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Too Much of a Good Thing? Update on Fish Consumption and Mercury Exposure

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While there is a significant amount of data showing health benefits of increased fish consumption, there are conflicting reports about the cardiovascular risks of mercury in seafood. A recent long-term study attempted to resolve this controversy, providing an opportunity to balance recommendations from the US Environmental Protection Agency for mercury with those from the American Heart Association for fish consumption.

Key words: cardiovascular disease, coronary heart disease, docosahexaenoic acid, eicosapentaenoic acid, mercury, methylmercury, omega-3

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BENEFITS OF FISH CONSUMPTION

The benefits of fish consumption, particularly for the cardiovascular system, include the prevention of cardiovascular disease, myocardial infarction, and arrhythmia. There have also been reports of decreases in serum triglyceride levels, blood pressure, and platelet aggregation. For example, one study that included data collected from 36 different countries showed that fish consumption was associated with a reduced risk for both ischemic heart disease and stroke.[1] These data were significant for both men and women between the ages of 45 and 74. The beneficial effects of dietary fish, which have recently been reviewed,[2-4] have largely been attributed to the fact that many seafoods provide a significant dietary source of cardioprotective omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[5]

While some studies have not reported the same degree of cardiovascular protection as others,[6] the strength of the data supporting protection led the American Heart Association (AHA) to recommend consumption of at least two 3-ounce servings (3 ounces cooked weight equals 4 ounces uncooked weight) of fish per week, with a particular recommendation to consume fatty fish. For patients with documented coronary artery disease, the AHA recommends omega-3 fatty acid intakes of approximately 1 g/d.[7] This amount can nearly be met (0.9 g/d) by consuming one fatty fish meal each day.[2]

DANGERS OF MERCURY IN FISH

Atmospheric deposition is the predominant source of mercury in lakes, rivers, and coastal waters. This mercury has been released into the environment by natural processes and via emissions into the atmosphere from human activities, principally mining and smelting of mineral ores, combustion of fossil fuels (coal, oil, gasoline, natural gas), incineration of wastes, and the use of mercury itself. It is now recognized that many fish species are contaminated with the toxic metal mercury.

While there are several different forms of mercury, including mercury vapor, inorganic divalent mercury, ethylmercury, and methylmercury, apart from occupational exposure, seafood consumption is the only significant source of mercury for humans.[8] The predominant form of fish mercury is methylmercury, a highly toxic and bioaccumulative form. Methylmercury is neurotoxic, with the developing nervous system as a particular target. It also impairs neuronal stem cell division and differentiation, and disrupts the neuronal migration that takes place during normal fetal development and childhood.[8] Thus, mercury intake and consumption should be limited in infants and children, pregnant and nursing women, and women who may become pregnant.

In adults, mercury is concentrated in the heart,

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kidney, brain, and liver. While mercury-related risks include disruption of glutamate-mediated neurotransmission, calcium homeostasis, and microtubule assembly, the most significant concerns about mercury exposure in adults arise from the known roles of mercury in binding to thiol groups and the precipitation of insoluble selenium-mercury complexes. This leads to the destruction of a number of thiol-containing cellular components such as glutathione (resulting in glutathione depletion), coenzyme A, and cysteine. Furthermore, because both glutathione and selenium, via the selenium-dependent enzyme glutathione peroxidase, participate in cellular antioxidant pathways, mercury exposure increases oxidative processes and oxidative damage to cellular constituents such as DNA.[9] Interestingly, oxidative processes have been implicated in the development of coronary heart and artery disease. For example, oxidized low-density lipoprotein (LDL) has been recently been identified as a strong risk factor in atherogenesis.[10] Because of the health risks of mercury exposure, the US Environmental Protection Agency has established a reference dose for methylmercury of 0.1 μg/kg body wt/d. Additionally, the World Health Organization (WHO) has set the tolerable weekly dose at 1.6 μg/kg body wt/week (0.23 μg/kg body wt/d).

