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Abstract: Because Great Lakes sport fish are contaminated with several toxicants, the Great Lakes states individually issue advisories, principally based on Food and Drug Administration (FDA) action levels, that suggest limiting or eliminating consumption of contaminated fish. We describe the procedures the states use to determine when to issue consumption advisories and we evaluate the associated cancer risks using EPA-IARC-OSTP risk assessment procedures. Projected cancer risks are high for consumers of small

Introduction

Contamination of the sport fishery in the Great Lakes basin (Lakes Michigan, Huron, Superior, Erie and Ontario and their connecting waters) has been a highly sensitive environmental and human health problem. Since the early 1970s, states in the Great Lakes basin (Illinois, Indiana, Michigan, Minnesota, New York, Ohio, Pennsylvania, Wisconsin) individually have issued annual consumption advisories that suggest reduction or elimination of the consumption of contaminated sport fish. Following the Great Lakes Toxic Substances Control Agreement, states were partially successful in implementing coordinated advisories in 1986. These advisories are based on Food and Drug Administration (FDA) action levels for commercial fish and vary substantially among the states. Whether the consumption advisories protect the population is not known.

In this report, we describe the different consumption advisories, which are dependent upon tissue concentrations of contaminants in local fish populations and we use quantitative cancer risk assessment to evaluate their efficacy.

Methods

We calculated risk projections for two contaminants of Great Lakes sport fish, DDT (1,1,1,-trichloro-2,2-bis[p-chlorophenyl]ethane) and dieldrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-endo-exo-1,4,:5,8-dimethanonaphthalene), partly because of recent regulatory action on these materials.^{1,2}

Projected risks were calculated following the guidelines of the US Environmental Protection Agency (EPA),^{3,4} Office of Science and Technology Policy (OSTP),⁵ and the International Agency for Research on Cancer (IARC).⁶ We used data from the studies of mammalian toxicity for DDT and dieldrin conducted by Cabral, *et al*,⁷ Tomatis, *et al*,⁸ and Walker, *et al*.⁹ We used the multistage model¹⁰ (Global 82) for extrapolation from high to low doses and rodent to human scaling factors. For each combination of fish consumption quantities of sport fish contaminated with DDT or dieldrin at their respective action levels. Projected risks at concentrations that are common but below the action levels are also substantial. We propose that sport fish with tissue concentrations of DDT or dieldrin one-fifth and one-third of the action levels should be covered by consumption advisories to warn consumers of the potential adverse health impacts. (Am J Public Health 1989; 79:322–325.)

and contamination level, we computed four cancer risk estimates by using either rat or mouse experimental data and either surface area or body weight scaling to estimate 95 per cent upper bound risk projections.

Concentrations of DDT (expressed as total DDT) and dieldrin in the edible tissue of Great Lakes sport fish (coho, chinook and king salmon, and lake trout) varied widely throughout the Great Lakes during 1986 (0.01 mg/kg (ppm) to 1.5 mg/kg for total DDT and 0.01 mg/kg to 0.2 mg/kg for dieldrin, Michigan Department of Natural Resources and Wisconsin Department of Natural Resources, unpublished data). Both DDT and its metabolite DDE are found in Great Lakes sport fish, with long range atmospheric transport acting as a continuing source of DDT to the Great Lakes. We chose intermediate tissue concentrations of DDT (total) and dieldrin (1.0 mg/kg and 0.1 mg/kg) to represent those found in many Great Lakes sport fish in 1986 and to be used for comparisons with FDA action levels. The FDA action level for DDT in fish is 5.0 mg/kg (ppm) and 0.3 mg/kg for dieldrin.

Three levels of consumption used in the risk assessment range from the US national average (6.5 g/day or less than oneportion per month weighing one half pound)¹¹ to 96 g/day (approximately three, half pound portions per week) over a lifetime. Surveys suggest that the average consumption rate of sport fish by anglers and their families in the Great Lakes basin ranges from 10 to 50 g/day¹²⁻¹⁴ but that some individuals may consume sport fish at least three times per week (96 g/day).¹⁵

Results

States surrounding Lake Michigan issue consumption advice for sport fish based on the number of fish sampled with edible tissue concentrations that exceeded the FDA action level for individual contaminants (Table 1). States surrounding the other Great Lakes generally issue advice based on the mean tissue concentration for individual contaminants. Consumption advice is modified by the states annually and is issued on a location, species and size-class specific basis.

