal. As it did, his mood swings vanished and he got his energy back. Ever since, customers at his store don’t buy fish without being informed about mercury.



Source: Witherspoon (2004)¹¹

(4) Lee Flynn



Lee Flynn, now 64, is an anthropologist and filmmaker in Sausalito, CA, just across the Golden Gate from San Francisco. She led a healthy lifestyle, but for more than a decade she suffered from chronic fatigue, headaches, and stomach aches. Her hair began falling out and she was losing her memory. Flynn ate fish an average of nine times a week, often choosing tuna, halibut, sea bass and swordfish. A doctor suspected mercury poisoning, and found 21 ppb of mercury in her blood. Now, several years later, after eliminating high-mercury fish from her diet, her blood mercury level is normal, her memory is fine, and she feels healthy again.



Source: Allen (2003)¹²

(5) Arnold Michael



Arnold Michael, a 48-year-old video photographer from Fort Lauderdale, Florida, ate tuna steaks and canned tuna as part of a healthy-diet regimen he was following. He estimated that he ate tuna at least four times a week. He developed dizzy spells, and consulted a doctor; a blood test showed he had high mercury levels. He went on a tuna-free diet, and his symptoms gradually disappeared.



Source: Roe and Hawthorne (2005)¹³

(6) Wendy Moro



Wendy Moro, 40 at the time her case was reported, is a marketing consultant living in a suburb of San Francisco. She was active, fit, and energetic; she ran every day, danced ballet, and lifted weights. She also ate fish two to five times a week, both at home and in restaurants, believing it was a healthy choice. Her lunch was often canned tuna, and her family would regularly have fish for dinner; they favored steaks, such as ahi tuna or halibut. In the spring of 2001, Moro began feeling severe fatigue. She started having pain and weakness in her arms and legs, which got so bad she could barely stand up. A series of doctors failed to find what was causing these symptoms. Finally, one doctor tested her blood for mercury, and found it was three times the safe level. She stopped eating fish, and her symptoms slowly began to disappear. When her case was reported, she felt “about 85 percent back to normal.”

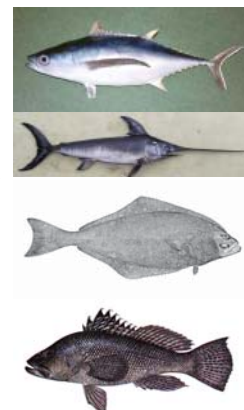


Source: Manning (2002)¹⁴

(7) Susie Piallat



Susie Piallat, a former sales manager for an airline, (shown here with her son, Cristophe) is very health-conscious, energetic and petite. She ate fish eight or nine times a week, usually choosing tuna, swordfish, halibut or sea bass. For years, she had felt chronic “flu-like” symptoms, including fatigue, muscle and stomach aches. She was having trouble concentrating, and was losing her memory and her hair. Nothing she tried made her feel better. A doctor finally asked about her fish consumption, and tested her blood for mercury; the level was 76 ppb, 13 times the EPA’s “safe” reference level. It took almost a year of avoiding mercury-laden fish for her mercury level to drop into the safe range, but she now feels much better.



Source: Kay (2002)¹⁵, Hightower (2009)¹⁶

(8) Will Smith



Will Smith, a geophysicist, couldn’t think any more. He couldn’t do even simple math, and he was forced to quit work. His speech was slurred, he was losing his memory and his balance, and he couldn’t even watch TV without getting dizzy. He experienced a metallic taste, constantly. When he’d go out, he’d lose his car, or get lost himself, in a city he had lived in for decades. He had tremors, and he was always tired. Smith reported eating tuna “all the



time,” for lunch, for business dinners. He ate sushi often, tuna steaks, and canned tuna several days a week as a snack. His doctor diagnosed mercury poisoning, and put him on a no-fish diet. He started getting better almost immediately, but the process was long and slow. Neurological testing showed that he had suffered some permanent brain damage, of a type his doctors said is almost always associated with heavy metal poisoning.



Source: Raines (2002)¹⁷

(9) Marilyn Winston



Marilyn Winston, 66, of New Brunswick, NJ, plays the guitar. A few years ago, she noticed that she was losing her ability to play the instrument. Although she was working out with weights, she was getting weaker, not stronger. Her hair was thinning and falling out, and she had hand tremors. She was losing her hearing and felt lethargic, irritable and impatient. Winston had always been very health-conscious, had not eaten red meat for 15 years, and had stopped eating poultry a few years later. She ate tuna steaks and swordfish four to five times a week. She had her hair analyzed by a naturopathic physician; it showed 13.3 ppm mercury, a high level (normal is about 1 ppm). She then visited the Environmental and Occupational Health Sciences Institute at nearby Rutgers University, where the doctors found that her blood had 38 ppb of mercury, and diagnosed her problems as methylmercury poisoning. She eliminated high-mercury fish from her diet, and over the next several months her symptoms gradually disappeared, and she felt much better.



Source: Bates (1999)¹⁸

(10) Daphne Zuniga



Daphne Zuniga, 45, an actress, is very health conscious. She meditates, does yoga, runs and hikes. She doesn't eat meat, and for years has relied on fish as her protein source. Tuna on Caesar salad and yellowtail sushi were among her favorites. She was suffering from headaches, inability to concentrate, depression, blurred vision, muscle aches, cramps in her hands and feet, chills and tingling in her legs, back, neck and head. After eating sushi three nights in a row, she broke out in a severe rash. Her doctors could not figure out what was causing her illness. She saw a news story about mercury in fish, had her blood tested, and it had more than twice the level considered safe. She replaced her favorite fish choices with low-mercury varieties, and was given chelating drugs every three weeks. Over a period of three months, she reported in an article she wrote later about her experience, her cramps and chills subsided, her other symptoms improved, and her depression lifted.



Source: Zuniga (2005)¹⁹

(11) Anonymous



A 40-year-old lawyer living in Madison, Wisconsin was experiencing problems sleeping and a loss of concentration severe enough to affect his ability to work. He and his family followed a meatless diet, but they ate fish three or four times per week. They ate several varieties repeatedly, including Lake Superior whitefish, salmon, trout, and their favorite, Chilean sea bass, all bought at a local market. Their family physician diagnosed mercury poisoning in the man, based on a hair mercury test that showed 12 ppm, a high level, and a blood mercury level of 58 ppb, which is 10 times the US EPA's "reference level," the definition of "safe" exposure. Two samples of the Chilean sea bass the family had been eating, tested by the Wisconsin Bureau of Public Health, contained 0.60 ppm mercury. The family said they ate sea bass twice a week, and the man estimated that he consumed about 8 ounces per meal. The man's wife and son both had blood mercury levels of 37 ppb, but neither experienced any symptoms. Health officials advised the family to stop eating sea bass. Within six months, the two adults' blood mercury levels had dropped to 5 and 3 ppb, and the man's symptoms disappeared.



Source: Knobeloch et al. (2006)²⁰

(12) Anonymous, Family



A mother, father and child who live on a ranch in the California wine country began losing their hair. They saw a dermatologist, who suspected heavy metal poisoning. Blood tests revealed that all three had elevated mercury levels. An intensive search of their property found no mercury sources in their home, drinking water or soil. The dermatologist referred the patients to an internal medicine specialist, who tested the woman's blood for mercury (18.5 ppb), and noted that she suffered from nausea, fainting spells, loss of concentration, fatigue and other symptoms, as well as hair loss. The doctor asked about their fish consumption. Yes, they ate a lot of seafood, particularly tuna and swordfish. Once the source of their exposure was known, they were advised to avoid high-mercury fish, and they gradually got better.



Source: Kay (2002)²¹, Hightower (2009)²²

(13) Anonymous



A 53-year-old woman contacted the federal Agency for Toxic Substances and Disease Registry (ATSDR) in 1999, after tests by her physician revealed a very high blood mercury level (125 ppb). She had been eating fish 10 or more times per week for over nine years. She ate swordfish about twice a week, and a variety of other (unspecified) fish. After two years on her high-fish diet, she had developed reddened skin. Her doctor tested her hair for mercury because of her high fish consumption; it contained 68 ppm, a very high level.

The doctor advised her to reduce her fish intake, but the woman believed fish was essential to her health and continued to eat it daily. She subsequently developed mouth sores, tremors, and a ringing sensation in her ears and head. She then got her blood tested, and her diagnosis of mercury poisoning was confirmed. She was still reluctant to believe fish could be poisoning her, and contacted ATSDR to ask for help locating her source of mercury exposure. After investigation ruled out other sources, the agency concluded that her fish consumption was indeed the problem and advised her to reduce her fish intake substantially. Unfortunately, she moved away and further follow-up was not possible.



