

Methylmercury and Seafood

Reflections and recommendations on the risks and benefits of fish consumption by pregnant and breastfeeding women

Introduction

Tuna or not tuna? That was the question.

In the realm of children's environmental health, some issues are clear-cut while others are more murky. The conflict over seafood consumption for women who were pregnant, planning to become pregnant, or breastfeeding belongs in the latter category. On one hand, seafood is considered near universally to be an excellent food. Research about omega-3 fatty acids, plentiful in fatty fish, as well as other nutrients like fat-soluble vitamins, confirms what cultures around the world have known for countless generations: that seafood is a healthful, even optimal, part of diet. However, in an era when industrial emissions pollute waterways from small lakes to the ocean, "healthful" is no longer so simple. Consumers of fish face exposure to contaminants like lead, PCBs, and methylmercury, meaning that eating a wholesome food now comes with side effects: the risks inherent in exposure to toxins, particularly during fetal development or early childhood.

To add to the confusion, some fish have much higher levels of contaminants than others, even within a species. Some types of tuna, for instance, have been found to contain significant levels of mercury, while others have been determined to be lower risk. The question is not just "tuna or not tuna" but which tuna? How much? How often? And for whom?

The "for whom" is an essential question. The conflict between risk and benefit becomes more complex when considering exposure to young children and to the developing fetus, by maternal consumption. Due to their stages of physical and central nervous system development, fetuses and young children are impacted uniquely by such exposure. In particular, compounds like methylmercury have been found to have profound impacts on fetal development, as research in Minamata Bay, Japan indicated as early as 1958.¹ On the other hand, those beneficial

omega-3 fatty acids and other nutrients in fish are especially beneficial for young children and expecting or new mothers.

While no group is in favor of children facing birth defects or other detriments to health and development, advocates from industry, health, and community groups have viewed differently the question of what to tell the public. On one end of the spectrum, some felt that publishing recommendations that highlighted contaminants in fish or recommended the public, or certain populations, avoid certain fish, would put an unnecessary burden on industry. On the other end, others held that the levels of mercury contamination in certain fish were significant enough to merit recommendations limiting the intake of fish, particularly certain species, and particularly by pregnant or breastfeeding women.

The differing recommendations from the Environmental Protection Agency (EPA) and Food and Drug Administration (FDA) have reflected this controversy. The EPA placed its reference dose (RfD) recommendation nearly a decade ago at 0.1 µg/kg/day whereas the FDA placed its at the much higher level of 0.5 µg/kg/day.

A committee from the National Academy of Sciences (NAS) faced the task of reviewing the research regarding methylmercury exposure and seafood consumption, and determining whether the EPA's more stringent recommendations were based on sound science. By looking at the studies this committee considered, the original FDA and EPA guidelines, more recent research, and the latest (January - April 2009) conflict between the agencies, we are able to determine reflections on the controversy and recommendations of our own for individuals, government, and industry.

Overview of studies considered

Assorted studies were considered in determining the NAS committee's recommendations for an appropriate RfD. After considering a selection, including a study from New Zealand, one from the Faroe Islands, another from Iraq, and one from Seychelle Islands, the committee determined that the Faroe Islands data were the most appropriate for determining an accurate RfD. However, each study contributes a different component to the growing body of research and debate regarding seafood consumption, mercury exposure, and maternal and child health.

The study from Minamata Bay, Japan in 1958 first raised public awareness of the drastic consequences of fetal exposure to mercury in seafood. Published in the journal *Lancet*, the study traced the relationship between mercury from seafood, a result of factory runoff into Minamata Bay, to devastating developmental and neurodevelopmental problems, particularly of children exposed in utero. The research determined that sensitivity in utero was significant enough that resulting brain lesions from exposure were far more prolific and widespread than those appearing in adults who had eaten contaminated fish. Children born after fetal exposure also displayed profound and similar birth defects. Inspiring the early name “Minamata disease,” this study was a significant first step in awareness, prevention and research.

