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JES JOURNAL OF ENVIRONMENTAL SCIENCES

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Benefits and risks associated with consumption of Great Lakes fish containing omega-3 fatty acids and polychlorinated biphenyls (PCBs)

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ARTICLE INFO

Available online 19 December 2015

Keywords:
Environmental epidemiology
Polychlorinated biphenyls (PCBs)
Omega-3 fatty acids
Thyroid cancer
Dietary exposure
Food contamination
New York fishermen

Focusing on a group of sport fishermen in New York, Haslam et al. (2015) examined the effects of estimated consumption of omega-3 fatty acids and PCBs on the risk of thyroid cancer over a 17-year span from 1991 to 2008. The study concluded that consumption of Great Lakes fish, with the concomitant PCBs, did not increase the risk of thyroid cancer in New York fishermen. The study results also suggest that long-term consumption of omega-3 fatty acids may protect against the development of thyroid cancer.

Introduction

Assessment of environmental health effects arising from exposure to multiple substances is often very challenging. This is particularly true when humans are exposed to a mixture that contains both beneficial and harmful substances. A good example relates to the risk and benefits of fish consumption. Fish contain a variety of essential nutrients, such as omega-3 fatty acids and proteins, which are beneficial to human health. Fish may also contain trace amounts of environmental contaminants, such as polychlorinated biphenyls (PCBs), which can disrupt endocrine function. How would environmental health studies confront the challenges of assessing the adverse and beneficial effects from food consumption? A recent study (Haslam et al., 2015) published in the *Journal of Environmental Sciences* demonstrates an example of an approach based on environmental epidemiology to tackle this complex problem.

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1. Sources and occurrence of PCBs

PCBs are a group of organic compounds consisting of 209 possible congeners. These congeners vary by the number and position of chlorine atoms on the biphenyl rings (Fig. 1). For their stability and low flammability, PCBs were used widely in many industrial processes, such as the manufacturing of electrical equipment, heat exchanges, and hydraulic systems (Erickson and Kaley, 2011). Because of a variety of industrial incidents and food contamination events, the production and use of PCBs were banned by the United States in 1979 and by the Stockholm Convention on Persistent Organic Pollutants in 2001 (Porta and Zumeta, 2002).

Because of their stability, slow biotransformation, and significant bioaccumulation in lipids, PCBs persist in the environment for long periods of time (Li et al., 2009; Xu et al., 2013; Wang et al., 2012; Malisch and Kotz, 2014). The persistence and bioaccumulation of PCBs in organisms results in their biomagnification along the food chain, with increasing concentrations of PCBs in the organisms as the trophic level increases.

The Great Lakes are in close proximity to many industrial plants and factories where PCBs were heavily used in the past.

http://dx.doi.org/10.1016/j.jes.2015.12.002

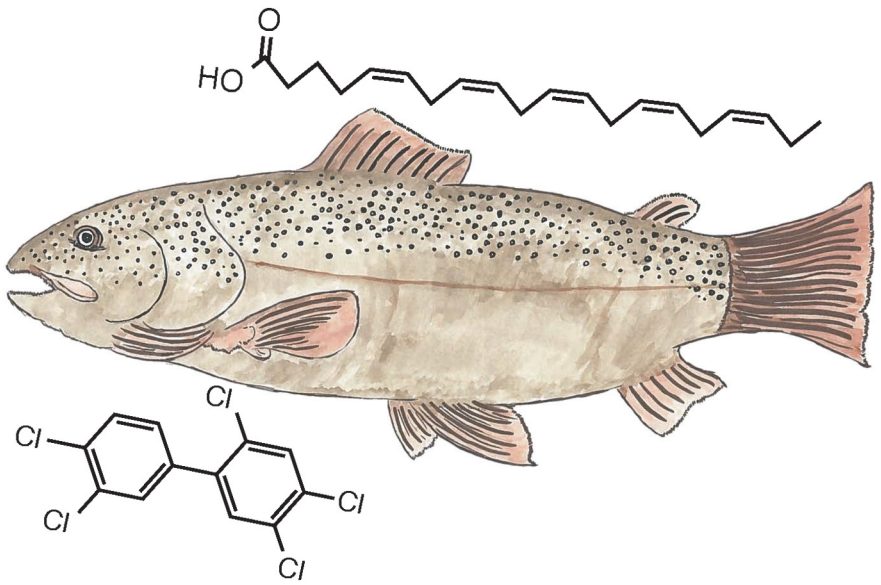

Fig. 1 – Fish from Great Lakes contain both beneficial omega-3 fatty acids (structure above the picture of the fish) and potentially harmful polychlorinated biphenyls (structure below the picture of the fish). The picture of the fish was drawn by Ms. Yi Li, University of Alberta.

