

Balancing the Risks and Benefits of Fish Consumption

Most Americans know that eating fish is good for their health. Studies from the past 2 decades have repeatedly linked the consumption of fish—especially fish that is high in ω -3 fatty acids—with healthier hearts in the aging population (1). Scientists have also found associations between fish consumption and a reduced risk for stroke, dementia, asthma, kidney disease, and diabetes. Americans have responded to the news: U.S. fish consumption per capita increased 50% since 1980, according to the U.S. Department of Agriculture. Consumption of salmon alone, the country's third most popular fish, increased 23% between 1987 and 1999.

But Americans have heard less about, and perhaps paid less attention to, various health warnings associated with fish consumption. Studies have linked overconsumption of certain fish (particularly popular ones such as swordfish, tuna steaks, Chilean sea bass, and some kinds salmon) to neurologic deficits, cancer, autoimmune and endocrine disorders, and even some heart disorders. The risks stem mainly from 2 toxins: mercury, which accumulates over the lifetime of larger, longer-living fish, and polychlorinated biphenyls (PCBs), which are found in fish living in polluted waters and in some farmed fish.

The idea that certain fish can be both beneficial and harmful is difficult for many people to understand, and they're not getting much help, according to environmental health experts. The federal government doesn't provide straightforward guidance: For instance, it has recommended that people eat salmon because it is high in ω -3 fatty acids without mentioning that farmed salmon commonly contains high levels of PCBs. Grocery stores seldom label fish that are likely to have a high content of toxins. Consumers must read state advisories to learn which noncommercial local fish are safe to eat.

Many Americans have simply ig-

nored the warnings about fish, perhaps holding the popular idea that lots of food today seems to pose some health risk. Others have stopped eating fish altogether because of the potential dangers of eating too much of the wrong ones. "The consumer is totally confused because the messages have not been comprehensive or consistent," said David O. Carpenter, MD, a professor of environmental health and toxicology at the State University of New York at Albany. "But the message is certainly not to avoid eating fish, just to eat it carefully."

Certainly, many fish pose no known health risks to any consumers. These include flounder, farmed rainbow trout, sole, anchovies, and farmed clams and shrimp. Other fish are fine to eat in moderation—approximately once a week—such as cod, farmed catfish, mahi mahi, wild salmon, tilapia, and canned chunk tuna. Environmental health experts generally agree that most Americans would benefit from consuming more of these safe fish. "You don't have to eat carcinogens and neurobehavioral toxicants in order to get your omega-3 fatty acids," Carpenter said. But telling Americans to eat more of some fish and less of others is not a simple message, and many physicians are not certain how to guide their patients.

MERCURY EXPOSURE AND THE ROLE OF THE INTERNIST

Much of the research on risks from fish has focused on mercury, a substance long known to be harmful to humans. Exposure to one form of mercury, methylmercury (the organic form of mercury that is found naturally in the environment and is released mainly through industrial practices, including the burning of fossil fuels and solid wastes), comes almost solely from eating fish. Methylmercury reaches its highest levels in large, predatory species, such as shark, tilefish, and tuna, and in bottom-feeders, such as crab.

(Two other forms of mercury—inorganic and elemental—pose a danger to humans when inhaled rather than ingested; exposure is usually occupational, such as from mining and processing mercury ores or from work with scientific instruments, batteries, and fungicides.)

Many Americans are believed to have dangerous levels of methylmercury in their bodies, according to federal research; this includes an estimated 5% to 8% of American women of childbearing age. Levels higher than 5 $\mu\text{g/L}$ in blood or higher than 1 $\mu\text{g/g}$ in hair are potentially hazardous to a developing fetus, according to U.S. Environmental Protection Agency (EPA) and National Academy of Sciences recommendations. This level corresponds to a reference dose of approximately 0.1 $\mu\text{g/kg}$ of body weight per day of methylmercury exposure. The U.S. Food and Drug Administration (FDA) recommends that a 120-pound person consume no more than 38.5 μg of mercury per week (77 μg for a 240-pound person). Just a single 6-ounce serving of some fish can exceed that level. For instance, 6 ounces of swordfish can contain more than 200 μg of mercury. "I've seen a patient eat a pound of swordfish every week for some months and get levels up to 50 micrograms per liter blood mercury," said Rose Goldman, MD, MPH, chief of occupational and environmental health at Cambridge Health Alliance in Cambridge, Massachusetts. The reference dose is based on levels determined to be dangerous for a fetus or very young child and thus contains a large margin of safety for adults, according to experts in environmental health.