The subsequent study hailed from research in Iraq in 1976², examining an incident in which grain treated with methylmercury, intended for seed and not for human consumption, had accidentally entered the human food supply. As a result of household bread baking and consumption, exposed infants and children showed symptoms such as delayed speech and motor development and impaired autonomic function and hearing. The symptoms manifested differently than those in Minamata nearly two decades prior. This was attributed largely to the fact that the Iraq incident stemmed from a single exposure rather than a long-term result of daily exposure, as in Minamata. The Iraq study revealed that hair sampling provided a strong measure of mercury level at the time of exposure.

Research from New Zealand³ informed the next phase of learning. This study looked at longer-term consequences, at age four, of exposure in utero, from mothers consuming fish three or more times per week during pregnancy. Using measures of social, mental/academic, linguistic, and physical development, it found significant differences between children exposed and those not exposed.

A 1995 - 2003 series of studies⁴ of a population in the Seychelle Islands, in the Indian Ocean, yielded some surprising results. This research looked at effects at 6, 19, 29 and 66 months. It found that associative symptoms correlating exposure to outcomes like attention deficit hyperactivity decreased over time. The data from the studies did not support the idea that seafood-sourced dietary methylmercury exposure in utero significantly increases neurodevelopmental disorders. The study was a basis of the RfD recommendation from the

Center for Disease Control (CDC)'s Agency for Toxic Substances and Disease Registry (ATSDR). However, some have raised questions about other confounding variables. As opposed to the subsequent 1997 study taking place in the Faroe Island, in which people consumed significant amounts of whale meat, Seychelle Islands residents consumed primarily fish. Some industry groups have chosen to interpret this as a sign that it is whale meat, and not fish, that is detrimental⁵, although they do not offer data to support a causal relationship. There are other factors that may potentially account for the difference, including other dietary differences between the population as well as region of the world. Vitamin D might be a factor; Faroe Island, at a significantly northern latitude, may have a population at higher risk for vitamin D deficiency than the tropical Seychelle Islands. Vitamin D has been shown to increase levels of glutathione, a peptide whose deficiency is associated with autism, a disorder also linked to mercury exposure.⁶

The Faroe Island study focused on a population eating significant amounts of whale meat. This research measured cord and hair levels of mercury exposure, and followed children from prenatal development to seven years of age. The data showed significant correlation between exposure level and impaired development in markers of motor function, attention, visuospatial, language and memory.

To determine a recommended RfD, the NAS committee focused on the data from the Faroe Island study, since it was a recent, comprehensive, long-term piece of research using rigorous markers of dose. The group also evaluated data from animal studies, which showed similar effects to those on humans of moderate to high exposure on primates and small mammals.

Looking at the data from the Faroe Island study, the committee sought to determine a benchmark dose (BMD) as a first step towards establishing their RfD recommendation. After adjusting for PCB exposure, the committee determined the median point from the Faroe Island study at 12 ppm (measured in hair level), and determined that this marker, stemming from a maternal blood level of 48 µg/L, should be used to determine the RfD. They calculated factors of dietary intake, cord blood concentration, elimination, blood volume, absorption, uptake, body weight, and an uncertainty factor to yield a final recommended RfD of 0.1 µg/kg per day.

FDA and EPA guidance

Notably, the committee's recommendations paralleled those of the EPA, the body whose recommendations the committee was asked to evaluate, and which also set its RfD at 0.1 µg/kg per day. However, the FDA and EPA offered different RfD. The FDA's recommended RfD was five times higher than that of EPA, at 0.5 µg/kg per day. Differences may be attributed to different data studied, competing influences, and political factors, including the federal administration in place at the time.

In 2004, the FDA and EPA issued a joint advisory⁷, suggesting consumers avoid certain types of fish and limit intake of others. Fish to avoid included predatory species such as shark, swordfish, king mackerel, and tilefish. The report also recommended limiting intake of species like albacore/white tuna.