Cancer risk projections (Table 2) range as high as 1.05×10^{-2} (one excess occurrence of cancer during the lifetimes of 100 exposed individuals living to age 70) for dieldrin and as high as 2.8×10^{-3} for DDT when consumption is 96 g/day (three portions per week) and fish are contaminated with DDT and dieldrin at their respective action levels (5.0 mg/kg, 0.3 mg/kg).

When 10 per cent to 50 per cent of sampled Lake Michigan sport fish are contaminated with DDT or dieldrin at or above action levels, consumers are advised to reduce consumption of

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Lake	Advice					
	Unrestricted Consumption (Category 3)	Restrict Consumption* (Category 2)	Do Not Eat (Category 1)			
Michigan	0-10% of fish sampled exceed Action Level	11–50% of fish sampled exceed Action Level	>50% of fish sampled exceed Action Level			
Huron	Mean Tissue Concentration < Action Level	Mean Tissue Concentration > Action Level	Mean Tissue Concentration > 2X Action Level			
Erie	Mean Tissue Concentration < Action Level	Advice Not Given	Mean Tissue Concentration > Action Level			
Superior	variable**	variable**	Mean Tissue Concentration > Action Level			
Ontario	None	All fish ^a Mean Tissue Concentration 1.5–3 X AL ⁵	Mean Tissue Concentration > 3X AL ^b			

TABLE 1—Process for Developing Sport Fish Consumption Advisories for the Great Lakes (excludes Ontario)

Note: All advice is based on the concentration of contaminants in edible tissue of individual sport fish species or size classes of individual species.

¹⁰Call species.
¹⁰States advise that women of child bearing age, pregnant women, and children do not eat any fish in this category.
**Advice for these categories is based on FDA Action Levels but the procedure for applying action levels is highly variable within and between states.

aNew York issues general advice that all fish should not be consumed more than once per week.

^bThis advice is based on an additivity formula where concentrations of more than one contaminant in fish tissue are combined. Where this combination of contaminants is 1.5–3X the combined action level, New York advises that these fish should not be eaten more than once per month.

these species and size classes of fish to not more than one portion per week. When more than 50 per cent of sampled fish contain contaminants above the action level, no consumption is recommended. Cancer risk projections associated with consumption of one portion per week (32 g/day) of fish with tissue concentrations at action levels range as high as 9.4×10^{-4} for DDT and as high as 3.8×10^{-3} for dieldrin (Table 2).

edible tissue of Great Lakes sport fish were below action levels in 1986, cancer risk projections associated with tissue concentrations of 1.0 ppm DDT or 0.1 ppm dieldrin range as high as 5.7×10^{-4} for DDT and 3.7×10^{-3} for dieldrin. At a fish consumption rate of 32 g/day, risk projections associated with these tissue concentrations range as high as 2.0 \times 10^{-4} for DDT and 1.5×10^{-3} for dieldrin.

Although concentrations of DDT and dieldrin in the

All of the projections cited above were derived using a

TABLE 2-95 Per Cent Upper Bound Cancer Risk Projections In Humans Exposed to Fish Contaminated with **DDT or Dieldrin**

Fish Con- sumption (g/d)*	SCLª	ANM ^b	Tissue Concentration (PPM)			
			DDT		Dieldrin	
			1.0 PPM	5.0 PPM [†]	0.1 PPM	0.3 PPM [†]
	BW	M	3.6 × 10 ^{−6} 1.7×10 ^{−6}	1.5 × 10 ⁻⁵ 7.0×10 ⁻⁶	4.51 × 10 ⁻⁵	9.02 × 10 ⁻⁵
6.5	SA	M R	4.8×10 ⁻⁵ 9.5×10 ⁻⁶	2.0×10 ⁻⁴ 3.9×10 ⁻⁵	5.86×10 ⁻⁴	1.04×10 ⁻³
	BW	M R	1.5×10 ^{−5} 7.2×10 ^{−6}	7.1×10 ^{−5} 3.3×10 ^{−5}	1.13×10 ⁻⁴	2.93×10 ⁻⁴
32.0	SA	M R	2.0×10 ⁻⁴ 4.0×10 ⁻⁵	9.4×10 ⁻⁴ 1.9×10 ⁻⁴	1.49×10 ⁻³	3.76×10 ⁻³
	BW	M R	4.3×10 ^{−5} 2.0×10 ^{−5}	2.1×10 ^{−4} 9.9×10 ^{−5}	2.93×10 ⁻⁴	7.89×10 ⁻⁴
96 .0	SA	M R	5.7×10 ⁻⁴ 1.1×10 ⁻⁴	2.8×10 ^{−3} 5.5×10 ^{−4}	3.65×10 ⁻³	1.05×10 ⁻²

