

A Fishy Paradox

Fish and shellfish contain high amounts of protein, nutrients, and omega-3 fatty acids which are important for heart health and neurological development. Because of this, expectant mothers, mothers who are breastfeeding and young children are generally encouraged to include fish in their diets. However, all fish also contain the neurotoxicant methylmercury (MeHg) and some fish contain higher levels than others, so there is some concern that consuming fish could also have adverse health effects from MeHg. Since these adverse effects are presumed to be more likely to occur prenatally, the United States Food and Drug Administration (USFDA) and Environmental Protection Agency (EPA) recommend that women of childbearing age and young children avoid fish that are typically higher in MeHg.

This apparently conflicting advice - that fish is important for health but that chemicals in fish could pose health risks - could be confusing to those trying to choose how much and what kinds of fish are safe to eat. Ongoing research aims to understand both the benefits of fish consumption and the potential health risks of MeHg. Research on the adverse effects of MeHg exposure started with case studies in Minamata and Niigata, Japan and in Iraq where populations inadvertently consumed food contaminated by high levels of MeHg. These studies demonstrated that very high dosages of MeHg can cause neurological impairment, and that prenatal exposures posed the greatest risks. The exposures that occurred in Japan and Iraq were very high - much higher than might occur from consuming even large quantities of typical ocean fish. Many of the subsequent studies addressing the effects of low-level, long-term pre-natal exposures, such as those that might occur in people who consume large amounts of ocean fish, have been inconclusive. Little research has been done on post-natal exposure. Thus, despite decades of study, many uncertainties remain about the benefits and risks posed by fish consumption.

A team of researchers from the University of Rochester Medical Center has been conducting a longterm study in the Republic of Seychelles, an Indian Ocean nation, to determine whether exposure to MeHg from high fish consumption has adverse consequences for child development. The Seychelles Islands were selected primarily because fish consumption is very high and many factors that typically complicate epidemiological studies



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are minimal (health care and education are free and readily available, malnutrition is nonexistent, and there are no other toxicant exposures). Mothers enrolled in the study consume about 10 times more fish than the average American. The area is also westernized but largely undeveloped, so little to no industrial pollution is introduced to the local food chain. These factors allow researchers to study developmental effects at naturally-occurring levels of mercury. The study



Photo courtesy of Dr. Philip Davidson

started in the mid 1980s under the direction of Dr. Thomas W. Clarkson in the Department of Environmental Medicine. Following Dr. Clarkson's retirement, the study has continued under the leadership of Dr. Philip W. Davidson of the Department of Pediatrics and Dr. Gary J. Myers of the Department of Neurology. This study includes researchers from the University of Rochester, The University of Ulster in Northern Ireland, and the Republic of Seychelles. The study is funded by several National Institutes of Health grants and in-kind contributions from the Republic of Seychelles.

The Seychelles Child Development Study (SCDS) began with the goal of examining the impact of low-level pre-natal exposure to MeHg on developing brains. Since then, the study has evolved to include several cohorts and to examine many facets of MeHg exposure, including the potential effects of post-natal exposures.



Photo courtesy of Dr. Philip Davidson

Results to date support past findings that consuming fish is beneficial to health, but that MeHg may reduce this benefit. The question that still eludes scientists is at what particular dose, and in which situations, does MeHg pose a health threat? Complicating this question is the fact that not all species acquire contaminants the same way, and that chemicals and concentrations vary geographically.

So what is one to do? The relative benefits and risks of fish consumption are still unclear. Current information suggests that if there are adverse health effects from MeHg in fish that women of childbearing age and young children are at highest risk. However, it also suggests that limiting fish consumption

may prevent them and their unborn children from getting nutrients that are important for human health and brain development. Until more answers are available, it is probably wise to consume species of fish that are high in fish oils, and if young or pregnant to avoid large predatory fish that are generally higher in MeHg.

The FDA and EPA jointly publish information about MeHg and how to choose safer fish: http://www.epa.gov/waterscience/fish/advice/index.html

For more information on the Seychelles Child Development Study, visit: http://www.urmc.rochester.edu/pediatrics/research/Seychelles/

Chemical Contaminants in Lake Ontario Fish

Although freshwater lake fish can contain mercury, these tend to also contain organic chemicals that are known to pose risks to human health. For example, New York State Department of Health (DOH) advises that women of childbearing age and children under the age of 15 should not eat fish from Lake Ontario and connecting waters because of high levels of PCBs, dioxins and mirex. The state also recommends that others limit consumption of most species of locally-caught fish to one 8 oz. meal per week. Although the advisories are widely available in print and electronic form (in English), anecdotal evidence and surveys conducted in other communities indicated that people may still be consuming excessive amounts of contaminated fish.