Source: Risher (2004)²³

(14) Anonymous



A plastic surgeon living in the San Francisco area had hand tremors so severe that she feared she would have to stop performing surgery. She also had numbness and tingling in her hands and feet, and was losing her memory. Her hair was falling out. She ate a varied diet, including meat, chicken, and fish—fresh tuna steaks—just two or three times a month. Despite her rather modest fish consumption, her blood mercury level was above 35 ppb. Her doctor told her to stop eating tuna. Within a few months, her blood mercury level came down into the acceptable range, and her symptoms simply disappeared.



Source: Raines (2002)²⁴

(15) Anonymous



A 61-year old retired research manager told his physician in Scarsdale, NY that his feet often felt numb, especially in bed at night, with a sensation like wearing tight socks (his doctor called that “sock and glove paresthesia”). A finger or two on each hand would sometimes lock in the flexed position, a phenomenon the doctor called “trigger finger.” Occasionally he would feel dizzy or lose his balance, and he was having arthritis-like pains in his hands and knees for the first time. His doctor

ordered a blood mercury test and asked about his fish consumption. The patient had been pursuing a healthier diet and ate fish five to seven times a week. He and his wife ate fresh or frozen salmon, tilapia or sole once or twice weekly for dinner, and he had sushi for lunch almost every day. Tuna was his favorite sushi choice. The blood mercury test showed a level of 9 ppb, not especially high. Nevertheless, he stopped eating tuna, and chose only low-mercury varieties of fish and sushi. A year later, his blood mercury had decreased to 3 ppb, and his symptoms were virtually gone.



Source: Anonymous (2008)²⁵

Group 2: Adults Eating Sport-Caught Fish

(16) Henry Henk



Henry Henk, of Windigo, Wisconsin loved to fish, and to eat fish. He ate fish twice a day, almost every day, consuming an estimated forty fish a month. He caught lake fish, especially northern pike. At age 61, Henk began feeling seriously ill. He could no longer walk, and he began hallucinating. He lost weight, and suffered from excruciating pain in his back and legs. He seemed to be dying, and his doctors could not figure out why.

In a hospital in Duluth, he was eventually diagnosed with methylmercury poisoning. He was given chelation therapy, to remove mercury from his system, and he eliminated fish from his diet. Within a few days, his hallucinations stopped, and he began to feel better. Several weeks later, he was walking again, with the use of a walker. He gained back most of the weight he had lost, and got some relief from his pain. But nerves in his legs were permanently damaged. Henk says he has only himself to blame—he knew about the state’s advisories about mercury levels in fish from certain lakes, but he ignored the warnings—he just loved to eat fish.



Source: Stanich (1993)²⁶

(17) David Wright



David Wright, a 56-year-old pool maintenance contractor from Rancho Cucamonga, CA, loves fishing. He took week-long trips out on the Pacific Ocean and would catch and eat “big fish,” including yellowtail and (occasionally) bluefin tuna. He estimated that he ate 50 pounds of fish a year. For several years, Wright had severe headaches, mood swings, and joint pain. When a fellow fisherman suggested mercury might be causing his health problems, Wright had his blood tested; it contained more than 120 ppb of mercury (the “safe” level is about 6 ppb). Wright cut back the amount of fish he ate, and switched to eating smaller varieties. His headaches stopped, and his other symptoms improved, but four years later, his blood mercury level was still above 10 ppb.



Source: Greene (2005)²⁷

(18) Anonymous



A 55-year-old recreational fisherman living in Two Rivers, Wisconsin caught and ate fish from a local lake. He caught pan fish, walleye, bass and northern pike. He reported that he had been eating fish he caught twice a week, on average, for at least 10 years, and that he ate on average 8 ounces of fish per meal. Average mercury levels in the fish he caught were estimated to be 0.7 ppm in walleye, 0.3 ppm in bass and northern pike, and 0.2 ppm in pan fish. He had seen his physician because he suffered from irritability, tiredness and depression. The doctor diagnosed mercury poisoning and prescribed chelation therapy. The patient’s pre-chelation blood mercury level was estimated to be about 7 ppb. His symptoms improved with treatment and his blood mercury was lowered even further.



Source: Knobeloch et al. (2006)²⁸

(19) Anonymous



A 65-year-old resident of Rhinelander, Wisconsin had his hair tested for mercury in response to an announcement from the Wisconsin Bureau of Public Health. He had a high hair level, 8.78 ppm. In a follow-up interview, he said he ate sport-caught fish, northern pike and bluegill, three times a week; he estimated that he ate about 50-60 northern pike in a year. His blood mercury level was 29 ppb. Three northern pike he provided had an average mercury level of 0.76 ppm. The man suffered from vision problems, confusion, and loss of balance. His doctor gave him chelation therapy and put him on a fish-free diet. After 38 days, his blood mercury level decreased to 13 ppb and his health was markedly improved. The man's brother, who fished with him and ate the same fish, had hair and blood mercury levels of 9.45 ppm and 24 ppb, respectively, and although he had not experienced symptoms of mercury toxicity, he also underwent chelation treatment.



Source: Knobeloch et al. (2006)²⁹

Group 3: Children Eating Commercially Caught Fish

(20) Matthew Davis



Matthew Davis, a 10-year-old fifth grade student in Berkeley, CA, shown here with his mother, Joan, was having problems in school. He couldn't focus, labored at simple tasks, and missed assignments. He had been a straight-A student, and his struggles came as a shock to his parents. He also began having problems with his hands. His fingers curled, he had tremors, and could no longer catch a football or hit a baseball. His parents took him to a doctor who diagnosed methylmercury poisoning, confirmed by a high blood mercury level (over 60 ppb). The source: Tuna fish. Starting a year or so before he was diagnosed, Matthew had begun eating canned albacore tuna about twice a day. His parents were delighted that he chose tuna—a “brain food”—over “junk foods.” What they didn't know was that the large amount of albacore Matthew was eating contained 12 times the safe dose of mercury for his 60-pound body. Matthew stopped eating canned tuna. His blood mercury dropped to an undetectable level in a few months. Today, he's fully recovered, a high school freshman, playing varsity football, doing well academically and involved in several extracurricular activities



Source: Waldman (2005)³⁰, Davis (2007)³¹

(21) Sophie Waldman

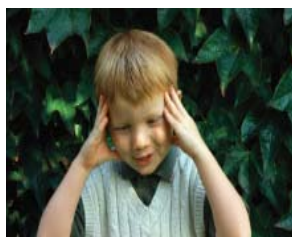


When Sophie Waldman was 5, in 2000, she seemed to stop learning. She had been an early walker and early talker, and her parents, both of whom are accomplished novelists, were understandably proud of their very bright child. Then she started “slowing down,” as her mother described it. She forgot how to tie her shoes and couldn’t remember words, and her hair stopped growing. Sophie loved tuna fish sandwiches, and was eating two cans of albacore tuna a week. When tests found a blood mercury level of 13 ppb, she was taken off the tuna fish. Her blood mercury level came down, and her physical and verbal abilities returned. She had what her mother called “a huge developmental upsurge.”



Sources: Roe and Hawthorne (2005)³², Raines (2002)³³

(22) Anonymous



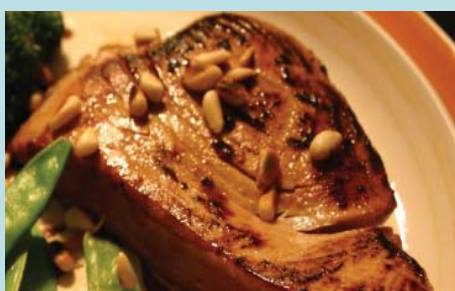
A 7-year-old boy had developed normally through the age of three, when he began eating fish. The child simply loved fish, and regularly ate canned albacore tuna, albacore and ahi tuna steaks, and king mackerel. Soon after he started eating a fish-heavy diet, his development began to decline. He stopped playing with other children, and would sit by himself, “totally lost, in a fog,” as his mother described it. He couldn’t remember classmates’ names, and lost his ability to express complete thoughts. He lost fine motor skills and became somewhat “uncoordinated.” He also had stomach aches, headaches, reddened skin, and was lethargic. When a doctor finally tested his blood for mercury, the level was above 75 ppb. He stopped eating fish, and after eight months, his blood mercury level dropped into the normal range. His condition also improved, steadily and markedly. But extensive neuropsychiatric testing revealed that he had suffered some permanent brain damage.



Source: Raines (2002)³⁴, Hightower (2009)³⁵

Does Methylmercury Cause a Skin Rash?

Dr. Paul Dantzig thinks so. Dantzig, a dermatologist at Columbia University's School of Physicians and Surgeons, experienced a specific type of severe skin rash himself after eating a meal of teriyaki tuna steak about seven years ago. Since he had no known allergies to fish, he suspected a toxic reaction, and had his blood tested. The mercury level was "sky high." He stopped eating fish, and took chelating drugs to lower his mercury level. His rash went away, his health improved in other ways as well, and he developed a new research interest.