*32 g/day = 1/2 pound/week

[†]FDA action level.

aSCL - BW = body weight scaling factor, SA = surface area scaling factor

^b ANM - M = mouse, R = rat

rodent to human scaling factor based on surface area. A body weight scaling factor reduces risk projections, generally by an order of magnitude for any consumption level and tissue concentration. Use of a body weight scaling factor results in risk projections greater than 1×10^{-5} for all consumption rates of dieldrin and greater than 1×10^{-6} for DDT (Table 2). Use of a body weight scaling factor results in risk projections as high as 7.9×10^{-4} for dieldrin and 2.1×10^{-4} for DDT when fish contaminated at the action level are consumed three times per week. Risks associated with consumption of fish contaminated at current levels range as high as 2.9×10^{-4} for dieldrin and 4.3×10^{-5} for DDT at a consumption rate of 96 g/day. Thus, while the use of a body weight scaling factor results in lower cancer risk projections, these projections are still high for all but the lowest consumption rates and tissue concentrations.

Finally, the use of toxicological data derived from a rat study for DDT results in differences in risk projections of less than an order of magnitude compared with risk projections derived from toxicological data from the mouse study. This is true for comparisons within any consumption level and tissue concentration.

Discussion

Our projections suggest that current consumption advisories for Great Lakes sport fish are inadequate and that consumers of those fish may face substantial excess cancer risks when tissue concentrations of DDT or dieldrin in fish are at or near the FDA action level. They may even face excess cancer risks at one-third to one-fifth of the action level if they consume fish at least weekly. By implication, advisories to restrict or avoid consumption may be necessary when tissue concentrations are one-third to one-fifth of the FDA action levels.

Several caveats apply to our modeling of risk. First, the problems inherent in extrapolation from rodent experiments to humans, the use of the multistage model, the use of benign or malignant tumors, species, sex and organ differences in tumor development rates, and the fact that DDT and dieldrin may act as promoters in the formation of cancer^{16–21} may all result in inaccurate predictions of human cancer rates. The US EPA states that actual cancer rates may be much lower than the 95 per cent upper bound estimates and may actually be as 'ow as zero. We have followed the EPA-IARC-OSTP guidelines for handling these specific points. Models are currently under development to incorporate methods of action as well as metabolic, physiologic and biochemical considerations,^{22,23} but they have not been adopted or endorsed by the US EPA or FDA.

A second problem is the inconsistent data from more than 30 animal studies on the carcinogenicity of DDT, DDE and dieldrin. Even among the few studies that meet EPA-IARC-OSTP guidelines for acceptable cancer studies, not all report positive results. On the other hand, it is reassuring that the use of rats or mice and the use of DDT or DDE changes risk projections by less than one order of magnitude.

Third, the model used here may underestimate cancer risk by ignoring concurrent exposure to other contaminants.²⁴ Great Lakes sport fish carry several chlorinated organic contaminants in their tissues.

Fourth, the risk assessment model used here does not incorporate consideration of any benefits that may be associated with fish consumption such as reduced blood cholesterol levels and reduced risk of heart attack. Nor does it consider that proper cleaning and cooking procedures may reduce the level of some, but not all, contaminants (for example, cooking does not reduce mercury levels in fish tissue).

Finally, the risk assessment model used here does not address other toxicological endpoints. Exposure to chlorinated organic toxicants have been shown to affect visual recognition memory (PCBs),²⁵ motor immaturity and other neonatal endpoints (PCBs),²⁶ duration of breast feeding (DDE),²⁷ and the occurrence of chronic lymphatic leukemia (DDT),²⁸

We propose that a standard, risk assessment based approach be adopted for the development of fish consumption advisories. This approach should be used to project cancer risks and combined with risk management decisions such as acceptable levels of risk and the level of acceptable economic impact, if any. This approach is appropriate until epidemiological data are available to validate current risk assessment models or until improved modeling techniques are adopted that incorporate consideration of all human health impacts as well as pharmacokinetic information, risk associated with exposure to multiple contaminants, and any risk/benefit trade-offs that are associated with consumption of sport fish.