What's in my fish?

Locally caught fish can provide a cheap source of protein and is culturally important for many communities. Most people know that fish promotes neurological development and improves heart health, but they also need to understand that some fish contain harmful chemicals that pose serious health risks to fetuses, babies, and children. The primary chemicals of concern in Lake Ontario fish are PCBs, mirex and dioxin.



Visit the EPA website to learn more about contaminants found in local fish: http://www.health.state.ny.us/environmental/outdoors/fish/fish.htm



A local angler and her daughter catch perch in the Genesee River, Charlotte. *Photo courtesy of Richard Baker*

The EHSC Community Outreach and Education Core (COEC) developed and conducted a rapid assessment this past summer to determine whether the community is aware of and understands the published advice. In total, 301 general community members were surveyed and 73 anglers were interviewed about their fishing and fish consumption habits. About 70% of all anglers interviewed said they had seen or heard of consumption advisories, yet only about 15% were able to correctly answer a short list of True or False questions related to the published advice.

The results of this rapid assessment suggest that many anglers either do not understand, believe in, or know of the advisories. We also found different consumption patterns among ethnic groups in Rochester. We plan to share these results with our community partners and get their input on how best to inform consumers about the health risks of eating local fish, and suggest strategies to reduce these health risks such as carefully selecting species, and filleting or grilling the fish to reduce organic chemicals.

Environmental Health Research Receives ARRA Boost



As of November, 113 projects at the University of Rochester have received American Reinvestment and Recovery Act (ARRA) funding, including 18 projects in the EHSC (totaling over \$6 million in funding for center research). Two EHSC awards are for researching the impact of developmental exposure to the plasticizer bisphenol A (BPA).



Dr. Paige Lawrence's (top left) study, "Developmental toxicity of bisphenol A and immune-mediated diseases," aims to provide the most detailed analysis to date of the impact of BPA on immune system development. She will test whether developmental BPA exposure increases susceptibility to influenza A, asthma and inflammatory bowel disease later in life. Drs. Lawrence Saubermann and Steve Georas are co-investigators for this study. Drs. Shanna Swan (middle left) and Bernie Weiss (bottom left) are researching "Prenatal bisphenol A and sexually dimorphic neurodevelopment." This project will provide unique information on how exposure to BPA before birth can alter masculinization and feminization of the brain during prenatal development. Later-life studies may show persistent effects. The research is being conducted in children and in a corresponding rat model. Drs. Troy Zarcone, Sander Stern and Heather Patusaul (North Carolina State) are co-investigators.



Other EHSC faculty members who received ARRA funding are (left to right) Drs: Phil Davidson, Alison Elder, Mark Frampton, Karl Kieburtz, Dina Markowitz (two ARRA awards), Margot Mayer-Pröschel, Kerry O'Banion, Richard Phipps, Gloria Pryhuber, Edward Puzas, Randy Rosier, Patricia Sime (three ARRA awards), and Kim Tieu.



The American Reinvestment and Recovery Act of 2009 was enacted to support short-term scientific research to stimulate the economy, create jobs, and open doors for a wide array of future research. The National Institute of Environmental Health Sciences (NIEHS) granted \$10 million in ARRA funding for Research and Research Infrastructure "Grand Opportunities" grants, prioritizing research on Engineered Nanomaterial Safety and Bisphenol A.



EHSC Publication Awarded "2009 Paper of the Year"

"Decrease in Anogenital Distance among Male Infants with Prenatal Phthalate Exposure", authored in 2005 by The Study for Future Families Research Team led by Dr. Shanna Swan, was awarded *Environmental Health Perspectives*' (EHP) 2009 Paper of the Year for its significance in research and political impact. The team was the first to demonstrate a link between prenatal exposure to phthalates (found in several common household items) and decreased anogenital distance (an indicator of masculinization) in human males. The team used a process translated from a standard animal exam to humans.

Since publication in 2005, the study has been replicated by Dr. Swan and incorporated into various ongoing research programs such as the National Children's Study. The paper has also been cited in support of legislation or mentioned in 15 U.S. states, been used in congressional hearings, and has influenced national phthalate legislation (the Consumer Product Safety Improvement Act of 2008).

