Measurement of Mercury Levels in Concentrated Over-the-Counter Fish Oil Preparations

Is Fish Oil Healthier Than Fish?

Stacy E. Foran, MD, PhD; James G. Flood, PhD; Kent B. Lewandrowski, MD

• ***Context.*—Fish consumption has been associated with a decreased risk of coronary artery disease. Recent studies have illustrated that the high mercury content in cold-water fish may negate the cardiovascular benefits of fish meals. Fish oils have similar antiatherogenic properties to fish, and similar studies should be performed to determine the level of mercury in fish oils.**

***Objective.*—To determine the concentration of mercury in 5 over-the-counter brands of fish oil.**

***Results.*—The levels of mercury in the 5 different brands of fish oil ranged from nondetectable (<6 μg/L) to negligible (10–12 μg/L). The mercury content of fish oil was similar to the basal concentration normally found in human blood.**

***Conclusions.*—Fish are rich in omega-3 fatty acids, and their consumption is recommended to decrease the risk of coronary artery disease. However, fish such as swordfish and shark are also a source of exposure to the heavy metal toxin, mercury. The fish oil brands examined in this manuscript have negligible amounts of mercury and may provide a safer alternative to fish consumption.**

(*Arch Pathol Lab Med.* 2003;127:1603–1605)

Epidemiologic studies have demonstrated that the Greenland Eskimos have a comparatively low incidence of coronary artery disease (CAD). This low incidence of heart disease is attributed to the consumption of greater than 400 g of fish per day. Presumably, this protection results from the high level of omega-3 polyunsaturated fatty acids (*n*-3 PUFAs) in oils derived from deep cold-water fish.[1,2] This discovery underscores the important role of diet in the development of CAD and has prompted research on the potential benefits of fish consumption in the general population. For example, the Diet and Reinfarction Trial showed a 29% reduction in overall mortality rates in survivors of a first acute myocardial infarction who consumed fish rich in omega-3 fatty acids at least twice weekly for 2 years.[3] Similar studies corroborate these results.[2,4,5] Consequently, fish intake has been recommended to decrease the incidence of CAD.[6] Although many studies have found that regular fish intake benefits cardiovascular function, some reports have not confirmed these conclusions and question the recommendations on fish intake.[7]

A potential issue arises from the fact that some fish may also contain relatively high levels of toxic heavy metals. For example, fish intake is a major source of exposure to mercury, primarily methylmercury. Large carnivorous fish that are high in the food chain, such as swordfish and shark, have the highest tissue concentration of mercury (1 μg/g), whereas tuna, trout, pike, and bass have intermediate concentrations (0.1–0.5 μg/g). In contrast, invertebrates, such as shellfish, have low concentrations of mercury.[6–8] Mercury may promote atherosclerosis by increasing free radical production or by inactivating several antioxidant mechanisms. Recent studies show that toenail mercury levels are directly associated with the risk of an acute myocardial infarction.[2,6,7] One study found no significant correlation between toenail mercury and CAD, but a trend did exist.[9] The association between the amount of fish consumed and mercury levels has been documented. Data regarding the cardiovascular benefits of fish have been inconsistent. These conflicting results may be explained by the variable amounts of mercury contained in different fish, which may negate the beneficial effects of *n*-3 PUFAs.[6,7]

Fish oils contain concentrated forms of *n*-3 PUFAs. Regular consumption of fish oils also appears to reduce the risk of CAD. In one study, patients with CAD who ingested 1.5 g of omega-3 fatty acids per day for 2 years had less disease progression than did comparable patients who ingested placebo.[10] The magnitude of effect of fish oil consumption on CAD is similar to the benefit of low-density lipoprotein cholesterol–lowering therapy, lifestyle change, and vigorous exercise.[10] Studies also suggest that the effects of fish oil supplements are comparable to fish consumption. Fish oil supplements also permit the administration of large doses of *n*-3 PUFAs, which may produce a decrease in blood pressure in patients with hypertension and a stabilization of mood in bipolar disorder and depression.[11–13] However, data concerning the level of mercury in commercial fish oil supplements are sparse. These data are critical if fish oil supplements are to be

Accepted for publication July 30, 2003.