Why is mercury dangerous? Among adults, methylmercury poisoning causes symptoms such as tremor, difficulty with concentration, vision deficits, and numbness and tingling. Such symptoms have usually been described in adults with blood levels of 200 $\mu\text{g/L}$ or greater, and sometimes in those with blood levels as low as 50 $\mu\text{g/L}$. At levels

lower than that, it is difficult to link symptoms specifically to a measurable level, Goldman said. Methylmercury is absorbed from the gastrointestinal tract and binds readily with proteins; the highest levels in the body are found in the kidneys. It is also known to cross blood-brain barriers. Methylmercury is slowly transformed into other forms of mercury and is excreted mainly in feces, urine, and breast milk, mostly within a few weeks to a few months after exposure.

Children born to women exposed to high levels of methylmercury during or before pregnancy may face numerous health problems, including brain damage, mental retardation, blindness, and seizures. Lower levels of methylmercury exposure in the womb have caused subtle but irreversible deficits in learning ability. Animal studies have suggested that methylmercury exposure in the womb may also alter male reproductive organs and increase risk for cancer.

Most physicians don't think of mercury poisoning as a common diagnosis in daily office practice. Jane M. Hightower, MD, an internist at the California Pacific Medical Center in San Francisco, tested 89 patients who came for an office visit in a 1-year period and, on the basis of a history of fish consumption, were at risk for mercury exposure. Statistical analysis of these patients found mercury levels of 2.0 to 89.5 $\mu\text{g/L}$. The mean ($\pm\text{SD}$) for 66 women was $15 \pm 15 \mu\text{g/L}$, and the mean ($\pm\text{SD}$) for 23 men was $13 \pm 5 \mu\text{g/L}$; 89% had levels exceeding the reference dose (2). Hightower's cohort included many middle- to high-income patients who frequently ate tuna steaks, swordfish, and Chilean sea bass, among other fish.

To diagnose mercury poisoning, physicians should ask patients about nutrition during the history and physical examination. "People have strange diets, and you don't know if you don't ask," Hightower said. She described 1 patient who ate a tuna steak almost every night for dinner. After having trouble concentrating, feeling sluggish, and experiencing hand tremors, he saw 5

doctors who ruled out cancer, chronic fatigue syndrome, lupus, Parkinson disease, and multiple sclerosis. Some suggested that the problems might be psychological. Finally, after hearing about Hightower's study, the patient scheduled a visit with her and received testing for mercury poisoning. Laboratory tests showed high levels of mercury, and Hightower recommended that the patient change his diet. After a few months, the symptoms receded.

Adults sometimes have elevated mercury levels from fish yet have no symptoms, according to a study by Goldman and her colleague, Stephen N. Kales, MD, MPH (3). Goldman and Kales reported on 1 patient who ate a can of tuna every day for lunch for 5 years and had no clinical symptoms of mercury poisoning. At the urging of his wife, he was tested and found to have a blood mercury level of 52 $\mu\text{g/L}$. Various factors might influence individual response to mercury exposure, including genetics, age, sex, health status, nutritional supplements or dietary interactions, and intensity of mercury exposure, Goldman noted.

For patients who frequently consume high-risk fish and who want to know their mercury exposure, Hightower and Goldman recommended ordering a blood and urine test for mercury, which costs less than \$20. (Measuring mercury in hair or nail samples is another way to test for mercury poisoning, but experts said that the findings can be less accurate and harder to interpret.) If the blood test shows elevated mercury levels but the urine test does not, then organic mercury from fish consumption is probably the source. The methylmercury in fish is mostly excreted in feces, not urine. When both the blood and urine test results are positive for mercury poisoning, the diagnosis is probably inorganic mercury exposure, usually from job exposure.

Mercury poisoning is treated by eliminating the source. Since the only important source of organic methylmercury is contaminated fish, removing high-risk fish from the diet is the key to eliminating exposure. Goldman

warned physicians who are unsure how to interpret mercury test results to ask about fish consumption. Sometimes physicians will recommend removal of dental fillings without even asking the patient about the source of mercury exposure, such as fish consumption. (Despite common belief, dental fillings rarely cause mercury exposure or poisoning since this inorganic form of mercury is dangerous only when inhaled, not when swallowed; in addition, the difference between the exposure from inorganic mercury in dental fillings rather than from organic mercury in fish should be clear from laboratory tests.) She also warned about chelation therapy, which has not been found to be beneficial for treating low-level methylmercury exposure. The body will excrete low-level mercury exposures on its own, over a few months, and medications that may have side effects are unnecessary. (Physicians treating patients with high levels of mercury might appropriately prescribe chelation therapy to enhance excretion of mercury from the blood and to avoid distribution of mercury in the body.)