After his own experience, Dr. Dantzig began noticing a similar rash in patients with a skin condition called Grover's disease. Some had been suffering from their skin problems for as little as one week, others for as long as two years. Dantzig took careful dietary histories and when they revealed that a patient regularly ate large amounts of fish, he tested their blood for mercury. In patients who had elevated mercury levels, he ruled out other sources of mercury exposure and allergy to fish as possible causes of their rash. In 2003, he published a report describing 11 patients with a skin rash he had diagnosed as caused by exposure to methylmercury from fish consumption. Two of the patients also experienced neurological symptoms (dizziness in two cases, memory loss in one). The blood mercury levels in the 11 patients ranged from 6 to 19 ppb. Dantzig told the patients to stop eating high-mercury fish, and in several cases gave the patient chelation treatments to remove mercury from their systems. In all 11 patients, blood mercury levels decreased and their skin rash cleared up, over periods of one to six months.

Dr. Dantzig's conclusion that this specific skin rash is caused by methylmercury in fish needs to be confirmed by other researchers. If it is, both the list of symptoms of methylmercury poisoning and the likely number of cases that occur will be expanded.

Source: Bartelme (2007)⁴⁸, Dantzig (2003)⁶⁶

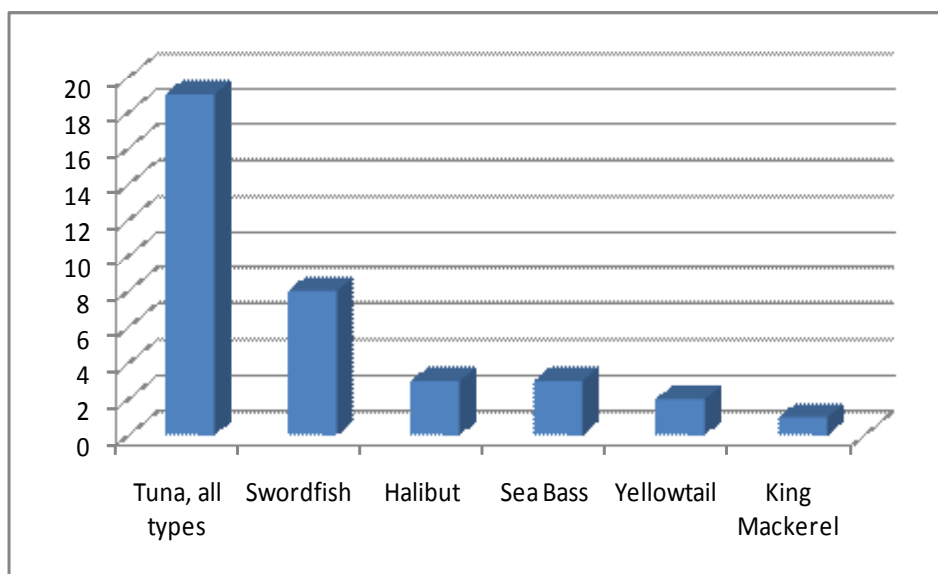
APPENDIX B

Types of Fish Involved in These Cases

The specific fish that patients ate are identified in the published records of each of the cases in **Appendix A**, except for the patients with a skin rash described in the sidebar. The 22 cases include 24 patients (a family of three is involved in **Case 12**). Twenty individuals ate commercially caught fish, purchased at local markets and restaurants, and four ate sport-caught fish. One of the sport fisherman (**Case 17**) ate ocean game fish that are also sold commercially; the fish he ate have been included with the commercially-caught group for this analysis, raising the number of patients in that group to 21. The other three patients were sport anglers who ate a variety of Wisconsin lake fish.

The 21 patients eating commercially caught fish reported consuming only six different fish varieties. **Figure B-1** shows the fish involved and the number of cases in which each one was named as a source of methylmercury exposure. (The total exceeds 21 because most patients ate more than one variety of mercury-containing fish.)

Figure B-1: Fish varieties consumed by patients
Eating commercially-caught fish
(Number of cases reported as eating each fish)



Tuna fish, in one form or another, contributed to the mercury exposure of 18 of the 21 patients in this category (86 percent). In nine of those cases (43 percent), tuna was the only identified source of mercury exposure. Some cases simply report that the patient ate “tuna,” while others specify canned tuna, tuna steaks, tuna sushi, or some combination of those (**Case 8**, for example, liked tuna sushi, canned tuna and tuna steaks.). Three cases specify that the patients ate canned albacore tuna, while four others refer simply to “canned tuna.” (We assumed the product involved in those latter cases was canned light tuna, in creating **Table B-1**, below, although it may in fact have been albacore, or a combination of both types.)

Swordfish contributed to the methylmercury exposure of eight of the 21 patients who ate commercially caught fish (38 percent), and was the only source specified in two cases.

Halibut and sea bass were each sources of exposure in three cases; Chilean sea bass was the only known high-mercury fish consumed by the patient in **Case 11**. Yellowtail was involved in two cases (as sushi in **Case 10**, as sport-caught fish in **Case 17**). One of the child patients (**Case 22**) ate king mackerel, as well as tuna.

The three remaining cases (**16, 18, 19**) involving sport-caught fish are quite similar; all three men lived in Wisconsin and ate several different lake fish. Northern pike was a common source in all three cases. This sample is too small and too geographically homogeneous to support further analysis of the fish types involved.

Table B-1 presents data on average mercury levels in the fish varieties that were sources of exposure in these cases. As the table shows, swordfish, which has long been recognized as an important source of mercury exposure, contains about 1 part per million (1 ppm), one of the highest average levels among commercially sold fish. King mackerel, involved in one case, also has a high mercury level, 0.73 ppm. But the other fish consumed by the patients in these cases—halibut, sea bass, yellowtail, and most forms of tuna—generally contain only about one-fifth to one-half of the mercury level in swordfish. These moderately high mercury levels (roughly 0.2 to 0.5 ppm) have not been the focus of advice aimed at preventing methylmercury poisoning.

Tuna in various forms is a very popular American fish choice. Canned tuna (all varieties combined) is the top-selling US finfish product (outsold only by shrimp among all seafood items). About 38 percent of the canned tuna sold is higher-mercury albacore,³⁶ although canned light tuna may vary in mercury content, and some samples contain levels well above the FDA’s reported average of 0.118 ppm, shown in the table. For instance, 6 percent of canned light tuna samples contain more than the average methylmercury level found in canned albacore tuna.³⁷ Tuna steaks and fillets account for a small part of the total amount of tuna consumed, but the volume sold is still greater than for most other fresh and frozen fish. Tuna sushi is a popular choice, on which data have only recently begun to appear.^{38,39}

Based on limited data reported in the news articles just cited, bluefin tuna appears to contain mercury levels comparable to those found in swordfish. The FDA is collecting data on mercury levels in bluefin, but none are in its current database. Tests done for the newspaper reports found an average of about 1 ppm mercury in tuna sushi, as shown in **Table B-1**. Tuna sushi is often bluefin. Sushi chefs prize larger fish, which are older and tend to have higher mercury levels.

TABLE B-1. Mercury Levels in Fish Consumed in Case Studies

<u>Fish Variety</u>	<u>Mercury, ppm</u>	<u>Case(s)</u>
<u>Commercially Caught</u>		
Canned tuna, albacore	0.353	20,21,22
Canned tuna, not specified†	0.118	2,5,6,8
Tuna fillets and steaks	0.383	5,6,8,9,14,22
Tuna sushi*	0.10-2.76	8,10,15
Other tuna, unspecified**	0.383	3,4,7,10,12,12,12,17
Swordfish	0.976	1,4,7,9,12,12,12,13
Sea bass, Chilean	0.386-0.60	11
Sea bass, all types	0.219	4,7
Halibut	0.252	4,6,7
Yellowtail	0.484	10,17
King Mackerel	0.730	22
<u>Sport-Caught</u>		
Bluefin tuna*	1.0	17
Yellowtail	0.484	17
Northern Pike	0.3-0.76	16,18,19
Walleye	0.700	18
Bass	0.300	18
Bluegill	0.150	19

† Type of canned tuna not specified in these cases. Mercury level shown here is for canned light tuna

* Tuna sushi samples with higher levels are most likely bluefin tuna; rough average for bluefin sushi used to estimate level for intact fish

** Assumed to be fresh/frozen tuna in terms of mercury level indicated here

Data Sources: Unless otherwise noted, US FDA data.⁴⁰ Tuna sushi and bluefin tuna data from New York Times⁴¹ and Houston Chronicle.⁴² Chilean sea bass data from Knobeloch et al.²⁰ Yellowtail data from Florida Fish and Wildlife Conservation Commission.⁴³ Data on mercury levels in sport-caught lake fish are presented in those case study reports (See Appendix A and references for individual cases).