However, the controversy over the difference between FDA and EPA's approach is still fresh. Recently, in January of 2009, FDA issued its draft of a risk/benefit report updating the agency's view on the risks and benefits of seafood consumption and methylmercury exposure. The new language focused on the benefits of seafood consumption and downplayed the risks of mercury exposure, favoring the former over the latter. This sparked anew a conflict between that agency and the EPA. An April 2009 *Newsweek* article⁸ featured on the Environmental Working Group website covers the latest aspects of the FDA/EPA conflict. In January 2009, the article explains, the FDA broke from the recommendations it had shared with the EPA about limiting mercury intake from fish consumption, to suggest instead that the benefits of fish consumption outweighed any risk from mercury exposure. In the ensuing comment period, among 248 responses from the public, EPA issued a long response to the FDA's new recommendations⁹.

The EPA response is sharply-worded and not complimentary. It criticizes the new FDA proposed recommendations for, among other things, a failure to implement a collaborative, peer-reviewed formal analysis, citation of poor-quality studies, failure to look at the full spectrum of coronary heart disease, and species-specific differences in fish contamination and exposure. Clearly the relevance of this issue has far from faded.

Results of recent studies

A number of studies published since the NAS committee proposed its RfD have introduced new data and questions. A 2006 study¹⁰ followed up on the Faroe Island research, evaluating the original study's participants at age fourteen. These data indicated that the neurophysiological outcomes found at age seven were still present at age fourteen, and thus were likely permanent. Another pair of studies¹¹ looked at the relationship between fish intake and mercury intake on infant cognition. This research suggested that higher maternal fish intake resulted in improved child cognition, but that higher mercury intake via fish resulted in impairments on the same measures of cognition. The researchers concluded that, in line with the current EPA view, the best solution is for expecting and breastfeeding mothers to eat seafood, but to limit intake of fish with high levels of methylmercury. A follow-up to the original study found that benefits decreased after consumptions of two servings a week. Another study¹² found an association between maternal methylmercury exposure via seafood consumption and increased risk of preterm birth. This study specifically isolated high risk seafoods, including certain canned fish.

Additional research supported the idea that consumption of non-contaminated or less-contaminated fish or fish oil during pregnancy was associated with healthier development. This study posited that omega-3 fatty acids and other nutrients available in seafood were responsible for the outcomes. Other research in the period since the NAS committee's recommendations have supported the idea that omega-3 fatty acids, particularly DHA, and lower intake of omega-6 fatty acids, are crucial for healthy development, metabolism, nutrient availability, and functioning.

Notably, as research on omega-3 fatty acids has increased, studies have identified other non-fish sources for DHA and EPA. These include grass-fed beef¹³ and lamb and organ meats from these animals, as well as eggs from chickens fed flaxseed¹⁴, as the chickens are able to convert the flaxseed's ALA into DHA.

Finally, a 2007 study¹⁵ suggested that only when expecting mothers consumed more than 340 grams/week of seafood did their children experience the benefits of increased omega-3 fatty

acid intake. This study proposed that advice to limit seafood intake during pregnancy could actually be detrimental.

These additional studies strengthen the committee's recommendations for the RfD, particularly the follow-up study that confirms the Faroe Islands data on which the RfD was based. The latter 2007 study and the research on omega-3 fatty acids may suggest some additional information be coupled with the RfD recommendations, such as emphasizing the benefits of fish consumption, increasing consumption of lower-risk fish, and seeking out additional sources of DHA and EPA omega-3 fatty acids.

Risks and Benefits

Determining how to balance the risks and benefits of eating seafood — particularly seafood contaminated with methylmercury — during pregnancy and breastfeeding is not simple. The dilemma stems from the fact that the common dietary source of methylmercury, seafood, is also extremely valuable to women who are pregnant, planning to become pregnant, or breastfeeding. A number of sources have studied the question of how to reconcile the benefits of seafood with the risks of toxic exposure.

A 2006 NAS brief¹⁶ weighed the risks and benefits. On one hand, the report suggested, seafood contains important nutrients and vitamins, as well as good quality fats, and a healthful fatty acid profile with significant proportions of omega-3 fatty acids. The report noted that consumption of omega-3 fatty acids during pregnancy is associated with developmental benefits post-birth. On the other hand, the risks include detriment from assorted contaminants, unknown long-term effects beyond the scope of existing studies, the reality of consumer choices, and different effects on different populations.