The FDA provides the following advice about eating fish: Do not eat shark, swordfish, king mackerel, or tilefish because they contain high levels of mercury. Eat up to 12 ounces (2 average meals) per week of a variety of fish that are lower in mercury; 5 of the most commonly eaten fish that are low in mercury are shrimp, canned light tuna, salmon, pollock, and catfish. Check local advisories about the safety of fish caught by family and friends in local lakes, rivers, and coastal areas; if no advice is available, eat up to 6 ounces (1 average meal) of that fish per week, but don't consume any other fish during that week.

PCB EXPOSURE AND THE ROLE OF THE INTERNIST

Like mercury, PCBs are also dangerous to adults as well as unborn and very young children. Fish are the main sources of concentrated PCB exposure. The highest dietary levels of PCBs are found in farmed salmon, and fish

caught by anglers in various local lakes and ponds may also carry high levels of PCBs. (They are also found in meat, poultry, and dairy products.)

Flame retardants, electrical equipment, pesticides, paints, varnishes, and inks were made with PCBs until the manufacture of the organochlorine compounds was banned in 1979. Materials containing PCBs that were in service at the time of the ban, however, were not removed from use, and some are still used today. In addition, although the ban led to a dramatic drop in levels of PCBs in the environment, they persist as a common pollutant because of their low solubility in water and low volatility. They are released from sediments that serve as environmental reservoirs, according to the EPA.

The EPA has identified PCBs as a probable carcinogen. However, the effects of PCBs on adults are poorly understood, mostly because of the long latency period required for cancer induction and epidemiologic limitations. PCBs appear to affect the central nervous system as well. In 1 study, 101 adults who annually ate more than 24 pounds of sport-caught fish from Lake Michigan had markedly elevated levels of PCBs, and they performed significantly worse on several measures of memory and learning compared with a control group (4).

Animal studies have also associated PCB exposure in adults with liver and breast cancer, neurologic and endocrine problems, and possibly even increased risk for heart disease. In children, PCB exposure in utero and from breast milk consumption has been linked with neurodevelopmental delays, impaired cognition, immune problems, and alterations in male reproductive organs.

Exposure to PCBs is hard to detect in office practice. Although PCBs in very high levels cause an acne-like rash, the effects at lower levels are generally not detectable. Testing PCB levels costs more than \$1000 and is generally not recommended. A careful history is considered the best way to detect PCB poisoning. "Doctors ought to take a di-

etary history just as they take an occupational history. They ought to ask if patients are eating fish more than 2 times a week, and if so, what kinds of fish. Doctors might advise some patients to cut back on or to avoid eating the highly contaminated fish. People who avoid the highly contaminated fish should be okay," said Henry Anderson, MD, Chief Medical Officer for Environmental Health for the Wisconsin Division of Public Health in Madison, Wisconsin.

Physicians should be aware that people who frequently eat certain non-commercial fish caught in local waters are at especially high risk for PCB poisoning. Fish affected by PCBs vary according to where they live, and consumers are advised to follow their local state advisories (www.epa.gov/waterscience/fish/states.htm). Because of PCBs, people are advised not to eat white bass, carp, or sturgeon caught in Wisconsin's Green Bay, for instance, or largemouth bass caught in various Florida waterways, or any fish at all caught in New York's Nassau Lake. Generally, freshwater fish that live in inland lakes, such as bluefish, lake trout, and smelt, are more likely to be contaminated.

Commercially farmed fish are now receiving a lot of attention as a source of PCBs. In a study published early in 2004, the highest levels of dietary PCBs occurred in farmed salmon sold in the United States and Canada (5). The farmed salmon, fed mostly PCB-contaminated ground-up fish, contained about 30 parts per billion of PCBs, which was 2 to 10 times more than the level in beef and about 5 times the amount that the EPA guidelines say is safe. Fish eaten twice a week should contain no more than 4 to 6 parts per billion of PCBs, according to the guidelines. These guidelines are based on the amount of PCBs thought to cause 1 additional cancer case in 100 000 people over a 70-year lifetime. Any more than a single 8-ounce portion of farmed salmon a month posed an "unacceptable cancer risk" to consumers, the authors concluded.