The predominance of tuna as a source of methylmercury poisoning in these cases is striking. Tuna was a source of exposure in 86 percent of the cases, more than twice the frequency of swordfish (38 percent). Because of tuna's popularity, a substantial fraction of Americans who eat a lot of fish are likely to eat a lot of tuna. The near-universal involvement of tuna in this (relatively limited) set of cases suggests that people who eat tuna often (as well as those who prefer other fish involved in these cases, such as halibut, sea bass, swordfish, and yellowtail) need to be better informed about the potential health hazards associated with their mercury content.

Compared to the mercury levels in most of the fish shown in **Table B-1**, many of the most widely consumed fish and seafood choices in the US diet, including salmon, shrimp, tilapia, pollock, sole, flounder, whiting, clams, oysters, scallops, haddock, sardines, herring and anchovies, contain less

than 0.05 ppm mercury.⁴⁴ Even canned light tuna, with an average level of 0.118 ppm, contains far more mercury than many other choices. Although FDA has listed canned light tuna as a “low-mercury” fish, for reasons that were more political than scientific, a more appropriate description of canned light tuna and the other varieties of fish involved in these cases is “moderate to high mercury” fish, while a few—bluefin, swordfish, king mackerel—are actually “very high mercury” fish.



APPENDIX C

How Do We Know It's Methylmercury Poisoning?

Each case described in **Appendix A** was diagnosed by a physician as methylmercury poisoning, based on three factors: The patient's symptoms, the level of mercury in their blood or hair, and their history of eating large amounts of fish varieties known to contain relatively high mercury levels.

Nevertheless, it can be argued that something else could have caused these patients' illnesses. Most of the symptoms they experienced can be caused by other toxic agents or diseases, and in truth, it is almost never possible to prove cause-and-effect relationships beyond all doubt in environmental health. In this Appendix, we examine the scientific evidence and reasoning that supports the conclusion that these cases are exactly what they appear to be: Methylmercury poisoning from eating too much fish that was too high in mercury.

The classical description of methylmercury poisoning comes from studies of the pollution incidents in Minamata and Niigata, Japan in the 1950s.⁴⁵ An incident in Iraq in the 1970s, when wheat treated with methylmercury fungicide, intended for planting, was mistakenly used as food, poisoning thousands of people, provided additional observations of this disease.⁴⁶ The symptoms, which are typical of the effects of a heavy metal on the nervous system, include prickling or tingling sensations in the arms and legs; impaired vision, hearing, taste and smell; slurred speech; loss of balance and coordination; unsteadiness of gait; tremors; muscle weakness and fatigue; irritability; memory loss; depression; and difficulty sleeping.⁴⁷

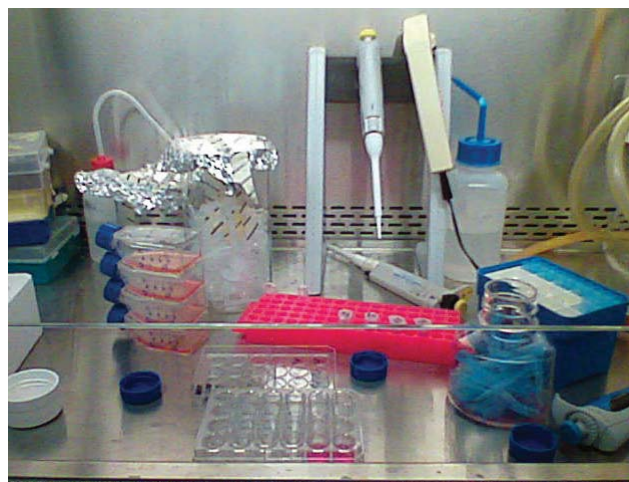


Table C-1 (next page) lists the symptoms experienced by the patients in the cases described in **Appendix A**. While no individual patient had all the symptoms, most patients had several symptoms, and most symptoms were observed in several cases. Taken as a whole, the symptoms of these 24 patients match quite closely with the clinical picture known as Minamata disease, or methylmercury poisoning.

The first two categories of symptoms in **Table C-1** are signs of effects on the brain and central nervous system. They include cognitive effects, such as confusion and memory loss; sensory effects, such as changes in vision, hearing, speech, or taste; balance loss; and headaches. The third category of symptoms results from toxic effects on the peripheral nervous system (the nerves in the body, arms and legs) and muscles, including pain, muscle weakness, spasms and cramping; tingling sensations or numbness; tremors of the hands; and curling of the fingers.

TABLE C-1. Symptoms Reported in Case Studies

<u>Symptoms</u>	<u>Number</u>	<u>Cases</u>
<i>Cognitive & Behavioral</i>		
Fatigue, loss of energy, lethargy	9	2,3,4,6,7,8,9,10,12,18,22
Memory loss	5	4,7,8,14,21,22
Inability to concentrate, confusion	6	7,8,10,11,12,19,20,22
Mood swings, irritability	4	3,9,17,18
Depression	2	10,18
Hallucinations	1	16
Difficulty sleeping	1	11
Difficulties in school (in children)	3	20,21,22
<i>Central Nervous & Sensory</i>		
Loss of balance, dizziness, fainting	4	5,8,12,15,19
Headaches	4	4,7,10,12,17,22
Impaired vision	2	10,19
Hearing loss, ringing in head & ears	2	9,13
Slurred speech	1	8
Metallic taste	1	8
Seizures	1	2
<i>Peripheral Nervous & Musculo-skeletal</i>		
Tremors	6	2,8,9,13,14,20
Chills, tingling, numbness	4	7,10,14,15
Loss of motor coordination	3	9,16,20,22
Pain in arms and legs, joint pain	6	2,6,7,10,15,16,17
Muscle weakness	3	6,9,16
Muscle spasms, cramps, curled fingers	4	2,10,15,17
<i>Skin and hair</i>		
Reddened skin, rash, mouth sores	2	10,13,22
Hair thinned, fell out, stopped growing	7	4,7,9,12 (3 pts), 14,21
<i>General, non-specific</i>		
Disability (could not work)	7	2,6,8,10,11,14,16
Stomach ache/nausea	1	4,7,12,22
Chronic flu-like symptoms	1	7
Weight loss	1	16

A few patients experienced skin problems associated with their high mercury exposure. Two developed skin redness or a rash; eight began losing their hair. The sidebar in Appendix A cites the work of Dr. Paul Dantzig, a dermatologist, who has observed at least 11 additional cases of skin reactions that he has diagnosed as caused by mercury poisoning. In an interview with a reporter, Dr. Dantzig said he sees as many as three or four cases of patients with this novel form of mercury poisoning every week.⁴⁸ If other investigators confirm this diagnosis in other patients, the list of symptoms associated with methylmercury poisoning and the number of cases may expand considerably.

Other symptoms listed in **Table C-1** included some general signs, such as fatigue, the most commonly reported symptom (in 11 cases) and stomach ache.

The symptoms ranged from very mild (perhaps more annoying than distressing) in a few of the cases to severe and disabling in several cases. For most of the patients involved in these cases, their illness substantially diminished their health and their ability to function. Symptoms were reversible in most cases and abated once mercury exposure was reduced or eliminated, but in three cases (**8**, **16** and **22**), permanent brain or nervous system damage occurred.

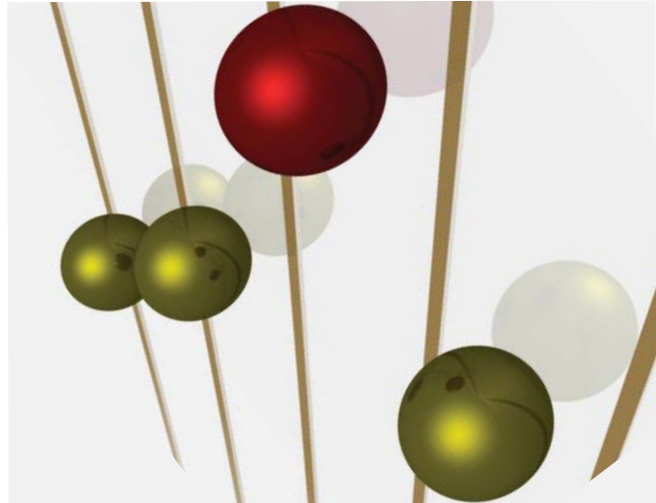
While many of the symptoms in **Table C-1** were experienced by multiple patients, no single “symptom profile” fits all the patients. Several things can account for this variability. The doses of mercury involved, as indicated by blood mercury level where available, varied nearly 40-fold across the cases (See **Appendix D**). More importantly, individuals are different, and toxic effects on the central nervous system can be expressed differently in different people. For instance, one person may experience memory loss, while another suffers from confusion and a third from inability to concentrate. Mercury affects the brain in all three cases, but how that toxicity is expressed varies. There are also subjective differences in how a patient might describe a symptom, and how a physician or a reporter might subsequently interpret and describe it.

