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The impact of environmental epidemiology/toxicology and public health practice in the Great Lakes

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The Great Lakes basin comprises one fifth of the total freshwater on the earth's surface; it is a valuable natural resource for both the United States and Canada. Approximately 25% of the Canadian population and 10% of the United States population live within the Great Lakes basin. For more than 200 years, the Great Lakes has been used as a resource for industry, agriculture, shipping, and recreation. The physical nature of the basin and the long retention time of chemicals in the lakes combine to make this huge fresh water resource a repository for chemical by-products of these activities (Hicks, 1996).

In 1985, 11 of the most persistent and widespread toxic substances were identified as "critical Great Lakes pollutants" by the International Joint Commission (IJC). The critical pollutants are: polychlorinated biphenyls (PCBs), dichlorodiphenyl trichloroethane (DDT), dieldrin, toxaphene, mirex, methylmercury, benzo[*a*]pyrene (a member of a class of substances known as polycyclic aromatic hydrocarbons [PAHs]), hexachlorobenzene (HCB), furans, dioxins, and alkylated lead (IJC, 1983). All 11 of the persistent toxic substances (PTSs) tend to bioaccumulate in organisms, biomagnify in the food chain, and persist at elevated levels in some areas of the ecosystem of the Great Lakes. Because of the persistence and ubiquitous presence of the Great Lakes chemicals in the environment, toxic effects in wildlife have been demonstrated and results from early epidemiologic investigations suggest the potential for adverse human health effects, i.e., developmental, neurologic, and immunologic (Fry and Tonne, 1981; Gilbertson, 1986; Jacobson et al., 1990a,b). Given the implications of the association between pollutants in the Great Lakes and the potential for adverse human health outcomes, the U.S. Congress amended the Great Lakes Critical Programs Act in 1990 to investigate this human health concern.

The Agency for Toxic Substances and Disease Registry's (ATSDR) Great Lakes Human Health Effects Research Program (GLHHERP) was initiated in 1992 and is designed to characterize exposure and investigate the potential for short- and long-term adverse health effects from exposure to PTSs via consumption of contaminated Great Lakes fish. This research program focuses on the "eleven critical Great Lakes pollutants" identified by the IJC as well as other chemicals of concern, i.e., cadmium and arsenic in the Great Lakes basin. The program assesses human exposure to these toxic chemicals and associated potential health effects including behavioral, reproductive, developmental, neurologic, endocrinologic, and immunologic end points. Future assessment may examine genetic end points as is warranted by the research findings.

The ATSDR's GLHHERP has identified several human populations who may be at particular risk because of greatest exposure to Great Lakes pollutants via fish consumption. Predisposition to toxic injury in these populations can be due to behavior (e.g., degree of contaminated fish consumption), nutritional status, or physiology (e.g., developing fetuses), and other factors. These communities of concern include subsistence fish anglers, American Indians, pregnant women, fetuses, nursing infants of mothers who consume contaminated Great Lakes sport fish (GLSF), young children, the elderly, the urban poor, and those with compromised immune function (Tryphonas, 1995; Weisglas-Kuperus et al., 1995).

ATSDR's strategy for its GLHHERP is built on the five traditional elements of disease prevention: identification of a pattern of disease or other adverse health effects, evaluation of the causal factors potentially contributing to these patterns of disease and adverse effects, interventions to control or mitigate the causal factors, dissemination of information, and development of an infrastructure (De Rosa and

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Johnson, 1996). This research strategy has been endorsed by the Council of Great Lakes Research Managers and has been adopted by the IJC as a framework for the study of human and ecosystem health in the Great Lakes basin.