From the Division of Laboratory Medicine, Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, Mass.

Reprints: Kent B. Lewandrowski, Division of Laboratory Medicine, Massachusetts General Hospital, 55 Fruit St, GRJ 5, Boston, MA 02114 (e-mail: klewandrowski@partners.org).

Mercury Content of 5 Preparations of Fish Oil	
Fish Oil Brand Name	**Mercury Level, μg/L**
CVS	10
Kirkland	<6
Nordic Ultimate	<6
Omega Brite	12
Sundown	<6

recommended in patients with CAD, bipolar and affective disorders, and for cardioprotective benefits in the general population. In this study, we measured the level of mercury in 5 commercial over-the-counter brands of fish oil to assess the risk of mercury toxicity from consumption of these dietary supplements.

METHODS

Five commercial over-the-counter brands of fish oil supplements were purchased from retail or Internet sources. The brands included Nordic Ultimate (San Dimas, Calif), Omega Brite (Waltham, Mass), Sundown (Boca Raton, Fla), Kirkland (Houston, Tex), and CVS (Woonsocker, RI). The capsules were punctured using a trace metal–free device, and the liquid contents were sent in trace metal–free containers to National Medical Services (Willow Grove, Pa) for mercury analysis. The mercury level was measured by cold vapor atomic absorption spectroscopy. The lower limit of detection of mercury for this assay is 6 μg/L.

RESULTS

The results of the mercury analysis are shown in the Table. None of the 5 brands contained significant amounts of mercury. No mercury was detected in the Nordic Ultimate, Sundown, and Kirkland brands. The Omega Brite brand had 12 μg/L of mercury, and the CVS brand contained 10 μg/L.

COMMENT

Humans are normally exposed to very low levels of mercury in the environment. Healthy patients have an average of 3 to 6 μg/L of mercury in their blood, while cold-water fish typically contain 0.5 to 1.0 μg of mercury per gram of fish.[14] The mean daily mercury intake of a 70-kg adult in the United States is 3.5 μg. In other areas of the world, such as Finland, more fish is consumed, which increases the daily intake of mercury to 7.6 μg.[7] Typical blood mercury levels in nonoccupationally-at-risk humans are approximately 2.0 μg/L in subjects who do not consume fish and 8.4 μg/L in those consuming greater than 2 to 4 fish meals per week.[15] A limited amount of research has been done on the levels of mercury in fish oils. A few studies were performed in the 1970s and 1980s, but they used less standardized methods for the determination of heavy metals.[16–18] The levels of heavy metals in cod liver oil and fish oils were examined. In 1978, Van de Ven reported that the ''normal use'' of cod liver oil produced a weekly intake of 8 μg of mercury, compared to weekly fish meals, which contained 125 μg of mercury.[18] The 2 other articles found negligible levels of heavy metals in fish oil preparations.[16,17] A letter reported that selected fish oil supplements were without detectable mercury.[19]

This study examined 5 popular brands of over-the-counter fish oil whose mercury content has not been reported previously. The mercury levels in fish oils obtained in this study are similar to those normally found in the serum of human subjects who consume regular amounts of fish. The 5 fish oil supplements tested have negligible amounts of mercury, suggesting either that mercury is removed during the manufacturing of purified fish oil or that the fish sources used in these commercial preparations are relatively mercury free. Our study results also suggest that even large doses of concentrated fish oil should not cause mercury toxicity. For example, 6 Omega Brite capsules contain 0.072 μg of mercury. This is equivalent to 2.1% of the mean daily mercury intake in the typical American population.

The consumption of fish rich in the essential *n*-3 PUFAs has been linked to a decreased risk of CAD. Omega-3 PUFAs are considered essential because humans cannot synthesize omega-3 fatty acids and must consume them in their diet. Omega-3 PUFAs are richest in cold-water fish, such as salmon, swordfish, shark, sardines, mackerel, and herring. Docosahexaenoic acid, docosapentaenoic acid, and eicosapentaenoic acid are the *n*-3 end-product fatty acids found in fish and have been associated with a decreased risk of acute coronary events[2] and a reduced risk of sudden death among men without evidence of prior CAD.[4,5,20] In addition, adipose tissue levels of docosahexaenoic acid are inversely associated with the risk of acute myocardial infarction.[6] The *n*-3 PUFAs may help clear cholesterol and triglycerides from the blood and prevent cholesterol deposition in the arteries.