Despite these expected sources of variability, the full set of symptoms reported in these cases is quite typical of people suffering from methylmercury poisoning. Several other environmental and food contaminants could also cause such effects, but most of these patients were tested extensively by their doctors, who looked for and ruled out diseases and other toxic agents. All of them ate a lot of mercury-containing fish and had an elevated blood mercury level. Each patient was diagnosed with methylmercury poisoning by one or more physicians. All were told to avoid eating the fish suspected of causing their problems; some also had chelation drug treatments to remove mercury from their systems. And in every case in which the patient did reduce their fish intake, their blood mercury level declined and their symptoms improved or disappeared completely. These facts clearly point to mercury exposure from fish as the cause of their symptoms.

Of course, it is still theoretically possible that something else, not mercury, caused the problems in every case. The patients may have gotten better once they stopped eating mercury-laden fish because of a placebo effect, or mere coincidence. Proper scientific caution requires that such possibilities be acknowledged. But are they likely? No, not at all. None of these patients had any other known toxic exposures or diseases that could cause their symptoms. Given the facts of these cases, mercury poisoning from fish consumption is not only by far the most likely cause of the patients’ symptoms; it is also the only cause for which there is any concrete evidence.

Individual case-histories are the “lowest” kind of evidence in environmental health. A stronger case for a causal relationship can be made by conducting a case-control study, in which a large number of cases (people with symptoms that could be mercury poisoning) are matched with controls (people of the same gender and age with much the same life circumstances, but without symptoms). Then a rigorous statistical analysis is done to determine whether cases ate more fish and had higher blood mercury levels, for instance, than controls, and whether symptoms are correlated with mercury exposure.

Still stronger evidence would come from a prospective study in which a very large group of people was enrolled at the start and followed for a number of years, keeping close track of what they ate and what health problems they had. Ideally, the study participants would be given a battery of tests for cognitive and neurobehavioral functions, and the results would be rigorously statistically analyzed. If such a study’s design included a substantial number of people who eat a great deal of fish, it might eventually be able to determine whether and how often high-end fish consumers exhibit signs of mercury poisoning, and perhaps to show approximately how large this risk is for people who eat much greater than average amounts of fish.



Unfortunately, however, very few such studies have been done to try to better define the relationship between high-end fish consumption and the risk of mercury poisoning. One study, done in Italy, compared 22 adult men who habitually ate tuna fish with 22 matched controls.⁴⁹ The tuna-eaters had an average blood mercury level of 41.5 ppb, compared to 2.6 ppb for the controls. The men were tested for cognitive and neurobehavioral function with an array of different tests; the tuna-eaters’ performance was significantly worse on three tests. Statistical analysis showed that the difference in mercury exposure accounted for about 65 percent of the variance in test scores. The subjects of this study did not feel sick, and had no outward symptoms of mercury poisoning, but sensitive tests nonetheless revealed adverse effects on their brain and nervous system functions.

A similar study using multiple sensitive measures of neuropsychological function tested fish-eating adults in villages in the Amazon Basin where gold mining had contaminated local rivers with mercury.⁵⁰ One hundred twenty-nine subjects were selected randomly and given a battery of tests for memory, intelligence, attention, mood, and manual and mechanical ability. Their mercury exposure was determined by hair analysis. Hair mercury levels were correlated with fish consumption, and subjects with higher mercury exposure performed less well on tests for fine motor speed, dexterity, ability to concentrate, and some aspects of verbal learning and memory. The magnitude of the effects increased as mercury dose increased. The range of hair mercury levels of the subjects in this study overlapped considerably with the range measured in Americans. The study suggests

that U.S. adults who eat a lot of mercury-containing fish might exhibit effects on neuropsychological functions if they were tested with appropriately sensitive methods that could detect such effects.

Another study, done in San Francisco, reported elevated blood mercury levels in patients who ate a lot of fish, and observed that several patients had symptoms consistent with mercury toxicity,⁵¹ but that paper provided no rigorous analysis of cases and no details of individuals' symptoms. A long-term study cited in the introduction of this report (by Oken et al.) is exploring effects of mercury from fish a woman consumes while she is pregnant on her child's cognitive development. But if any studies are currently under way pursuing the possibility of mercury poisoning in US adults and older children who eat a lot of fish, none have been published yet. Clearly, more research on this topic is needed.

Why isn't more such research being done? One reason is that epidemiological studies are expensive, and resources are limited. Priorities need to be set, and usually are driven by what researchers are interested in and what problems are perceived as important. There are many environmental health concerns, many less well understood than methylmercury toxicity, competing for research funding and scientists' attention. But another reason may be a perception on the part of many scientists that there is no such problem as mercury poisoning from eating commercially caught fish. A Chicago Tribune reporter asked an official of the Great Lakes Commission why they weren't doing more testing for mercury levels in fish sold in regional markets. "Why should we spend resources looking for a problem we know doesn't exist?" was the official's reply.⁵² Sad to say, that attitude is probably relatively widespread.

One thing that could help overcome lack of awareness of the problem would be for more physicians who have encountered patients with mercury poisoning from fish consumption to publish case histories in medical journals. Given the many demands on a physician's time, the number of published reports is likely to increase only slowly at best.

Our bottom line, then, is that we are confident that the cases described in Appendix A are just what they seem to be, methylmercury poisoning from fish consumption. For further analysis of the amounts (doses) of mercury involved in these cases, see **Appendix D**, and for a discussion of how widespread such cases may be, see **Appendix E**.



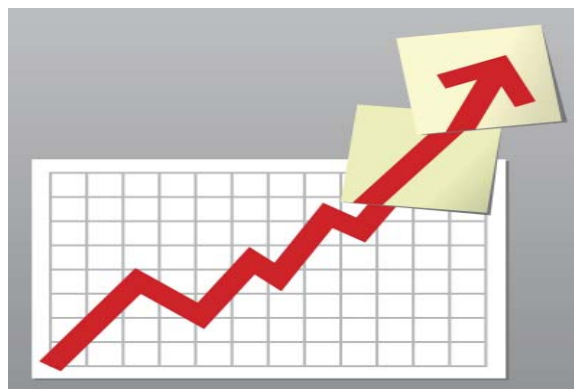
APPENDIX D

How Much Mercury Is Too Much?

What level of mercury exposure—or more specifically, what blood mercury level—poses a significant risk of mercury poisoning in adults and children? The cases reviewed here offer valuable insights into that critical question.

Blood mercury levels were reported quantitatively for only 17 of the 24 patients in these 22 cases. In other cases mercury levels were described qualitatively, for instance as “sky high” or “off the charts.” The reported numerical blood mercury readings range from 7 ppb (**Case 18**) to 228 ppb (**Case 1**). This sample size is too small to support rigorous statistical analysis to correlate different symptoms with different blood levels.

In fact, in this very limited set of data, there appears to be little if any correlation between measured blood mercury level and severity of the reported symptoms. On one hand, some individuals with only relatively mild symptoms (e.g., **Cases 15 and 18**) had among the lowest reported blood mercury levels. On the other hand, patients with the highest blood mercury levels did not always have the most severe symptoms.



Unfortunately, blood mercury levels were not specified for three patients (**Cases 2, 8 and 16**) who were among those most severely affected by toxic symptoms. The person with the highest blood mercury level (228 ppb, **Case 3**) had no symptoms at all. Four other patients with the four next highest reported blood mercury levels (**Cases 13, 17, 7, and 22**, at 125, 120, 76, and over 75 ppb, respectively) had symptoms that could be classified as moderately severe. But seven people with much lower blood mercury levels, from about 12 to 38 ppb (**Cases 4, 6, 9, 10, 12 14 and 21**) also suffered moderate to severe symptoms that seem, from the descriptions, at least as serious as those experienced by the patients with much higher blood mercury levels, just described.

Several of the adult patients experienced symptoms severe enough that they were to a large extent disabled, unable to work or live their normal lives (**Cases 2, 6, 8, 10, 11, 14 and 16**). In three of those (**Cases 2, 8, and 14**), a quantitative blood mercury value was not part of the case description, but in the other four cases, the blood mercury values ranged from 12 to 58 ppb, not exceptionally high levels.