FISH CONSUMPTION ADVISORIES FOR MERCURY

In the United States, individual states take primary responsibility for issuing fish consumption advisories. While advisories can be issued for 40 different contaminants, 98% of advisories in effect in 2003 involved five bioaccumulative contaminants: polychlorinated biphenyls (PCBs), chlordane, dioxins, DDT, and mercury. Mercury contamination of fish is by far the most common reason for the issuance of advisories, with 76% of all advisories being issued at least in part because of mercury contamination.[11] State advisories include "no-consumption" and "restricted-consumption" advisories for the general population and for sensitive subpopulations, and bans on the commercial harvest of specific fish. However, the basis for issuing advisories differs from state to state. In general, states issue advisories based on calculations using data on mercury concentrations in fish, methylmercury reference dose (reference dose), assumed median human body weight (for men, women, and children), and weight of fish consumed at a meal.[12]

In these calculations, the methylmercury reference dose (the daily methylmercury intake level designed to have no deleterious effects over a lifetime) is the parameter that is most variable among states. Table 1 demonstrates the range of assumed reference doses, about 4-fold for both the sensitive subpopulations, women of childbearing age and children, and the general population, other adults. It is of note that cardiovascular effects of methylmercury have not been a consideration yet for many states in regard to the setting of reference doses. The reference doses shown in Table 1 are supported by various agencies.[13-17] Of interest is that the variation in reference doses for sensitive subpopulations is largely explained by variations in the uncertainty (safety) factors—factors based on professional judgment—and used to derive reference doses. None of these reference doses is based explicitly on cardiovascular endpoints.

Table 1. Reference Dose of Methylmercury by State

Women of Childbearing Age and Children	Other Adults
μg/kg body wt/d	
1 state uses 0.4	3 states use >0.3
4 states use 0.3	25 states use 0.3
1 state uses 0.2	2 states use 0.2
23 states use 0.1	7 states use 0.1
4 states use <0.1	1 state uses <0.1

Reference doses obtained from US Environmental Protection Agency National Program Manager, National Fish and Wildlife Contamination Program by personal communication based on 2003 USEPA Survey of States.

Although human-caused mercury emissions in this country have dropped by almost 50% since 1990, increased monitoring of the nation's bodies of water has resulted in a quadrupling of the number of mercury advisories in terms of lake acres nationwide from 1993 to 2003, and a 14-fold increase in terms of river miles.[18] Forty-eight states issued fish consumption advisories in 2003, and 45 of these states issued advisories regarding mercury contamination. In that year, approximately 35% of the nation's total lake acreage, 24% of the total river miles, and almost 71% of the coastline (excluding Alaska) were under fish consumption advisories. Twenty-one states have issued statewide advisories for fish in freshwater lakes and/or rivers, and 11 states have statewide advisories for their coastal waters.

At the national level, the US Food and Drug Administration (FDA) has primary authority for regulating commercial seafood in the marketplace. The FDA, however, does not conduct significant testing of commercially caught fish, but rather tests both imported and domestically caught fish across the United States, with the fish types and numbers based on the needs to augment the FDA data sets on mercury levels in fish.[19-21] The FDA takes the approach that the best use of resources is to use education and outreach to target subpopulations of greatest concern (pregnant women,

women who may become pregnant, nursing mothers, and young children).

FISH OMEGA-3 FATTY ACIDS VS. MERCURY: THE CONTROVERSY

Several recent reviews have highlighted the ongoing controversy between recommendations to increase fish consumption to prevent heart disease and the possible role that mercury exposure from fish may play in the development of heart disease.[2-4] Beginning in 1995, there were a series of reports suggesting that high methylmercury consumption in fish not only abrogates the benefits of omega-3 fatty acids, but may be an independent risk factor for the development of cardiovascular disease.

The first large-scale population-based study to provide data for this hypothesis was conducted in approximately 1800 middle-aged Finnish men.[22] These subjects, who initially were free of cardiovascular disease, were eating a mean of 7.6 μg/d methylmercury. Interestingly, this is only slightly above the US Environmental Protection Agency reference dose for a 70-kg adult man, and at 0.77 μg/kg body wt/week, under the WHO weekly limit of 1.6 μg/kg body wt/week. Thus, the estimated methylmercury intakes in these men were not excessive by current standards. Measurements of hair mercury levels showed that men in the upper tertile for mercury had a significantly elevated risk of acute myocardial infarction ($P = 0.038$) and even greater risk of death from all causes ($P = 0.007$). Hair mercury was also strongly associated with oxidized LDL in these men. Furthermore, hair mercury was significantly correlated with thickening of the common carotid artery, a marker for arterial lipid deposition and coronary artery disease.[23] Two subsequent follow-up studies in this population[23,24] and an independent study in eight additional European countries and the Middle East[25] suggested that the increased risk associated with elevated mercury levels is the result of diminished protective effects of omega-3 fatty acids.