The PCB contamination of the Great Lakes has resulted in higher concentrations found in water, sediment, and aquatic life. Though PCBs have been banned in the United States for more than 35 years and their concentrations in the Great Lakes have declined steadily, their concentrations are still above wildlife protection values of 0.16 ppm (US EPA, 2012). Bioaccumulation of PCBs in fish is of particular concern, as fish is a common food for many who live in the area. PCBs have also been detected far away from manufacturing and production, such as regions north of the Arctic Circle and in the Tibetan Plateau (Tian et al., 2014), indicating their ability for long-range transport. New sources of PCBs that are of concern also originate from electronic waste processing (Li et al., 2015).

2. Toxicity of PCBs

The toxicity of PCBs varies considerably among congeners: coplanar PCBs tend to have dioxin-like properties and generally are the most toxic (Hutzinger et al., 1974). The common toxic effects of PCBs include hormonal interference, reproductive disorders, neurological disorders, and cancer (Louis et al., 2005; Meeker and Hauser, 2010; Schantz et al., 2003; Wolff et al., 1993; Høyer et al., 1998). In 2013, the International Agency for Research on Cancer classified PCBs as human carcinogens (IARC, 2015).

The carcinogenicity of PCBs has been studied in animal models, in which high concentrations of PCBs were found to induce tumors in the liver, lung, and oral mucosa in rats (Strauss and Heiger-Bernays, 2012). An epidemiological study by Pavuk et al. (2004) found a higher incidence of thyroid cancer in women living in a site with contamination from previous PCB production. PCBs act as endocrine disrupters, which is of particular concern because of their ability to promote development of thyroid cancer (Boas et al., 2012; Fein et al., 1984). Additionally, Zani et al. (2013) have shown an association between elevated blood levels of PCBs and non-Hodgkin lymphoma. However, studies on health outcomes of human exposure to PCBs are not all consistent. For example, epidemiological studies of people in Kyushu, Japan and Yu-Cheng, Taiwan who were exposed to high doses of PCBs through contaminated rice oil did not show significant adverse health effects (Tsai et al., 2007; Li et al., 2012; Onozuka et al., 2009; Yoshimura, 2012). Although there was increased PCB consumption in these populations, the data showed no definite increase in total cancer mortality and no association with any specific cancers.

3. Benefits of Omega-3 fatty acids

Fish consumption is beneficial as fish contain essential nutrients, such as iodine, selenium, vitamins, and proteins (Larsen et al., 2011). Additionally, fish contain high levels of omega-3 fatty acids that cannot be synthesized by the human body but are essential for normal metabolism. Omega-3 fatty acids have been shown to protect against inflammatory conditions and even cancer, because of their antioxidant activity (Tavani et al., 2003). Antioxidants act as scavenging molecules, removing free radicals that are formed in the body during many cellular processes. Otherwise, elevated levels of free radicals can damage major cell components, such as DNA, proteins, and cell membranes. Damage caused by these free radicals, specifically to DNA, plays a role in the development of cancer (Diplock et al., 1998; Valko et al.,

2007). One animal study found that consumption of omega-3 helped production of antioxidant enzymes, such as glutathione peroxidase, superoxide dismutase, and catalase (Iraz et al., 2005). Other health benefits of omega-3 include protection against heart attacks and strokes, slowing build-up of plaques, and reducing blood pressure (Calder, 2004; Eritsland et al., 1996; Kris-Etherton et al., 2002; Morris et al., 1993; Simopoulos, 2002; Wall et al., 2010). Because mammals cannot synthesize omega-3 fatty acids, we obtain omega-3 in our diet from sources such as fish.

4. Association of cancer risk with consumption of fish that contain PCBs and omega-3 fatty acids

Fish from the Great Lakes contain both harmful and beneficial components that may lead to contradictory health outcomes. Several epidemiological studies examining the association between consumption of Great Lakes fish and cancers have demonstrated the complexity of the problem (McElroy et al., 2004; Tomasallo et al., 2010; Haslam et al., 2015). Similarly, a number of earlier studies reporting consumption of fish from other areas have shown positive, negative, or no association with the risk of cancers, *e.g.*, breast cancer and colorectal cancer (Stripp et al., 2003; Gago-Dominguez et al., 2003; Holmes et al., 2003; Kato et al., 1997).