This seeming lack of correlation between blood mercury level and severity of symptoms reflects both the small number of data points available here and the known limitations of blood mercury level, especially at a single point in time, as an index of exposure and potential for toxic effects. On one hand, blood mercury levels in an individual can fluctuate, and high levels, in particular, may be

as likely to reflect a single recent meal as a chronic steady-state level. On the other hand, when an epidemiological study associates a particular effect with a specific blood mercury level, the dose-response relationship represents a statistical average. Individual people are known to vary widely in sensitivity to toxic effects. If a study reports that an effect is associated with a level of, say, 50 ppb of a toxic agent in blood, the data supporting that average may include some individuals who displayed the effect at 20 ppb or less, and others who did not display it even at 100 ppb or more.

The inconsistent relationship between symptoms in these cases and different doses of mercury indicated by blood mercury levels primarily reflects this wide variability of individual human beings in sensitivity to effects of toxic substances. To define clear-cut patterns relating particular dose levels to specific symptoms, hundreds if not thousands of cases would need to be statistically analyzed.

Early studies of methylmercury toxicity were done mainly in cases of severe poisoning, such as in Minamata and Iraq, as described in **Appendix C**. In those studies, mostly done 30 to 40 years ago, clear-cut neurotoxic effects in adults were generally associated with blood mercury levels of 200 ppb or higher, and subtler effects were generally not seen at levels below 50 ppb.⁵³ In contrast, the cases reviewed here suggest that moderate to severe symptoms of methylmercury toxicity can occur in sensitive adults with blood mercury levels well below 50 ppb.

Some observers may argue that the symptoms suffered by these patients cannot possibly be methylmercury poisoning, because their exposure is too low to cause such effects, based on previous knowledge. That argument goes against the common experience in environmental health research. It is quite typical, in fact, for effects of a toxic substance to be observed first in either severe poisoning incidents or in occupational exposures, where the doses are very high, and then later to be associated with much lower doses. This has been the case with lead poisoning, for example.

It has also already been documented with methylmercury poisoning, as described in detail in Hightower's recent review, cited above. The studies by Carta et al. and Yokoo et al., referenced in **Appendix C**, are also examples of this trend. Several factors explain why, as research advances, toxic effects of pollutants like methylmercury tend to be associated with progressively lower doses. The most basic reason is that methods for detecting effects and attributing them to a specific cause improve as research on a problem continues.

There has been no concerted effort to define a dose-response relationship for neurotoxic effects of methylmercury in a "normal" population with exposure from a diet rich in fish. Several studies have looked for possible effects on cardiovascular health, but few have focused on neurotoxic effects, which in the past have not been believed to occur at the dose levels people ordinarily encounter from their diets alone. Yet the evidence of these cases suggests that the problem does occur—at least occasionally—at doses that until now have been regarded by most authorities as harmless.

A fundamental principle of environmental health is that individuals vary widely in their sensitivity to toxic effects. The cases reported here may well represent individuals who are much more sensitive to mercury toxicity than average. Conversely, it is also relatively unsurprising that four individuals mentioned in these cases had blood mercury levels ranging from 24 to 228 ppb but showed

no symptoms of mercury poisoning (**Case 1**, and family members noted in passing in **Cases 11** and **19**). Those individuals are probably inherently less sensitive to toxic effects of methylmercury, for various (mostly genetic) reasons. Determining which group is more “typical” would require more research.

Carefully designed epidemiological studies using current sensitive evaluation methods—such as the tests of cognitive and behavioral functions used by Carta et al.⁵⁴ and Yokoo et al.⁵⁵—might demonstrate effects of methylmercury on the nervous system in adults at doses far below levels previously recognized as posing that risk. More such studies are clearly needed.

The cases reviewed here do not indicate a particular dose range in which symptoms of mercury toxicity may first begin to appear; that is, these data (which are very sparse, in terms of what would be needed for this purpose) do not suggest a threshold for methylmercury poisoning. Toxic symptoms occurred in seven cases with reported blood mercury levels as low as 7-21 ppb. The average blood mercury level in adult women in the US is about 1 ppb.⁵⁶ These cases therefore suggest that toxic effects may occur in people with exposure only about 10-fold higher than the national average, and in people whose only known source of mercury exposure is frequently eating fish with moderately high to very high mercury content. The public-health implications of this observation suggest that obtaining a better definition of this dose-response relationship should be an urgent research priority.



APPENDIX E

How Many Cases May Be “Out There”?

The cases presented in Appendix A are all readily accessible in published sources—scientific journals in some cases, newspaper accounts in others. These cases do offer compelling evidence that methylmercury poisoning does occur, in some people who eat a lot of fish. But they don’t indicate how often it may occur. Even within high-end fish consumers, symptomatic poisoning may be rare. In several cases reviewed here, people had high blood mercury levels but exhibited no obvious signs of toxic effects.

The two dozen cases reviewed here raise some obvious questions: How many additional cases may have occurred, but were not reported, or were not even diagnosed? How many people who eat a lot of fish may be suffering now from methylmercury poisoning? How many more cases will occur if Americans heed public health advice and substantially increase their fish consumption?

It is virtually certain that the patients in the cases described here are not the only people in the United States who ever got mercury poisoning from eating fish. In fact, they are probably just the tip of the proverbial iceberg. If we also consider the strong likelihood that additional people may be affected in subtle ways that diminish their ability to think and function, but who don’t exhibit any outward symptoms, as in the Italian and Brazilian studies cited in **Appendix C**, the number of people adversely affected by mercury in the fish they eat could be quite large.

How many such people could there be? Only some crude estimates can be made, but the question is nevertheless worth examining. There are several ways to approach this task. Most of them are imprecise, at best. However, by using several approaches we may be able to “triangulate” and get a rough, approximate estimate of the possible number of people at risk.

Methods for approximating an answer to this question include:

- Back-of-the-envelope calculations based on arbitrary (but probably reasonable) assumptions about fish consumption and other factors involved.
- Examining the few (small) published studies to see what they may suggest about the US population as a whole.
- Examining CDC/NHANES data (which tested for blood mercury, but reported no cases of methylmercury poisoning), to see what can be inferred from the size and composition of the NHANES sample regarding possible occurrence of harmful exposures to methylmercury in the US population as a whole.
- Identifying other kinds of data and analyses that could shed light on this question through more detailed research.

Back-of-the-Envelope Calculations: The cases of methylmercury poisoning reviewed in **Appendix A** shared two key characteristics. They ate far more fish than average, and they repeatedly ate fish that had much higher mercury content than average.

Per capita fish consumption in the US is about 16 pounds per person per year, or about one 5-ounce serving per person per week.⁵⁷ Anyone who eats fish twice a week is thus well above average for fish consumption, and people who eat fish four, five or even 10 times per week are very far indeed above average, what might be called “extreme” fish consumers. Unfortunately, data from surveys of fish consumption are not adequate to estimate how many Americans fall at specific above-average consumption levels, such as the 99th or 99.9th percentiles. Serving sizes also vary widely, so it is difficult to estimate amounts of fish consumed by any sector of the public with any precision.

Despite these limitations, estimates of the number of “extreme” fish consumers can be derived from relatively simplistic, arbitrary assumptions. For example, the US population is roughly 320 million. If we arbitrarily defined “extreme” fish consumption as above the 99th percentile (the person who eats the most fish out of 100 people), 3.2 million people would fall into the “extreme” category. If we instead defined it as people who fall above the 99.9th percentile—the one person out of a thousand who eats more fish than the other 999—the “extreme” category would include 320,000 people.

Few surveys show how much of particular types of fish Americans eat, either. While we can say, based on catch and sales figures, that, with the important exception of tuna, most high-mercury fish are consumed far less frequently than most low-mercury fish, there are not enough data to show how many people eat, for example, swordfish or tuna steaks once a week or more. Again, we can only make arbitrary assumptions to gain some crude insight into the question.

So, let us assume, first, that “extreme” consumers fall above the 99.9th percentile, and second, that from 1 to 10 percent of them prefer and repeatedly choose high-mercury fish. If so, the group considered “at risk” would be from 3,200 to 32,000 people.

These assumptions address only exposure. If we further consider that only a fraction of people with high exposures are sensitive enough to experience symptoms of mercury poisoning, the number of expected cases would be smaller. But we have too few data on the distribution of sensitivity to methylmercury toxicity to make even a rough stab at quantifying this last fraction. We can simply say, qualitatively, that only some within the extreme high-exposure population would be likely to experience toxic symptoms.

Obviously, this estimate is based on too few actual data to be terribly useful. However, these arbitrary but not unreasonable assumptions produce estimated numbers of cases in the range of thousands to tens of thousands. In fact, the assumptions we used may be too conservative. We cannot be very confident that no one below (even far below) the 99.9th percentile in fish consumption is at risk, for instance. Nor can we be confident that only 10 percent or less of those with high fish consumption might eat a lot of tuna, for example, given the popularity of that particular moderately-high-mercury fish.