Recent studies suggest that the mercury present in many types of fish may negate the cardiovascular benefits of eating fish.[2,6,7] Mercury is a highly reactive metal with no known physiologic role. Three forms of mercury exist: elemental, inorganic, and organic. Exposure to inorganic mercury occurs through certain dental amalgams and in at-risk occupations. Fish consumption is the main source of exposure to organic mercury, predominantly methylmercury.[6–8] Mercury levels of approximately 300 μg/L may produce acute overt symptoms from mercury toxicity. Symptoms of acute toxicity include fever, chills, dyspnea, metallic taste, pleuritic chest pain, lethargy, and confusion.[6,21,22] Chronic exposure to mercury after fish consumption may lead to the classic triad of tremors, gingivitis, and erethism (constellation of neuropsychiatric findings, such as insomnia, shyness, memory loss, emotional instability, depression, anorexia, uncontrolled perspiration, and blushing).[21,22] Due to the possibility of mercury toxicity, pregnant and breast-feeding women and infants and children have been advised not to consume large amounts of certain fish.[15,23] Pregnant or breast-feeding women are cautioned not to eat more than 2 medium-sized cans of tuna fish per week due to the risk that mercury might adversely affect the development of the fetal nervous system. Infants and children younger than 16 years should avoid shark, swordfish, and marlin.[22,23] In addition to the classic findings of chronic mercury toxicity, mercury specifically affects the cardiac vasculature. Increased toenail mercury levels have been associated with an increased risk of CAD.[6] Mercury may enhance free radical production and inactivate several antioxidant mechanisms, such as glutathione, catalase, and superoxide dismutase, leading to atherosclerosis. Mercury may also promote platelet aggregability and blood coagulability, and may induce lipid peroxidation.[6]

Fish oil is a possible substitute for eating fish and has been used pharmacologically in subjects at risk for CAD and in certain psychiatric populations. The effects of fish oil consumption on the risk of CAD are similar in mag-

nitude to low-density lipoprotein cholesterol–lowering therapy, lifestyle change, and vigorous exercise.[10] Supplements of omega-3 fatty acids significantly reduced cardiovascular mortality in patients who took 1 g daily of docosahexaenoic acid and eicosapentaenoic acid.[2] Another study showed that fewer aortocoronary venous bypass grafts became occluded after ingestion of fish oil concentrate, 4 g/day, for 1 year.[1,20] Omega-3 essential fatty acids in fish oil may also have dramatic impact on both emotional and physical well-being.[11–13,24] Fish oil has been reported to relieve depression,[11–13,24,25] improve gastrointestinal function in Crohn disease,[26] and act as an anti-inflammatory agent in cystic fibrosis.[27,28]

Due to the lower measured concentrations of mercury in commercial fish oil preparations, consumption of fish oil may be preferable to consuming fish. We have shown that mercury levels in 5 commercial fish oils are either below the limit of detection or do not contain a significant amount of mercury and therefore pose minimal risk of toxicity. Levels of mercury in fish oil are similar to basal human levels observed in the population. Some fish, on the other hand, may contain high levels of mercury that appear to counteract the positive effects of fish consumption on CAD. The additional benefit of fish oil is that large doses of *n*-3 PUFAs can be ingested easily in a capsule without risk of toxicity.

Finally, it should be cautioned that we tested only 5 preparations of fish oil for mercury content. It is possible that other brands may have more mercury, depending on the source of fish. To circumvent this possibility and to eliminate any risk of mercury toxicity, we recommend that routine labeling of fish oil preparations should include mercury analysis to ensure safety and efficacy.