In a recent study by Haslam et al. (2015), the effects of fish consumption on the risk of thyroid cancer in humans were examined. Prior to this study, there was no report on any association between ingestion of PCBs (from fish consumption) and thyroid cancer. The authors chose to focus on thyroid cancer because PCBs are known endocrine disruptors and have potential effects on thyroid functions. The authors recruited participants (135 sports fishermen and their spouses) from the New York State Angler Cohort Study (Vena et al., 1996). The ratio of male to female participants in the control group was matched with that of the participants in the thyroid cancer case group. The scientists asked the participants about their fish consumption patterns at the beginning of the study in 1991, and then followed the participants for 17 years (from 1991 to 2008), to observe incidences of thyroid cancer and to determine any differences between the fish consumers and non-fish consumers. A questionnaire also included the species of fish consumed, the size of the fish, and the frequency of fish consumption. Using this information, the authors estimated exposure to PCBs and the intake of omega-3 fatty acids from fish consumption. When constructing logistic regression models to predict thyroid cancer association with consumption of Great Lakes fish, intake of omega-3 fatty acids, and exposure to PCBs, the authors adjusted for sex (cases and controls were matched by sex), age, and cigarette smoking. They took into account these possible confounding factors because other studies found that women were more likely to develop thyroid cancer (Aschebrook-Kilfoy et al., 2011), that the median age of thyroid cancer diagnosis was 46 years old (Davis and Welch, 2006), and that smoking has been associated with thyroid hormone abnormalities (Soldin et al., 2009). In total, 27 cases of thyroid cancer were reported with 108 control participants. Results from statistical analyses indicated that there was no significant association between total fish consumption or the estimated PCB intake from Great Lakes fish and the incidence of thyroid cancer. However, those who had a higher long-term estimated omega-3 fatty acids consumption from Great Lakes fish had lower incidences of thyroid cancer than those with a lower omega-3 fatty acids consumption. These results suggest that long-term intake of omega-3 fatty acids from Great Lakes fish may protect against the development of thyroid cancer.

5. Further perspectives

The Great Lakes have been contaminated with PCBs and other potentially harmful chemicals. Concerns over the health effects of PCBs and other contaminants have led to fish consumption advisories in the Great Lakes area, *e.g.*, the US EPA National Listing of Fish and Wildlife Advisories (US EPA, 2014). Although the concentrations of PCBs in the Great Lakes have declined significantly, at least 5% per year between the years 1975 and 2006 (US EPA, 2012), the fish advisories have remained in place. Consuming the contaminated fish is a trade-off, as the PCBs have been shown to have adverse health effects, but the omega-3 fatty acids have health benefits. The study by Haslam et al. (2015) supports the risk-benefit analysis conducted by Neff et al. (2014) who concluded that the benefits of consuming the fatty acids in certain species of Great Lakes fish, primarily smaller-sized species, could outweigh the risks of possible PCB exposure from these fish, within the limits of the current fish-consumption advisories.

Further research on this topic could benefit from an improved determination of individual exposure to PCBs and omega-3 fatty acids from all dietary sources. This may be done through serum analysis, combined with more detailed dietary records. Additional research should aim to elucidate and separate the effects of harmful PCBs from beneficial omega-3 fatty acids, both occurring in fish. Further, it would be useful to include a longer follow-up time for the study, as the participants in the study by Haslam et al. (2015) were relatively young (mean age of 32 years) and most cases of thyroid cancer are diagnosed before the age of 55. It would also be beneficial to include a longer follow-up time spanning more than one generation to observe potential health effects on subsequent generations. This would provide insight into protective advantages of the long-term intake of omega-3 fatty acids over exposure to the concomitant PCBs in fish.

Despite the co-occurrence of environmental contaminants and beneficial nutrients in food, moderation in food consumption and a balanced diet with a variety of food remains good health advice. This is true for such food as fish that contain both PCBs and omega-3 fatty acids and rice that contains trace amounts of arsenic (Newbigging et al., 2015). In the case of fish consumption, it is important to consider that larger fish and other organisms at higher trophic levels are more likely to have higher concentrations of PCBs due to bioaccumulation and biomagnification. Thus, eating smaller fish and those lower on the food chain in moderation would potentially reduce exposure to PCBs.

Acknowledgments

We thank Alberta Health, Alberta Innovates, the Canada Research Chairs Program, the Canadian Institutes of Health Research, and the Natural Sciences and Engineering Research Council of Canada.

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