New Funding to Understand the Involvement of Circadian Rhythm in COPD

Dr. Irfan Rahman, associate professor in Environmental Medicine, has been awarded NIH R01 funding from the US Department of Health and Human Services to study the cellular and molecular mechanisms of peripheral (not associated with the central nervous system) lung functions that are coupled with the body's 24-hour circadian rhythm. Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of chronic illness and death in the United States. As COPD progresses, patients develop more frequent and severe symptoms, and have an increased rate of emergency room visits and hospitalizations. Increased events occur particularly in the night time and early hours; this time of day is when lung function is lowest, and treatments such as steroids and bronchodilators are least effective. Patients with COPD have abnormal circadian rhythm, reflected in daily changes in the size of the airway and respiratory symptoms.

With support from this funding, Dr. Rahman aims to identify a new target for treatment of COPD that works in phase with the patient's biological clock (chronotherapy) that will "cue the lung clock" so that treatments for COPD will work more effectively. This unique funding opportunity will support research to understand the role of the biological clock in physiological lung changes in patients with COPD. This research is supported through collaboration with the Department of Environmental Medicine (Dr. Troy Zarcone, Dr. Paige Lawrence) and Pulmonary Unit (Dr. Patricia Sime) of the University of Rochester via the R01 grant. Preliminary data for this research was gathered by Dr. Rahman, with assistance from fellows Dr. Hongwei Yao and Dr. Sangwoon Chung.

The Infant Development and Environment Study

A team of researchers led by Dr. Shanna Swan received funding to conduct a multicenter pregnancy cohort study to look at the relationships between concentrations of urinary phthalate metabolites and genital development in the first year of life. The team has applied for supplemental funding to examine BPA and to include females in post-natal follow-up.

Summer Undergraduate Student Received Poster and Presentation Awards

Ms. Brittany Black (Xavier University, Cincinnati), a student in the Summer Undergraduate Research Fellowship (SURF) exchange program with the University of Rochester Department of Environmental Medicine, won the SURF prize for best poster and ranked in the top 3 for oral presentations. Brittany did her research in the laboratory of Dr. Irfan Rahman, examining the process by which cigarette smoke results in Chronic Obstructive Pulmonary Disease (COPD).

Brittany's work is supported by co-authors David Adenuga and Samuel Caito. The awards are an outstanding achievement for Ms. Black and highlight the significant role Dr. Irfan Rahman's lab has played



Left to right: David Adenuga, Brittany Black, Dr. Irfan Rahman

the significant role Dr. Irfan Rahman's lab has played in nurturing future scientists at the Department of Environmental Medicine, Lung Biology & Disease Program.

The World Health Organization (WHO) predicts that COPD will be the third leading cause of mortality worldwide by 2030, and 75 – 80% of COPD-related mortalities in the US are directly linked to cigarette smoking. Brittany found that cigarette smoke-induced oxidative stress results in the movement of the proteins Re1A and p65 into the nucleus and causes epigenetic modifications, leading to the release of the cytokine IL-8 (which induces inflammation) in normal lung cells. Knowing the biological pathways that are activated as a result of cigarette smoking and are known to result in COPD is one of the first steps in designing drugs to prevent COPD.

Selected Recent EHSC Publications

Adibi, J.J., R. Hauser, P.L. Williams, R.M. Whyatt, A.M. Calafat, H. Nelson, R. Herrick, S.H. Swan. 2009. Maternal urinary metabolites of di-(2-ethylhexyl) phthalate in relation to the timing of labor in a U.S. multi-center pregnancy cohort. In press, *American Journal of Epidemiology* 169(8): 1015-1024.

Gollenberg, A.L., F. Liu, C. Brazil, E.Z. Drobnis, D. Guzick, J.W. Overstreet, J.B. Redmon, A. Sparks, C. Wang, S.H. Swan. 2009. Semen quality in fertile men in relation to psychosocial stress. In press, *Fertility and Sterility*.



Zarcone, T.J., R. Chen, and S.C. Fowler. 2009. Effects of differing response-force requirements on food-maintained responding in C57BL/6J mice. *Journal of the Experimental Analysis of Behavior* 92(2): 257-274.

Swan, S.H., F. Liu, M. Hines, R.L. Kruse, C. Wang, J.B. Redmon, A. Sparks, and B. Weiss. 2009. Prenatal phthalate exposure and reduced masculine play in boys. *International Journal of Andrology* 32: 1-9.

If you have questions or comments about this newsletter, please contact Valerie George@urmc.rochester.edu