"The salmon study was important psychologically because it overturned

some of our preconceived notions. In the past, farmed fish were felt to be universally better than wild fish, and yet this study indicated that some may be more contaminated," said Peter Orris, MD, MPH, a professor of internal and preventive medicine at Rush University Medical School in Chicago. More than 90% of the salmon consumed in the United States is farm-raised; it is available year-round and is less costly than wild salmon. Orris noted that in response to the results of the study, the industry has already started to change the way that it feeds farmed fish.

The FDA and the fishing industry have, however, disputed the importance of the study's findings. Contaminant levels in salmon have declined by 90% since PCBs were banned, the FDA noted. The FDA notes that the salmon contained no more than 50 parts per billion of PCBs, far lower than the FDA standard of 2000 parts per billion. The FDA and others have also repeatedly emphasized that the benefits of eating salmon—a high-protein content and the favorable effects of ω -3 fatty acids on cardiovascular health—outweigh the risk from PCBs.

As with mercury, the only treatment for PCB poisoning is removal of the source. However, it is almost impossible to completely eliminate exposure since PCBs occur in many foods besides fish. The FDA and EPA advise consumers to avoid eating fatty fish caught locally. For consumers of these fish, the agencies advise reducing exposure by removing fatty areas, such as the belly, back, and dark side meat, before cooking since PCBs occur mostly in fat. Other precautions include removing or puncturing the skin and cooking the fish on a rack to allow fat to drain. Frying fatty fish is ill-advised. Lean ocean fish such as cod, flounder, and haddock are the least likely to be contaminated with PCBs.

UNRESOLVED QUESTIONS ABOUT TOXIC FISH

While mercury and PCBs in fish pose a danger to human health, many

Alternate Sources of ω -3 Fatty Acids

Although fatty fish are considered the best source of ω -3 fatty acids, there are alternatives. Flaxseed, canola, soybeans, and walnuts are high in short-chain omega-3 α -linolenic acids. It is not known whether the short-chain linolenic acids found in these foods are transformed into long-chain fatty acids in humans once consumed (they are in at least some animals), but they are believed to be as beneficial to health as the ω -3 fatty acids found in fish.

Nutritional supplements containing ω -3 fatty acids are also an option. "I'm not a big fan of supplements, but the omega-3 supplements can now be purified to remove any mercury or other toxins," David O. Carpenter, MD, said. He said that people with documented coronary artery disease might consider taking purified ω -3 fatty acid supplements as an alternative to eating lots of fish. It is possible to overdose on supplements, however, he noted, so patients are advised to check with their physicians on how much to take. Most physicians advise about 3 g per day, Carpenter said.

uncertainties remain about their role in human health. For instance, scientists don't know the exact level at which the contaminants in fish become detrimental to adult health. The first priority of current fish advisories is to protect the unborn fetus and young children. Furthermore, while it is generally believed that passage out of the human body takes 3 months to a year for mercury and up to 8 years for PCBs, the contaminants have a different half-life in different organs. They may linger longer, for instance, in the brain and kidneys than in the blood. Genetic susceptibility and synergy with other compounds in the body may play roles in determining at what threshold these contaminants prove dangerous to individuals.

In addition, the benefits from eating PCB-contaminated fish might outweigh the risks, at least among people at highest risk for heart disease. "There's absolutely no question that omega-3 fatty acids are very important in the prevention of sudden cardiac

deaths, and therefore adequate amounts of those fats in the diets of individuals of the age that should be concerned about heart attacks—men older than 45 and women older than 55—[are] extremely important," Carpenter said. "The area that is really gray is whether there are benefits for younger people." Scientists have conducted little research on the effects of fish consumption in the younger adult population, except its effects on fetal exposure during childbearing years.

FIXING THE PROBLEM FOR THE FUTURE

Despite many changes in environmental law, experts expect that mercury and PCBs will persist in fish for at least the next 50 years. While levels of PCBs have fallen in recent years, levels of mercury in fish continue to increase at a rate of 4.8% per year, according to estimates. Legislation such as the Clean Air Act and the Clean Water Act has helped to reduce toxins in the water,

but the effectiveness of such legislation relies on continued enforcement. Furthermore, the removal of PCBs in the food supply requires changes in the practices of commercial food producers. "Industry is recycling contaminated fats through the food that we feed the farmed salmon as well as other protein sources like beef, pigs, and chickens. If that food were cleaned up or a different food were used, the problem would be resolved," Carpenter said.

Overall, the public needs robust prospective studies in populations in which fish is a major part of the diet, experts say, and some are ongoing. Ideally, such studies would help shape federal dietary regulations as well as environmental regulations.

—Jennifer Fisher Wilson

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