In contrast, other studies have failed to find an association between elevated methylmercury and risk of heart disease. For example, in a study of over 50,000 European men, toenail mercury concentrations were significantly correlated with fish consumption ($P < 0.001$). However, there was no significant correlation between toenail mercury levels and cardiovascular disease or mortality from coronary heart disease.[26] Another study that monitored the serum mercury levels of almost 1500 women ages 38 to 60 over 20 years also found no correlation between mercury and elevated risk of a myocardial infarction or stroke.[27] Finally, a study published in 2001 described the results of a prospective, case-controlled study in men and women ages 30 to 60, in whom erythrocyte mercury and plasma concentrations of EPA and DHA were measured. Subjects with reported fish intakes of at least one fish meal per week had significantly ($P < 0.001$) higher concentrations of both erythrocyte mercury and plasma omega-3 fatty acids. Interestingly, the risk of myocardial infarction was reduced by either high mercury levels or high omega-3 levels, suggesting that the reduced risk associated with fish consumption is not diminished by mercury.[28]

A recent study[29] was specifically designed to address the controversy concerning the role of methylmercury from fish in the development of heart disease. Hair mercury, total serum fatty acids, and serum EPA and DHA concentrations were measured, as well as determinations of body mass index (BMI), in over 1800 Finnish men aged 42 to 60 years. Dietary intakes were determined using food intake records for 4 days after training by a nutritionist. The subjects were followed up after an average of 14 years, during which time there were 525 deaths, 257 (49%) of which were related to cardiovascular disease. Non-fatal coronary events such as myocardial infarction and coronary chest pain were all tracked during this period, as was a diagnosis of cardiovascular disease or coronary heart disease.

Because of the large range of hair mercury concentrations (3.3% of the men had undetectable levels), the subjects were divided into tertiles. Hair mercury concentrations were related to fish intake such that the fish intake of men in the highest tertile of mercury concentration was greater than 2 times higher than men in the lowest mercury tertile ($P < 0.001$). Using the Cox proportional hazards model, which enabled the data to be adjusted for age, family history of heart disease, blood pressure, BMI, alcohol intake, nicotine use (as measured by urinary nicotine metabolite excretion), nutrient intake (i.e., fiber, saturated fat, and antioxidant vitamins), and serum LDL, HDL, selenium, and EPA+DHA, the investigators found that each milligram of increase in hair mercury led to an

Table 2. Regional Variation in Mackerel Hg Concentrations

Fish	Region	Hg
		ppm
Mackerel	North Atlantic	0.05
	Pacific	0.09
	South Atlantic, Spanish	0.18
	Gulf of Mexico, Spanish	0.45
	Gulf of Mexico, King	0.73
Tilefish	Atlantic	0.15
	Gulf of Mexico	1.45

11% increase in the risk of an acute coronary event and to a 13% risk of death from coronary heart disease. This was in spite of the fact that the men with the highest levels of mercury also had the highest combined serum concentrations of EPA and DHA ($P < 0.001$), suggesting that mercury attenuates the benefits of the omega-3 fatty acids EPA and DHA found in fish.