We also should not limit our concern to people who would suffer outward symptoms of mercury poisoning. As studies cited earlier show, mercury poisoning at levels too low to cause clinical symptoms can adversely affect cognitive and neuropsychological functions. Since these latter effects occur at lower doses than those that produce overt illness, the population at risk for these subtler effects is correspondingly larger.

Estimation from Existing Studies: Hightower and Moore⁵⁸ screened all the patients their office saw in a year, about 720 in all, with a dietary questionnaire. They identified 123 individuals for further testing, based on their high fish consumption, and 89 percent of that subset had elevated blood mercury levels (above 5 ppb). They reported that “several” of those patients had symptoms consistent with mercury poisoning (and in fact, several cases described in **Appendix A** are Dr. Hightower’s patients.) In Wisconsin, the Division of Public Health published an announcement inviting people who ate a lot of fish to submit a hair sample for mercury analysis. About 2,000 people responded by sending in hair for analysis.⁵⁹ The Division then followed up on those individuals whose hair had high mercury levels. Overall, they identified seven cases summarized in their published paper, three of which were described here (**Cases 11, 18, and 19**).

If the “several” cases mentioned by Hightower and Moore is estimated as five, their incidence of cases would be 0.7 percent of their patient population (5/720). In Wisconsin, three people with symptoms were identified in 2,000 subjects, a rate of 0.15 percent. If all seven cases are included—four patients had elevated blood mercury but no symptoms—the rate would be 0.35 percent. Neither population is representative of the US as a whole. Wisconsin solicited participation by people who ate a lot of fish, while Hightower and Moore’s patients live in the San Francisco Bay Area, where seafood is abundant and fish consumption is probably above average. The case incidence estimated from these studies, 0.15 to 0.7 percent, is likely to be higher than the rate for the US as a whole.

With that caveat, it appears that the arbitrary assumption used above, to define “extreme” fish consumers as those above the 99.9th percentile, is fairly reasonable. (The population above the 99.9th percentile is 0.10 percent of the total population, or somewhat less than the case rate observed in Wisconsin, and far less than the rate observed by Hightower and Moore.)

Inferences From the NHANES Data: The NHANES II surveys, conducted by the Centers for Disease Control, tested for blood mercury in 5,214 women of childbearing age and children from 1999 through 2004.^{60, 61} CDC has reported that 6 percent of women had levels above 5.8 ppb, the EPA reference level. CDC did not report the 99th percentile blood mercury level, but it seems reasonable to assume that only a fraction of 1 percent of the sampled population had blood mercury levels above, say, 15 ppb, a level exceeded by most individuals with symptoms of mercury poisoning in the cases reviewed here.

The NHANES data include just younger women and children, while most patients in the cases described in Appendix A here were men and women over the age of 40. The NHANES sample also was not fully representative of the US as a whole, geographically or ethnically.⁶² The NHANES data therefore do not apply to the entire US population, nor to specific groups that were over-represented among our cases, i.e., middle-aged adults of both genders.

Nevertheless, much has been made of the fact that the NHANES surveys found no individuals with “methylmercury poisoning.” That is based on two observations. First, NHANES did not look for symptoms or try to diagnose disease conditions in the people examined; CDC merely took blood (and other) samples for analysis. Second, no one among the 5,214 people sampled by NHANES had a blood mercury level above 58 ppb, which the US EPA has defined as a “benchmark” for risk to the developing fetus (it is the lowest level at which statistically significant effects were observed in the Faroe Islands studies).⁶³

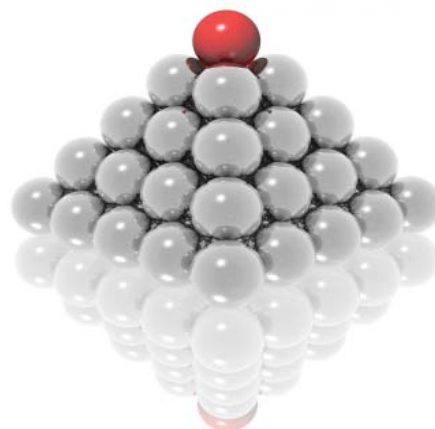
It is therefore worth examining what we can learn from these NHANES data. Does the failure of NHANES to find anyone with a blood mercury level above 58 ppb mean there are no such people in the US? That question can be answered by analyzing the statistical power of the NHANES survey.

The US EPA has used 58 ppb as a blood mercury level that justifies concern about effects on fetal development, and 58 ppb was in the middle of the range of blood mercury values recorded in people with symptoms of methylmercury poisoning in **Appendix A**. For this analysis, we ignored the fact that the NHANES does not represent the US population as a whole, and concentrated on its statistical power. In simple terms, we asked: How many people with blood mercury levels above 58 ppb could there be in the US population, without its being likely that at least one would be included in CDC's sample of 5,214?

The answer depends on simple calculations of probabilities. If the actual incidence of blood mercury levels above 58 ppb were 1 in 10,000, then 32,000 people in the US population would have levels that high (and 9,999 people out of every 10,000 would have levels below 58 ppb). The odds that a random sample of 5,214 Americans would not include even one person with a level above 58 ppb are 0.9999 raised to the 5,214th power, or 59.4 percent. That is, there could be 32,000 people with blood mercury levels above 58 ppb in the US population and it is still more likely than not that the NHANES survey would not have detected one.

If the actual incidence were assumed to be 10-fold higher, i.e., 1 in 1,000, the odds that no one tested by NHANES would have a level above 58 ppb are 0.9990 to the 5,214th power, or 0.54 percent. So we can be roughly 99.5 percent confident—extremely certain, in statistical terms—that the incidence is less than 1 in 1,000. These calculations suggest, though, that the incidence of blood levels over 58 ppb could easily be between 1 in 1,000 and 1 in 10,000, without a single case showing up in the NHANES sample.

Using similar methods, we can calculate how large the actual incidence of people with blood mercury above 58 ppb would need to be for the NHANES sample to have a 95 percent probability of including at least one case. That calculated incidence is 1 in 1,742. In other words, based on the NHANES data, we can assert with 95 percent confidence (the standard scientific measure of a statistically robust conclusion) that there are no more than about 184,000 ($320,000,000/1,742$) people in the U.S. with blood mercury levels above 58 ppb. The fact that NHANES found no blood levels above 58 ppb is therefore not particularly reassuring. It is even less comforting given that there is nothing magical (or safe) about the 58 ppb level; some patients in our cases with blood mercury levels well below 50 ppb still had moderate to severe symptoms of mercury poisoning.



With all its limitations, this analysis of the NHANES survey nonetheless is consistent with the other approaches explored above, in that it suggests an upper limit of about 0.06 percent of the US population (184,000 out of 320,000,000) at risk for mercury poisoning from fish consumption, if we assume that risk is associated with blood mercury above 58 ppb. Given that symptoms may occur only in sensitive individuals at any given blood mercury level, the actual number of expected cases could be much smaller. On the other hand, given that symptoms may occur at blood levels well below 58 ppb, the population affected might be much larger. Unfortunately, the available evidence does not enable us to be more precise than that.

Possible Research Opportunities: Some types of large-scale epidemiological studies that could shed light on this question were described in **Appendix C** (see page 32). Reasons why such studies have not been done to date and may be unlikely to be funded were also explored there. Clearly, more aggressive research on this question is needed.

Some simpler approaches could also shed light on this issue. In many states, physicians who encounter a case of mercury poisoning are supposed to report it to state health public health officials. State health departments could be surveyed to ascertain how many cases of mercury poisoning have been reported. Since mercury poisoning can occur in many ways (from exposure to a broken thermometer, for example), further investigation would be needed to determine how many cases were methylmercury poisoning from fish consumption. The quality of data reported might often be limited. Nevertheless, state data on mercury poisonings, if carefully analyzed, might yield some useful evidence.

Neurologists are likely to have been involved in most cases of methylmercury poisoning, often as specialists consulting with primary-care physicians. A survey of neurologists, contacted through professional societies or via web-based specialist rosters maintained by medical insurance companies, could yield an estimate of the number of cases seen by practitioners in this specialty in different geographical regions of the country. Surveys have limitations—many of the target group simply do not respond, and those who do may not be representative of the group as a whole—but this approach could generate at least a rough estimate of the number of methylmercury cases diagnosed by physicians.

These research possibilities will remain just that—possibilities—unless someone with an interest in this public health issue can find the money, time, and skill needed to carry out well designed studies. Meanwhile, although we lack satisfactory quantitative estimates of the number of cases of methylmercury poisoning from fish consumption, it is difficult, given this analysis, to conclude that the number is negligibly small.