ATSDR has awarded 10 research grants to state health departments and academic institutions to study adverse human health effects from consumption of contaminated Great Lakes fish. To strengthen analytical methods and enhance comparability across the health studies, ATSDR has implemented several infrastructure-enhancing strategies. These include harmonization and standardization of questionnaires, analytical protocols, human health end points to be assessed, and identified contaminants to be evaluated across studies. The Agency has also established a quality assurance and quality control (QA/QC) program and a tissue bank (Hicks and Spengler, 1996). This tissue bank may prove to be a key resource as research findings suggest the need for further analysis or as more robust analytical methods become available.

In implementing this research program, ATSDR continues to work with a number of partners in the Great Lakes region, including local and state health departments and academic institutions. In addition, our partnerships include a number of federal, national, and international organizations e.g., the U.S. Environmental Protection Agency, the Centers for Disease Control and Prevention, tribal governments, the IJC, and Health Canada. These partnerships are a key component in leveraging limited resources and extending the impact of research findings (De Rosa et al., 1999a). Perhaps most importantly, from a public health perspective, these partnerships involve working directly with individuals who serve as "gatekeepers" within communities of concern, including health care providers, spiritual leaders, and the general public.

Over the past 4 years, the ATSDR's GLHHERP has made significant progress in reporting and evaluating findings that address public health issues from exposure to contaminants in the basin. One primary reason for this progress is that the program has focused its research efforts on assessing health outcomes in communities of concern by virtue of their intrinsic physiologic sensitivity and/or elevated exposure to toxic chemicals in Great Lakes fish.

Key research findings in the Great Lakes basin have been described for the areas of exposure, sociodemographics, and health effects. (De Rosa et al., 1999b). In the area of exposure, the levels of PTSs in the Great Lakes basin have declined dramatically, particularly from the 1970s and into the 1980s. However, more recent trends are less clear, indicating that the levels of some PTSs have reached a plateau, while others appear to be increasing. One contributing factor to this increase in environmental levels for substances such as PCBs and DDT is atmospheric transport from sources outside the basin (IJC, 1997).

Increased attention to pollution prevention has been an important key in reducing exposure. This success story of pollution prevention has come about through partnerships among regulatory agencies, health agencies, and industry strategically implementing technologies that have reduced emissions into the environment (US EPA, 1997). However, that good news is tempered by the fact that we now recognize that body burdens of key pollutants, such as PCBs, methylmercury, and dioxins, in the general population have been identified at levels that are within an order of magnitude of effect levels determined in experimental settings (DeVito et al., 1995; Johnson et al., 1998). Furthermore, some Great Lakes sport fish still contain levels thought to be potentially harmful to human health, even though two decades of environmental regulation have significantly reduced chemical residues in waters, sediments, fish, and shellfish (US EPA, 1999). Body burden levels in the human population generally parallel these declines in ambient levels of chemical residues (Hovinga et al., 1992; Anderson et al., 1998; Hanrahan et al., 1999).

Other recent exposure findings indicate the following:

- Exposure to PTSs is continuing in communities of concern in the basin (Johnson et al., 1998).
- Body burden levels of some PTSs in at-risk populations are higher than in the general population. Body burdens for some of these contaminants are two to four times higher than those of the general U.S. population (Schantz et al., 1996; Anderson et al., 1998; Falk et al., 1999; Hanrahan et al., 1999).
- Residents in the Great Lakes basin eat more fish than the 6.5g/day often estimated for the U.S. population (Courval et al., 1996; Fitzgerald et al., 1996a,b; Schantz et al., 1996; Falk et al., 1999).
- Men consume more fish than women; men and women eat Great Lakes fish during most of their reproductive years (Courval et al., 1996; Fitzgerald et al., 1996a,b; Lonky et al., 1996; Waller et al., 1996).
- Maternal consumption of Lake Ontario Great Lakes fish increases the risk of prenatal exposure to the most heavily chlorinated PCBs (Stewart et al., 1999).