References

1. Harris WS. Nonpharmacologic treatment of hypertriglyceridemia: focus on fish oils. *Clin Cardiol.* 1999;22(6 suppl):II40–II43.
2. Rissanen T, Voutilainen S, Nyyssonen K, Lakka TA, Salonen JT. 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.
3. Burr ML, Fehily AM, Rogers S, Welsby E, King S, Sandham S. Diet and reinfarction trial (DART): design, recruitment, and compliance. *Eur Heart J.* 1989; 10:558–567.
4. Schmidt EB, Skou HA, Christensen JH, Dyerberg J. N-3 fatty acids from fish and coronary artery disease: implications for public health. *Public Health Nutr.* 2000;3:91–98.
5. Albert CM, Campos H, Stampfer MJ, et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *N Engl J Med.* 2002;346:1113–1118.
6. Guallar E, Sanz-Gallardo MI, van't Veer P, et al. Mercury, fish oils, and the risk of myocardial infarction. *N Engl J Med.* 2002;347:1747–1754.
7. 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.
8. Kales SN, Goldman RH. Mercury exposure: current concepts, controversies, and a clinic's experience. *J Occup Environ Med.* 2002;44:143–154.
9. 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.
10. von Schacky C, Angerer P, Kothny W, Theisen K, Mudra H. The effect of dietary omega-3 fatty acids on coronary atherosclerosis: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med.* 1999;130:554–562.
11. Peet M, Horrobin DF. A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. *Arch Gen Psychiatry.* 2002;59:913–919.
12. Freeman MP. Omega-3 fatty acids in psychiatry: a review. *Ann Clin Psychiatry.* 2000;12:159–165.
13. Stoll AL, Locke CA, Marangell LB, Severus WE. Omega-3 fatty acids and bipolar disorder: a review. *Prostaglandins Leukot Essent Fatty Acids.* 1999;60: 329–337.
14. Storelli MM, Giacominelli Stuffler R, Storelli A, Marcotrigiano GO. Total mercury and methylmercury content in edible fish from the Mediterranean Sea. *J Food Prot.* 2003;66:300–303.
15. Schober SE, Sinks TH, Jones RL, et al. Blood mercury levels in US children and women of childbearing age, 1999–2000. *JAMA.* 2003;289:1667–1674.
16. Bugdahl V, von Jan E. Quantitative determination of trace metals in frozen fish, fish oil and fish meal [in German]. *Z Lebensm Unters Forsch.* 1975;157: 133–140.
17. Koller H, Luley C, Klein B, Baum H, Biesalski HK. Contaminating substances in 22 over-the-counter fish oil and cod liver oil preparations: cholesterol, heavy metals and vitamin A [in German]. *Z Ernahrungswiss.* 1989;28:76–83.
18. van de Ven WS. Mercury and selenium in cod-liver oil. *Clin Toxicol.* 1978; 12:579–581.
19. Schaller JL. Mercury and fish oil supplements. *MedGenMed.* 2001;3:20.
20. Saldeen TG, Mehta JL. Dietary modulations in the prevention of coronary artery disease: a special emphasis on vitamins and fish oil. *Curr Opin Cardiol.* 2002;17:559–567.
21. Graeme KA, Pollack CV Jr. Heavy metal toxicity, part I: arsenic and mercury. *J Emerg Med.* 1998;16:45–56.
22. Mercury toxicity. Agency for Toxic Substance and Disease Registry. *Am Fam Physician.* 1992;46:1731–1741.
23. Evans EC. The FDA recommendations on fish intake during pregnancy. *J Obstet Gynecol Neonatal Nurs.* 2002;31:715–720.
24. Chiu CC, Huang SY, Shen WW, Su KP. Omega-3 fatty acids for depression in pregnancy. *Am J Psychiatry.* 2003;160:385.
25. Berk M, Segal J, Janet L, Vorster M. Emerging options in the treatment of bipolar disorders. *Drugs.* 2001;61:1407–1414.
26. Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. *J Am Coll Nutr.* 2002;21:495–505.
27. Beckles Willson N, Elliott TM, Everard ML. Omega-3 fatty acids (from fish oils) for cystic fibrosis. *Cochrane Database Syst Rev.* 2002:CD002201.
28. Furst P, Kuhn KS. Fish oil emulsions: what benefits can they bring? *Clin Nutr.* 2000;19:7–14.