There is a strong argument that the benefits of seafood consumption outweigh the risks. Cultures around the world have valued seafood, and likely with good reason. While research reveals specific components of seafood that are beneficial (e.g. omega-3 fatty acids), it is possible that there are benefits we are not yet aware of, meaning substitution with other sources of omega-3 fatty acids may not equal the benefits of fish consumption.

Some benefits stand out as particularly noteworthy. Mozaffarian et. al argue¹⁷ that increased fish oil and fish intake are strongly associated with decreased cardiovascular disease risk, including sudden death from coronary heart disease, and that this benefit is linked to intake of omega-3 fatty acids from fatty fish. Additionally, seafood contains important fat soluble vitamins, such as vitamins A, D, K and E, that are essential for childhood and pre-natal development. Those consuming seafood are less likely to consume less healthful/more detrimental foods to fill the gap avoiding seafood might leave. Fatty seafood consumption also may improve nutrient availability from otherwise-detrimental foods, such as those high in phytic acid.¹⁸

The benefits of fish consumption are complicated by various factors. Even within fish species, there are wide variations in omega-3 content, as in within different varieties of salmon.¹⁹ Complications include risks as well. Smith et al²⁰ provided data on different fish species' levels of omega-3 fatty acids and mercury contamination. These researchers concluded that due to the link between mercury presence in some, but not all, high omega-3 fish, those at risk for coronary heart disease or seeking to increase omega-3 content in their diets might be better served by a combination of fish consumption and fish oil supplementation.

Obviously, methylmercury exposure is a significant risk. The types of irreversible physical and neurophysiological detriments detailed in this paper are not to be considered lightly. There is the serious question of whether mercury exposure could not only counter the benefits of omega-3 intake, but create significant harm.

There are other risks as well. The NAS brief examined a number of risk factors for increased seafood consumption. The researchers noted that other contaminants, such as PCBs and dioxins, were also of concern to consumers of fatty fish, and particularly to infants whose mothers consume fish. Microbes were also of concern.

Some alleged risk factors seem to present less of an issue. There has been suggestion²¹ that excessive omega-3 intake may impair the immune system. However, the same study that raises this concern also acknowledges that such levels of consumption in the U.S. is rare. This data may also reflect omega-3 intake in isolation rather than in combination with naturally-occurring fat-soluble vitamins present in fatty fish.

Finally, from a public health promotion perspective, consumers may disregard or misinterpret information, leading an attempt to make recommendations to fail. This type of risk factor is related to awareness and effects of recommendations.

Awareness and Effects

In determining how to word an advisory or set of recommendations, it is essential to look at how such a document, presented in various media, actually affects behavior. Changes in actual practice (e.g. consumption of fish and types of fish consumed) is shaped by factors such as perceived threat (e.g. from mercury intake or from lack of fish intake), how individuals view the agency or group issuing the advisory, and confusion over available information.

A study of women of childbearing age²² found that knowledge and implementation of current advisories was limited, and that hair samples indicated a direct relationship between fish consumed recently and levels of mercury in the body. Another study²³ associated mercury levels with demographic factors, and examined the relationship between the consumption of sport fish and mercury. While no link was found for that aspect of data, the study noted that knowledge of current recommendations was not associated with changes in behavior and resulting mercury exposure. This suggests that public health promotion tactics must be refined in order to reach the population in a meaningful way. However, a different study²⁴ found that the 2001 federal advisory did have an impact on fish consumption and choices. Perhaps more research is needed in this area.

Guidance and Recommendations for women of childbearing age

It is, perhaps, easier to critique a set of guidelines and recommendations than to fold together existing data to determine one's own set of ideal guidelines. Yet the existing data, old and new, on methylmercury exposure and nutritional benefits from maternal seafood consumption, afford an increasingly clear picture.

I would recommend upholding the committee's proposed RfD of 0.1 µg/kg/day in light of the 14-year data on the Faroe Island study. I also support and appreciate the wording of the recommendations in the 2007 NAS report (p. 6-7), particularly that the public needs clear,

interactive tools to determine safe seafood consumption information, that agencies should work together to increase awareness of guidelines, and that risks and benefits should be framed in terms of specific types of fish to avoid, with emphasis on the positive aspect of consuming fish during pregnancy and breastfeeding.