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REFERENCES

- 1. US Environmental Protection Agency: Federal Register 1986; 51:46660.
- US Environmental Protection Agency: Federal Register 1985; 50:110078.
 US Environmental Protection Agency: Federal Register 1986; 51:3392-
- US Environmental Protection Agency: Federal Register 1986; 51:33992-34003.
- US Environmental Protection Agency: Guidance manual for assessing human health risks from chemically contaminated fish and shellfish. (Draft) Washington, DC: EPA, December 1987; 76pp.
- Office of Science and Technology Policy (OSTP): Chemical carcinogens: A review of the science and its associated principles. Federal Register 1985; 50:10371-10442.
- International Agency for Research on Cancer: Basic requirements for long-term assays for carcinogenicity. IARC Monograph Series, Suppl 2. Paris: IARC, 1980.
- Cabral JRP, Hall RK, Rossi L, Bronczyk SA, Shubik P: Effects of long-term intake of DDT on rats. Tumori 1982; 68:11-17.
- Tomatis L, Turusov V, Day N, Charles RT: The effect of long-term exposure to DDT on CF-1 mice. Int J Cancer 1972; 10:489–506.
- Walker AIT, Thorpe E, Stevenson DE: The toxicology of dieldrin. I. Long-term oral toxicity studies in mice. Food Cosmet Toxicol 1972; 11: 415-432.
- Howe RB, Crump KS: Global 82: A computer program to extrapolate quantal animal toxicity data to low doses. Washington, DC: Office of Carcinogen Standards, Occupational Safety and Health Administration, #41USC252C3. 1982.
- US Environmental Protection Agency: Water quality criteria documents; availability. Federal Register 1980; 45:79318-79379.
 Rupp EM, Miller FL, Baes CF: Some results of recent surveys of fish and
- Rupp EM, Miller FL, Baes CF: Some results of recent surveys of fish and shell fish consumption by age and region of US residents. Health Physics 1980; 39:165-175.
- Jones VB, Anderson HA, Hanrahan LP Olson LJ: Fish consumption habits and body levels of chlorinated hydrocarbons in Wisconsin sport fisherman. Abstract. Presented at the International Symposium on Environmental Epidemiology, Pittsburgh, PA 1987.
- Cordle F: The use of epidemiology in the regulation of dioxins in the food supply. Reg Toxicol Pharmacol 1981; 1:370-387.
- Humphrey HEB: Evaluation of humans exposed to water-borne chemicals in the Great Lakes. Washington, DC: US EPA (Report #CR-807192) 1983; 205pp.
- Maronpot RR, Haseman JK, Boorman GA, Eustis SE, Rao GN, Huff JE: Liver lesions in B6C3F1 mice: The National Toxicology Program experience and position. Arch Toxicol, Suppl 1987; 10:10-26.

- Reynolds SH, Stowers SJ, Patterson RM, Maronpot RR, Aaronson SA, Anderson MW: Activated oncogenes in B6C3F1 mouse liver tumors: Implications for risk assessment. Science 1987; 237:1309–1316.
- Tennekes HA, Edler L, Knuz HW: Dose response analysis of the enhancement of liver tumor formation in CF-1 mice by dieldrin. Carcinogenesis 1982; 3:941-945.
- Williams GM, Numoto S: Promotion of mouse liver neoplasms by organochlorine pesticides chlordane and heptachlor in comparison to DDT. Carcinogenesis 1984; 5:1689-1696.
- Kitagawa T, Hino O, Nomura K, Sugano H: Dose-response studies on promoters and anticarcinogenic effects of phenobarbital and DDT in the rat hepatocarcinogenesis. Carcinogenesis 1984; 5:1653–1656.
- Connery J: Report of the EPA workshop on the development of risk assessment methodologies for tumor promoters. Washington, DC: US EPA Report, Office of Research and Development, 1987.
- 22. Thorslund TW, Brown CC, Charnley G: The use of biologically motivated mathematical models to predict the actual cancer risk associated with

environmental exposure to a carcinogen. Risk Analysis 1987; 7:109–119.
23. Menzel DB: Physiological pharmacokinetic modeling. Environ Sci Technol 1987; 21:944–950.

- Clark JM, Fink L, DeVault D: A new approach for the establishment of fish consumption advisories. J Int Assoc Great Lakes Research 1987; 13: 367-374.
- Jacobson SW, Fein GG, Jacobson JJ, Schwartz PM, Dowler JK: The effect of intrauterine PCB exposure on visual recognition memory. Child Devel 1985; 56:853–860.
- Jacobson JL, Jacobson, SW, Schwartz PM, Fein GG, Dowler JK: Prenatal exposure to an environmental toxin: A test of the multiple effects model. Develop Psychol 1984; 20:523-532.
- 27. Rogan W, Gladen B: Duration of breast feeding and environmental contaminants in milk. Am J Epidemiol, Abstracts 1982; 116:565.
- Flodin U, Fredriksson M, Persson B, Axelson O: Chronic lymphatic leukemia and engine exhausts, fresh wood, and DDT: A case-referent study. Br J Indus Med 1988; 45:33–38.

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