APPENDIX F

How to Eat Lots of Low-Mercury Fish

Fish is part of a healthy diet, and eating fish several times a week is generally a smart choice. But people who eat fish very often should be aware of the risks associated with mercury exposure, and of the mercury content of different fish and seafood choices.

The chart on page 45 breaks fish and shellfish into four color-coded categories, based on their mercury content. We obtained information on mercury levels in each variety from the US Food and Drug Administration; details are available on the FDA web site.⁶⁴ Our categories are as follows: Green List (low-mercury) choices contain no more than 0.05 ppm mercury. Yellow List (low to moderate mercury) choices contain between 0.05 and 0.20 ppm mercury. Orange List (moderately high mercury) choices have between 0.20 and 0.60 ppm, and Red List (very high mercury) choices have over 0.60 ppm.

We offer these recommendations for consumers who eat fish often, based on their frequency of fish consumption:

- Adults who eat fish twice a week or less can choose any or all their meals from either the Green or the Yellow List, and can also eat fish from the Orange List once or twice a month without much concern. They might choose fish on the Red List now and then, but we recommend doing so no more than once a month.
- Adults who eat fish two to four times a week should choose mainly from the Green and Yellow Lists, and should limit their choices from the latter to no more than one meal per week. They may also choose from the Orange List, but no more than once a month. They should probably avoid Red List items altogether, or substitute one Red List item for two Orange List items (i.e., once in two months).
- Adults who eat fish five or more times per week should choose primarily from the Green List. Those who eat fish less than once a day can pick from the Yellow List once a week, but those who eat fish more than seven times in a week should cut their consumption of Yellow List items to twice a month. They should choose Orange List items no more than once every few months, and should avoid Red List choices.
- Children who eat fish more often than twice per week should be given items almost exclusively from the Green and Yellow Lists, and children who eat fish very often should have their Yellow List meals limited to no more than one per week.

Most Americans who eat a lot of fish appear to be already choosing mostly fish from the Green List, judging from recent market data. **Table F-1** presents data from the National Fisheries Institute (an industry trade association) on per capita US consumption of the 10 most popular fish and seafood items from 2005 through 2007.⁶⁵

Table F-1. Top Ten Seafoods 2005 - 2007
(Pounds Per Capita Edible Weight)

	2005		2006		2007	
	Species	Lbs	Species	Lbs	Species	Lbs
1	Shrimp	4.10	Shrimp	4.40	Shrimp	4.10
2	Canned Tuna	3.10	Canned Tuna	2.90	Canned Tuna	2.70
3	Salmon	2.430	Salmon	2.026	Salmon	2.364
4	Pollock	1.468	Pollock	1.639	Pollock	1.730
5	Catfish	1.025	Tilapia	0.996	Tilapia	1.142
6	Tilapia	0.848	Catfish	0.969	Catfish	0.876
7	Crab	0.643	Crab	0.664	Crab	0.679
8	Cod	0.572	Cod	0.505	Cod	0.465
9	Clams	0.435	Clams	0.440	Clams	0.449
10	Flatfish	0.366	Scallops	0.305	Flatfish	0.319
Total All Species		16.2		16.5		16.3

A comparison of these “Top 10” lists with our chart here shows that eight of these most heavily-consumed fish and seafood varieties (i.e., shrimp, salmon, pollock, catfish, tilapia, clams, flatfish [which includes sole, flounder, and plaice], and scallops [ranked 10th in 2006]) are on our Green List of low-mercury items, because they contain less than 0.05 ppm mercury. Two others (crab and cod) are on our Yellow List, signifying low-to-moderate mercury (between 0.05 and 0.20 ppm). Only one of these most popular seafood items, canned tuna, frequently contains higher mercury levels.

Canned tuna is sold in two main varieties. Canned light tuna is on our Yellow List, with an average reported mercury level of 0.118 ppm, while canned albacore tuna, with an average of 0.353 ppm, is on our Orange List (moderate to high mercury choices, limiting consumption is advised.) Because of the amount of it Americans consume, canned tuna is by far the largest source of methylmercury exposure in the US diet. People who eat a lot of fish therefore need to be cautious and limit the amount of tuna (including tuna steaks and sushi, which generally contain even more methylmercury than canned albacore) they consume.

Since individuals are so variable, it is difficult to apply simple rules to everyone. Each person, however, has a personal “maximum safe mercury dose.” That dose varies from one person to the next. Whatever the upper limit may be for a given person, eating a fish from the Red List uses up a large share of that “allowance.” Choosing an item from the Orange List also uses up a relatively big share, but less than a Red List choice. Items on the Yellow List use up smaller shares, while those items on the Green List use up the smallest shares of all.

The more fish meals a person consumes—the greater the number of shares one’s personal “mercury allowance” is divided into—the smaller each share must be to avoid going over the limit. Thus, someone who eats a Red List fish now and then but eats few other fish meals may not exceed their personal safe limit, while someone who eats Yellow-List fish every day may already be close

enough to their limit that adding just one or two meals from the Orange or Red Lists could put them well over a safe dose. People who exceed their personal safe mercury limit once in a while have less risk of mercury poisoning than people who do so day after day, week after week, and month after month.

As in most things, in choosing to improve one's diet by eating a lot of fish, moderation is essential. In this case, intake of fish that contain moderate to very high mercury levels needs to be moderated. This can be accomplished by giving consumers more facts about the mercury content of different seafood choices, and urging them to set sensible limits on how much they eat of varieties with significant mercury content, all in the context of their overall level of fish consumption.

* * * * *

Methodological notes: Deciding where to draw lines in creating the attached chart and in what advice to give people who eat differing amounts of fish required some essentially arbitrary judgments. Because the purpose here is specifically to advise people who eat a lot of fish, our definition of low mercury fish (for example) differs from the one used by the FDA and EPA in their 2004 advisory. FDA and EPA considered anything with less than 0.12 ppm mercury to be “low-mercury.” However, the agencies were offering advice to women who, they assumed, would eat no more than 12 ounces (or two six-ounce servings) of fish per week. When the advice is intended for people who eat fish more often than that—four, five, even 10 or more times per week—what is considered “low mercury” needs to be adjusted. We therefore considered “low mercury” fish and shellfish to be those that contained 0.05 ppm mercury or less.

Recommending how often people should choose from each of our color-coded categories also required subjective judgments. The risk of mercury poisoning in adults who eat a lot of fish has not been well quantified. The EPA Reference Dose (RfD), the definition of “safe” exposure, is based on prenatal effects on the developing brain, not on effects in adults such as those observed in the cases reviewed here.

The EPA RfD for prenatal effects is 0.1 microgram of mercury per kilogram of body weight per day (0.1 $\mu\text{g/kg/day}$). The RfD includes a 10-fold “uncertainty factor” to take into account variation in individual susceptibility. We assumed (arbitrarily, since there is virtually no evidence from epidemiological studies) that toxic effects in adults might be observed at twice the dose that produces effects on the developing brain. We then applied the same 10-fold “uncertainty factor” to our assumed dose, to take into account the wide variability of individual humans in sensitivity to toxic effects. That yielded an RfDA (RfD for effects in adults) of 0.2 $\mu\text{g/kg/day}$.

Our recommendations are generally designed to prevent high-end fish consumers from exceeding that RfDA of 0.2 $\mu\text{g/kg/day}$. Given the variability of individual body weights, fish portion sizes, and mercury levels in different samples of the same fish, guidelines of this sort are inevitably approximate, and individuals must therefore decide for themselves how cautious they wish to be.

RECOMMENDED SEAFOOD CHOICES
FOR PEOPLE WHO EAT A GREAT DEAL OF FISH

Low Mercury: Eat as often as you wish	Low-Moderate Mercury: Eat occasionally	Moderate-High Mercury: limit consumption	Very High Mercury: Avoid eating
Salmon	Butterfish	Sea bass	Swordfish
Tilapia	American shad	Sablefish	Shark
Ocean perch	Whitefish	Halibut	Tilefish
Whiting	Atlantic croaker	Sea trout	King Mackerel
Pollock	Freshwater trout	Weakfish	Bluefin tuna
Hake	Pacific mackerel	Scorpion fish	Tuna sushi
Flounder	Cod	Pacific croaker	Bigeye tuna
Sole	Jack smelt	Bluefish	
Plaice	Canned light tuna	Canned albacore tuna	
Haddock	Sheepshead	Fresh/frozen tuna	
Sardines	Skate	Tuna steaks	
Herring	Freshwater perch	Chilean sea bass	
Anchovies	Monkfish	Spanish mackerel	
Mullet	Mahi-mahi	Grouper	
Catfish	Snapper	Marlin	
Atlantic mackerel	Buffalofish	Orange roughy	
Shrimp	Blue crab	American lobster	
Clams	King crab		
Oysters	Snow crab		
Crayfish	Squid		
Scallops	Spiny lobster		

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