Table 3. Intake Frequencies of Specific Fish Species that Exceed Mercury Limits

Fish 3 oz Servings Hg Limit*	Hg†	Reference Male (70 kg)			Reference Female (50 kg)		
		2 × wk 1.6 μg/wk	Daily 1.6 μg/wk	One 0.1 μg/d	2 × wk 1.6 μg/wk	Daily 1.6 μg/wk	One 0.1 μg/d
	ppm						
Tilefish (gulf)	1.45						
Shark	0.99						
Swordfish	0.97						
Mackerel (king gulf)	0.73						
Grouper	0.55						
Orange roughy	0.54						
Marlin	0.49						
Tuna (fresh)	0.38						
Tuna (canned albacore)	0.35						
Bluefish	0.31						
Croaker (pacific)	0.29						
Bass (saltwater)	0.27						
Halibut	0.26						
Sable	0.22						
Snapper	0.19						
Monkfish	0.18						
Mackerel (Spanish, south Atlantic)	0.18						
Tilefish (Atlantic)	0.15						
Perch (freshwater)	0.14						
Tuna (canned, light)	0.12						
Cod	0.11						
Mackerel (Pacific)	0.09						
Whitefish	0.07						
Shad	0.07						
Squid	0.07						
Pollack	0.06						
Mackerel (North Atlantic)	0.05						
Flounder/sole	0.05						
Croaker (Atlantic)	0.05						
Catfish	0.05						
Mullet	0.05						
Herring	0.04						
Trout (fresh water)	0.03						
Haddock (fresh water)	0.03						
Sardine	0.02						
Tilapia	0.01						
Salmon (fresh)	0.01						
Ocean perch	ND						
Whiting	ND						

Fish species within the bar areas are acceptable based on intake frequency and established limit.
*World Health Organization upper tolerable limit = 1.6 μg MeHg/kg body wt/week; US Environmental Protection Agency reference dose = 0.1 μg MeHg/kg body wt/d.
†Average mercury (Hg) content in parts per million (ppm), US Environmental Protection Agency data.
ND = Not detected, Hg value too low for detection.

OMEGA-3 VS. MERCURY: GETTING THE RIGHT RATIO

Interestingly, men with low hair mercury concentrations combined with high serum concentrations of omega-3 fatty acids had a decreased risk of an acute coronary event, cardiovascular and heart disease, and death.[29] This suggests that we need recommendations for fish consumption that will maximize EPA and DHA intakes while limiting, as much as possible, methylmercury intake. Because methylmercury contamination varies widely from region to region, such recommendations would need to take into account the source of the fish as well as species differences. For example, Table 2 lists the mercury content of mackerel caught in different saltwater locations and shows that the mercury content of this fish ranges from a relatively low average concentration of 0.05 ppm in mackerel caught in the north Atlantic to 0.73 ppm in king mackerel caught in the Gulf of Mexico. Large regional differences are also seen in tilefish mercury concentrations (Table 2). These high mercury contents put gulf king mackerel and tilefish (also known as golden snapper) on the list of seafood, along with shark and swordfish, that should not be consumed.

Table 3 ranks commonly eaten fish by mercury content published by the US Environmental Protection Agency. Previous reviews have made similar calculations and rankings.[2] However, this listing adds a number of popular fished omitted from previous reviews and, more importantly, shows which fishes would be acceptable for men (70 kg) and women (50 kg) using the reference dose for mercury set by the US Environmental Protection Agency and the upper tolerable limit set by the WHO. It also makes separate calculations for mercury in daily compared with twice-weekly fish consumption. Because shellfish are among the most popular seafoods consumed,[2] we have included a separate table (Table 4) for them. As shown in this table, while each of these seafoods contain the omega-3 fatty acids EPA and DHA, many shellfish, including oysters, shrimp, and clams, have methylmercury levels that fall below the limits of detection.

Table 4. Common Shellfish Hg Concentrations

Shellfish*	Hg	EPA + DHA
	ppm	
Lobster	0.31	0.07
Crab	0.06	0.40
Crawfish	0.03	0.14
Oysters	ND	0.47
Shrimp	ND	0.27
Clams	ND	0.12
Scallops	ND	0.17

*3-oz portion.
ND = Not detected, Hg value too low for detection.

Table 5. Fish Omega-3 Fatty Acids Expressed as a Function of Hg Content

Fish	EPA + DHA/Hg
Salmon (fresh, frozen)	2.14
Herring	0.50
Sardine	0.49
Shad	0.34
Trout (freshwater)	0.31
Mackerel (n. Atlantic)	0.24
Whitefish	0.23
Mackerel (Pacific)	0.20
Flounder/sole	0.10
Pollock	0.09

Because it appears that mercury abrogates the cardioprotective effects of omega-3 fatty acids, recommendations for fish intake should consider both mercury and omega-3 contents. Table 5 shows the results of a calculation of omega-3 fatty acid (EPA+DHA) content divided by the mercury content in individual fishes, and reports the 10 fish with the highest EPA+DHA:Hg ratio. As illustrated in this table, fresh or frozen salmon have the highest ratio and thus would be expected to provide the most cardioprotection of any fish. However, caution should be used when purchasing salmon because it has now been shown that some farm-raised salmon have particularly high levels of PCBs and other organic toxins compared with wild, ocean-caught salmon.[30] Furthermore, it appears that salmon farmed in Europe have higher PCB concentrations than salmon farmed in South and Central America.