Certain sociodemographics trends and behaviors have been identified in some of the communities of concern. A recent survey of 8306 residents of the eight Great Lakes states indicated that approximately 4.7 million people consumed GLSF in a given year; 43.9% of the respondents were women (Tilden et al., 1997). Approximately 50% of the respondents who had eaten GLSF were aware of a health advisory for fish, and awareness differed significantly by race, sex, educational attainment, GLSF consumption level, and state of residence. For example, fish advisory awareness was greatest for white men with a college degree, who consumed greater than 24 GLSF meals a year, and who lived in either Wisconsin or Michigan. Tilden et al. (1997) also found to the contrary, that 80% of minorities who had eaten GLSF were unaware of the fish advisory, and awareness was especially low among women.

Fish is an essential component of the diets of African Americans, American Indians and other minority populations, and their choice of fish and cooking practices may increase their exposure to contaminants in fish. These cooking practices include not removing the skin nor the fatty portions of the fish prior to cooking, frying fish and the repeated use of the same cooking oils, and frying fish instead of broiling or grilling (Zabik et al., 1979; Voiland et al., 1991; Anderson et al., 1993). When we examine exposure levels in these populations, we find a significant trend of increasing body burden with increased fish consumption. For example, in the study of local fish consumption and serum PCB concentrations among Mohawk men, multiple regression analysis indicated that total serum PCB levels increased with age ($P<0.001$) and with cumulative lifetime exposure from local fish consumption ($P=0.006$) (Fitzgerald et al., 1999).

Research findings in the area of health effects include the following:

- Conception rate and the incidence of a live birth are lower in some women who are fish consumers (Courval et al., 1996).
- Reproductive function may be disrupted by exposure to PTSs. Significant menstrual cycle reductions were indicated in women who reported consuming more than one meal per month of contaminated GLSF (Mendola et al., 1997).
- Neurobehavioral and developmental deficits have been observed in newborns (12 to 24 h after birth and again 25 to 48 h after birth) of mothers who consumed approximately 2.3 meals per month of contaminated Lake Ontario fish (Lonky et al., 1996).
- The relationship between prenatal exposure to PCBs and performance on the Neonatal Behavioral Assessment Scale (NBAS) was assessed. The results indicated significant relationships between the most highly chlorinated PCBs and performance impairment on the habituation and autonomic tests of the NBAS at 25–48 h after birth. No significant relationship was found between PCBs of lesser chlorination, DDE, hexachlorobenzene, mirex or lead on any NBAS performance test (Stewart et al., 2000). The exposed children are now 3 years of age and initial test results for memory, verbal, and perceptual performance indicate their score is lower than children from mothers who consumed low amounts or no fish (Stewart et al., 1998).
- Self-reported liver disease, diabetes, and muscle/joint pain may be associated with exposure to PCBs and other contaminants via fish consumption (Dellinger et al., 1997).

These research findings in the areas of exposure, sociodemographics, and health effects are of public health concern (Johnson and De Rosa, 1999). The communities of concern identified in our program are at risk because of elevated exposures as well as possibly intrinsic physiologic sensitivity. For example, the developing fetus is highly sensitive to the effects of these chemicals during certain "windows" of development (Guzelian et al., 1992). Nursing infants, subsistence and sport anglers, as well as the elderly, are among these at-risk groups because of their elevated exposures (Yakushiji et al., 1984; Schantz et al., 1996; Patandin et al., 1997; Falk et al., 1999). It is further recognized that the body burdens of some fisheaters are two to four times higher than in the general population and that nursing infants may experience exposure rates anywhere from 10 to 40 times that of the general population (WHO, 1989).