I have additional recommendations as well. My recommendations for individuals, industry, government, researchers, and public health are as follows:

Individual level recommendations

- Uphold the RfD of 0.1 µg/kg/day
- Emphasize the benefits of fatty fish consumption, especially for pregnant and breastfeeding women.
- Eat fish that are high in omega-3 fatty acids. Avoid predator species like shark, tilefish, or king mackerel, and limit white tuna. Emphasize species like salmon, bass and trout which are high in omega-3 fatty acids and not necessarily in methylmercury.²⁵
- Be informed about mercury risks and seafood benefits. If you are concerned about mercury risks, in addition to consuming lower-risk fish, consider supplementing with lower-risk fish oil or foods such as grass-fed beef or lamb, grass-fed organ meats, or eggs from chickens fed flax seed. Flax itself, or vegetable sources of omega-3 are not acceptable substitutes.
- Reduce consumption of omega-6 fatty acids found in grain-fed meats and vegetable oils. Among other detrimental effects, high consumption of omega-6 fatty acids compromises DHA/omega-3 fatty acid levels in the brain and impairs neurodevelopment.²⁶
- Avoid farmed fish, which may be higher in contaminants
- Increase consumption of vitamin D3 and K2. These vitamins, in addition to important benefits for development, may mediate effects of mercury on glutathione²⁷²⁸
- Be aware of sources of information about mercury contamination. Some sources are strongly influenced by industry and financial concerns, and may be biased. Other sources may discourage any fish consumption whatsoever. A balanced consumption of carefully-selected fish is ideal.

Institutional level recommendations

- Clearly label fish choices in fish markets and supermarkets to make consumer awareness and choice easier. This may include labeling predator fish as not recommended for women of childbearing age, and other fish as safer choices. This may also include required labels on canned tuna specifying which varieties are safer. Additionally, having information cards about fish safety available and visible at fish counters may also increase awareness. Experiment with dissemination strategies which research suggests to be effective
- Study successful strategies of health promotion to increase risk/benefit awareness and practical effect of such awareness.
- Provide incentives and/or regulations to alter feeding practices of livestock to improve the omega 3:6 ratio, such as grass-feeding without feedlot-finishing, pasture-raising chickens, and supplementing chicken diet with flax.
- Fund further research into long-term effects of fish consumption, mercury exposure and dose, and a potential moderating effect on mercury exposure of adequate intake of fat-soluble vitamins, particularly vitamins D3 and K2 (MK-4).

Potential effect

Some of these more specific recommendations, such as the inclusion of alternate sources of DHA and clear labeling, may result in direct benefits to the consumer, and reduced anxiety about confusing information. Overall, however, the effect of the above recommendations depends on a number of factors. Most notably, the extent to which institutional change, such as federal regulations, industry labeling, and public health promotion, is realistic. If public awareness is reinforced, practical behavior might change due to increased ease of staying informed and making healthier choices. However, without significant institutional support, promotion of these new recommendations might increase healthy behavior to some extent, but not necessarily remedy the main issue, which is that a number of conflicting and often-changing recommendations lead to public confusion and failure to make changes. Even the most astute of health enthusiasts may forget her mackerel from her king mackerel, or which salmon is higher in

omega-3 content, or which can of tuna is the right one to purchase, resulting potentially in a third answer to our “tuna or not tuna” question: Something else.

And yet, the public has a right to accurate, health-promoting information, even if this results in confusion. Starting with accurate information is paramount. The techniques for disseminating that information to the public, even as it may evolve and change with new research, may be refined. The accuracy of information should not, in the process, be compromised.

NOTES

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⁵ <http://fishscam.com/fwhalemeat.cfm>

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⁷ <http://www.fda.gov/bbs/topics/news/2004/NEW01038.html>

⁸ <http://www.ewg.org/newsclip/Newsweek-Smackdown-EPA-FDA-and-Mercury-in-Fish>

⁹ <http://www.regulations.gov/fdmspublic/ContentViewer?objectId=090000648095bf51&disposition=attachment&contentType=msw8>

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