CONCLUSIONS AND RECOMMENDATIONS

The data reviewed here support the AHA recommendation for at least two 3-ounce servings of seafood per week. However, because mercury abrogates the cardioprotective effects of fish, the mercury content of the fish must be considered. Presently, human activities release mercury to the environment at a rate several times higher than in the pre-industrial era, and at rates exceeding those of natural inputs of mercury to the atmosphere. Depending on its speciation, mercury released from industrial processes or incineration can be deposited near sources, or travel long distances through the atmosphere, before depositing from the air onto the land and sea. It is thus clear that benefits would stem from reductions in mercury emissions to the atmosphere.

At the national level, the US Environmental Protection Agency and the FDA have issued a joint fish consumption advisory[20] that states in part:

1) Do not eat shark, swordfish, king mackerel, or tilefish;
2) Eat up to 12 ounces (two average meals) a week of a variety of fish and shellfish that are lower in mercury; and
3) Check state advisories about the safety of fish caught by individuals in local lakes, rivers, and coastal areas. If no advice is available, eat up to 6 ounces (one average meal) per week of fish you catch from local waters, but do not consume any other fish during that week.

Based on the data reviewed here, it is clear that these recommendations are not sufficiently specific or useful for avoiding the cardiovascular consequences of mercury exposure from fish. Taking into account mercury content, omega-3 fatty acid content, and PCB contamination, it appears that wild salmon can safely be recommended for both adult men and women, even for those consuming fish on a daily basis. However, for other fishes, we advise that choices take into consideration body weight, portion size, frequency of consumption, and the region or water body where the fish was caught or grown, even if no specific mercury advisories have been issued.

Furthermore, the type of fish consumed is of considerable importance. When feasible, selections should come from those fishes listed in Table 5. However, there is a need for better identification and labeling of commercial fish. For example, the marketing of fish as "grouper" or "mackerel" leaves undefined the actual species and its methylmercury content. Furthermore, there is a significant need for a more complete set of data on methylmercury content, particularly in oceanic fish. The variance in methylmercury concentrations is relatively low geographically and over time, making the dissemination of accurate information on contamination levels, and the implications for cardiovascular and overall health, feasible at the point of sale.