The reports of neurodevelopmental deficits and reproductive effects are especially compelling. The observed neurodevelopmental effects are subtle, but they can have profound implications for the affected populations, particularly for those individuals that make up the tails of the distribution curve of a measure of functional capacity like IQ (Schantz, 1996; Johnson et al., 1998). These are deficits that once incurred, unlike budget deficits, cannot be repaid. A roundtable discussion at the Montreal Health Conference '97 on the "Public Health Implications of Neurobehavioral Effects" specifically addressed the current human research in this area (De Rosa et al., 1999c). The results of studies on five human cohorts (Dutch, Michigan, North Carolina, Oswego, NY, and Yu-Cheng [Taiwan]) exposed to PTSs in utero, including PCBs and dioxins, were discussed. The limitations of these studies and the role of mercury as a possible confounder also were discussed. The majority opinion on the panel was that the weight of evidence supports PCBs (or more specifically a set of PCB congeners) as the agents responsible for neurodevelopmental effects in four studies and dioxins in the Dutch cohort. The weight of evidence from all five cohorts provides a coherent epidemiologic picture of neurodevelopmental effects related to PCBs/dioxins.

There is a difference in opinion regarding the implications of these findings from epidemiologic studies because of variations in experimental design, methodologies, and reported results. Yet there are remarkable parallels in some of the reported findings, and these findings transcend both geographic and phyletic boundaries (Johnson et al., 1999).

Responsible and prudent public health practice cannot wait for irrefutable scientific evidence to amass before preventive measures are taken. The public health community must be willing to assemble the evidence — in this case the data from laboratory experiments, wildlife studies, and epidemiologic investigations — and act on this weight of evidence by initiating efforts that put "the science into service." Efforts should now focus on ecological and human health programs (such as environmental restoration and public health intervention programs). In addition, there is a need to improve the effectiveness of fish consumption advisories for those individuals who are most at risk, e.g., pregnant women. Finally, there is a need to develop strategies for prudent public health interventions and new risk communication tools that are intended to reduce human exposures.

The research findings from the ATSDR GLHHERP have led to a number of success stories by using different public health strategies, e.g., regulatory and community-based. For example, recent health findings were instrumental in the implementation of a Uniform Great Lakes Sport Fish Advisory used by all eight Great Lakes states as well as other states. In another example involving American Indians, 97% of the men knew about fish advisories against consuming local fish prior to the study; however, 80% of the men ate local fish during the last 2 years before participating in the ATSDR study. To make the study populations aware of the hazards of consuming contaminated fish, ATSDR used various risk communication strategies, including organizing health fairs and public meetings, holding press conferences with tribal reporters, and providing information on cooking practices to reduce exposures; this information was then published in tribal newspapers and other printed media. Involving tribal representatives in the planning and implementation of the study was a key element in structuring the study, recruiting participants, and strengthening the research design (Hicks et al., 1996). During the first year of the study, the men reduced their consumption rate from an average of 98 meals per year to 28, and even lower during the second year. The serum PCB levels in men were significantly related to the number of local fish meals consumed per year. Therefore, a reduction in consumption led to lower PCB serum levels (Fitzgerald et al., 1996b, 1999). A similar trend was also found in the women of this group (Fitzgerald et al., 1996a, 1998).

With respect to the future, the time has come to promote the need for a strong surveillance system merged with an effective environmental contamination monitoring program. Research must also continue. The ATSDR's GLHHERP has documented exposure to a number of PTSs in communities of concern and have found body burden levels two to four times higher than the general U.S. population. Health intervention and education and risk communication strategies have been initiated in these communities of concern. Our health findings also indicate that in addition to assessing overt signs of toxicity, there is a need to assess subtle forms of toxicity (e.g., impaired cognitive performance from prenatal exposure to PCBs) observed only at the levels of populations as opposed to individuals. Much remains to be learned about adverse neurodevelopmental and reproductive health effects as well as other adverse health effects from exposure to PTSs. Despite these findings, we must still consider the health benefits gained from fish consumption while also evaluating the potential health implications. Fish provide a diet high in protein and low in saturated fats, and some studies suggest that eating fish each week is helpful in preventing heart disease (Albert et al., 1998). These counterbalancing risks and benefits pose a significant challenge in the development of health education and risk communication. Despite these challenges, pollution prevention strategies remain the key to reducing toxic chemical exposures.

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