REFERENCES

1. Zhang J, Sasaki S, Amano K, Kesteloot H. Fish consumption and mortality from all causes, ischemic heart disease, and stroke: an ecological study. Prev Med. 1999;28:520–529.
2. Smith KM, Sahyoun NR. Fish consumption: recommendations versus advisories, can they be reconciled? Nutr Rev. 2005;63:39–46.
3. Stern AH. A review of the studies of the cardiovascular health effects of methylmercury with consideration of their suitability for risk assessment. Environ Res. 2005;98:133–142.
4. Chan HM, Egeland GM. Fish consumption, mercury exposure, and heart diseases. Nutr Rev. 2004;62: 68–72.
5. Oh R. Practical applications of fish oil (omega-3 fatty acids) in primary care. J Am Board Fam Pract. 2005;18:28–36.
6. Ascherio A, Rimm EB, Stampfer MJ, et al. Dietary intake of marine n-3 fatty acids, fish intake, and the risk of coronary disease among men. N Engl J Med. 1995;332:977–982.
7. Kris-Etherton PM, Harris WS, Appel LJ, Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Arterioscler Thromb Vasc Biol. 2003;23:20–30
8. Clarkson TW, Magos L, Myers GJ. The toxicology of mercury—current exposures and clinical manifestations. N Engl J Med. 2003;349:1731–1737.
9. Castoldi AF, Coccini T, Manzo L. Neurotoxic and molecular effects of methylmercury in humans. Rev Environ Health. 2003;18:19–31.
10. Faviou E, Vourli G, Nounopoulos C, et al. Circulating oxidized low density lipoprotein, autoantibodies against them and homocysteine serum levels in diagnosis and estimation of severity of coronary artery disease. Free Radic Res. 2005;39:419–429.
11. US Environmental Protection Agency. The National Listing of Fish Advisories (NLFA). Available online at: http://www.epa.gov/waterscience/fish/advisories/index.html. Accessed February 8, 2006.
12. US Environmental Protection Agency. Fish Advisories: Where You Live. Available online at: http://epa.gov/waterscience/fish/states.htm. Accessed February 8, 2006.
13. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Mercury. Available online at: http://www.atsdr.cdc.gov/toxprofiles/tp46.html. Accessed February 8, 2006.
14. Food and Agriculture Organization of the United Nations. World Health Organization. Joint FAO/WHO Expert Committee on Food Additives. Available online at: ftp://ftp.fao.org/es/esn/jecfa/jecfa61sc.pdf. Accessed February 8, 2006.
15. National Research Council. Toxicological effects of methylmercury. Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, Commission on Life Sciences, National Research Council. Washington, DC: National Academies Press; 2000.
16. US Environmental Protection Agency. *Mercury Report to Congress Office of Air Quality and Standards*. Washington, DC: US Environmental Protection Agency; 1997.
17. US Environmental Protection Agency. *Integrated Risk Information System, Methylmercury*. Available online at: http://www.epa.gov/iris/subst/0073.htm. Accessed February 8, 2006.
18. US Environmental Protection Agency. *Fish Advisories: National Maps and Graphics*. Available online at: http://epa.gov/waterscience/fish/map.htm. Accessed February 8, 2006.
19. US Food and Drug Administration, Center for Food Safety & Applied Nutrition. *Mercury Levels in Commercial Fish and Shellfish*. Available online at: http://www.cfsan.fda.gov/~frf/sea-mehg.html. Accessed February 8, 2006.
20. US Food and Drug Administration and US Environmental Protection Agency. *What You Need to Know About Mercury in Fish and Shellfish*. Available online at: http://www.cfsan.fda.gov/~dms/admehg3.html. Accessed February 8, 2006.
21. US Food and Drug Administration, Center for Food Safety & Applied Nutrition, and US Environmental

Protection Agency. *Mercury in Fish: FDA Monitoring Program (1990–2004)*. Available online at: http://www.cfsan.fda.gov/~frf/seamehg2.html. Accessed February 8, 2006.
22. Salonen JT, Seppanen K, Nyyssonen K, et al. Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in eastern Finnish men. Circulation. 1995;91:645–655.
23. Salonen JT, Seppanen K, Lakka TA, et al. Mercury accumulation and accelerated progression of carotid atherosclerosis: a population-based prospective 4-year follow-up study in men in eastern Finland. Atherosclerosis. 2000;148:265–273.
24. Rissanen T, Voutilainen S, Nyyssonen K, et al. Fish oil-derived fatty acids, docosahexaenoic acid and docosapentaenoic acid, and the risk of acute coronary events: the Kuopio ischaemic heart disease risk factor study. Circulation. 2000;102:2677–2679.
25. Guallar E, Sanz-Gallardo MI, van't Veer P, et al. Heavy Metals and Myocardial Infarction Study Group. Mercury, fish oils, and the risk of myocardial infarction. N Engl J Med. 2002;347:1747–1754.
26. Yoshizawa K, Rimm EB, Morris JS, et al. Mercury and the risk of coronary heart disease in men. N Engl J Med. 2002;347:1755–1760.
27. Ahlqwist M, Bengtsson C, Lapidus L, et al. Serum mercury concentration in relation to survival, symptoms, and diseases: results from the prospective population study of women in Gothenburg, Sweden. Acta Odontol Scand. 1999;57:168–174.
28. Hallgren CG, Hallmans G, Jansson JH, et al. Markers of high fish intake are associated with decreased risk of a first myocardial infarction. Br J Nutr. 2001;86:397–404.
29. Virtanen JK, Voutilainen S, Rissanen TH, et al. Mercury, fish oils, and risk of acute coronary events and cardiovascular disease, coronary heart disease, and all-cause mortality in men in eastern Finland. Arterioscler Thromb Vasc Biol. 2005;25:228–233.
30. Foran JA, Carpenter DO, Hamilton MC, et al. Risk-based consumption advice for farmed Atlantic and wild Pacific salmon contaminated with dioxins and dioxin-like compounds. Environ Health Perspect. 2005;113:552–556.