Bisphenol A, EHSC Research, and the Rochester community

Bisphenol-A (BPA) is an organic chemical used in polycarbonate plastics (such as the hard plastics used to make water bottles and CDs), epoxy resins (including the linings of metal food cans), and the thermal paper used for many sales receipts, among other products. Because BPA is produced in large quantities and used in so many consumer products, it is not surprising that population studies have found BPA in most people’s bodies. It remains unclear, however, whether typical levels of BPA exposure cause health problems or not.

In 2009, the National Toxicology Program (a collaboration between NIEHS (NIH), NIOSH (CDC), and NCTR (FDA)) developed an integrated research program funded through the American Reinvestment and Recovery Act (ARRA) to focus on some of the unanswered questions about BPA. We highlighted two EHSC projects funded through ARRA in the Fall 2009 Issue of Your Health & the Environment. This issue summarizes ARRA-funded BPA research progress from the Lawrence and Weiss labs.

...Continued on page 2
Bisphenol A, EHSC Research, and the Rochester community, continued...

Dr. Paige Lawrence recently published results from her ARRA-funded study, “Developmental toxicity of Bisphenol A and immune-mediated diseases.” The Lawrence lab used a mouse model to study whether a mother’s exposure to BPA while pregnant can cause allergic asthma to be worse for her baby. Previous studies found that rates of asthma in people who work in industries using BPA have increased asthma and other allergic symptoms. However these studies did not identify that BPA is the cause. Other studies have found conflicting results about the effect of BPA on the immune system, but some used high doses while others only studied one cell type. Immune systems are very complex and have many different types of cells. Dr. Lawrence therefore believed it was important to study system-wide effects using a mouse model. To do this, Dr. Lawrence’s lab fed pregnant mice low doses of BPA (similar to typical human exposures). The study revealed no or minimal effects on the offspring’s immune system. Findings from this study specific to asthma showed that although there were small differences on the molecular level, there was nothing significantly different in airway constriction (indicating asthma) between control and experimental mice offspring.

Recent BPA Publications from EHSC


In another study, Dr. Bernard Weiss collaborated with principal investigator Dr. Shanna Swan (now at Mount Sinai School of Medicine) on a project entitled “Prenatal Bisphenol A and Sexually Dimorphic Neurodevelopment.” This study used both an animal model and human population data to look at the reproductive and nervous system effects of BPA. Dr. Weiss assessed the effect of developmental BPA...Continued on page 3
Bisphenol A, EHSC Research, and the Rochester community, continued...

exposure on rats. He used a wide range of doses since endocrine disruptors (such as BPA) may show different effects at varying doses. Initial (unpublished) results suggest that BPA led to weight gain in the rats, but only at smaller doses. Similarly, BPA seemed only to cause certain groups of the female rats to gain weight; others had no change or actually weighed less compared to control groups. Preliminary results from Dr. Swan’s component of the study correlates BPA exposures with aspects of offspring behavior. For this assessment, Dr. Swan used human behavior study results and urine samples collected from a prior study. Results from their work are still being analyzed.

Dr. Lawrence presented a summary of her results to the EHSC’s Community Advisory Board in May 2013. This presentation sparked a lively conversation about the scientific, policy, and personal implications of research on the health effects of BPA. CAB members remarked on how Dr. Lawrence’s study helped them understand the complexities of research on the effects of this chemical, and how negative study findings can lead to new ideas for further research. The group discussed different policy approaches in Europe and the U.S., and the particular challenge of how to remove BPA from products without replacing it with a new potentially hazardous chemical. At the level of personal action, the CAB discussed recommendations for citizen, government, and health groups about how to minimize one’s exposure to BPA from consumer products (see, for example, the NIEHS BPA fact sheet). The meeting concluded with a discussion of how to improve communication within our local community to help groups and individuals make decisions about consumer products, policy strategies, or information campaigns in situations with significant scientific uncertainties.

EHSC Research Summaries

The COEC now offers brief summaries of EHSC research publications. New center publications will be summarized and posted to the COEC News and Publications page. The first summary in this new series is of Dr. Lawrence’s 2012 paper “The effects of maternal exposure to bisphenol A on allergic inflammation into adulthood.”
Iron Deficiency & Lead Exposure Target Similar Populations

Iron, an essential metal for early brain development, is one of the most abundant metals on earth, yet iron deficiency (ID) is estimated to affect at least 30% of pregnancies in developed countries [1, 2]. Studies in offspring of iron deficient humans and animals have shown decreases in neuron myelination (the insulation for electrical signals traveling in the brain), learning/memory problems and behavioral abnormalities [2, 3]. ID is more common in low-income pregnant women and children due to lack of access to proper nutrition. These populations are also vulnerable to other environmental toxicants that can influence development, most notably lead (Pb^{2+}). Studies of lead exposure during development have produced similar results as ID in behavior, as well as in learning and memory [4, 5]. Since both ID and lead exposure occur in similar populations and affect the body in similar ways, the possibility that ID and lead combined cause even greater health problems is of great concern. The interaction of nutritional deficiencies and heavy metals is not a new concept, but little research has been done on their combined effects during early brain development [6]. In addition, most studies in children focus on the postnatal period, as opposed to the prenatal period (during pregnancy) when the developing brain is most sensitive. Thus, there is still a significant gap in knowledge of how these two factors (ID, and lead exposure) affect early brain development.

Insights from an Animal Study of ID & Lead Exposure

The Mayer-Pröschel lab conducted an experiment in which they fed one group of pregnant female rats a control diet (normal iron) and another group an iron-deficient diet. Half of the females in each group were also given water containing lead (Pb^{2+}). They found that pregnant rats that were exposed to lead and fed an iron-deficient diet had significantly higher blood and bone lead levels compared to pregnant rats that were exposed to lead and fed an iron-normal control diet. Maternal bone is a critical source of lead exposure for the developing fetus, so higher lead levels in the mother are likely to result in higher lead levels in the offspring.

...Continued on page 5
Iron Deficiency and Lead, continued…

The researchers were interested in studying ID and lead exposure after birth as well, because lifetime exposure is most relevant to at-risk human populations. Therefore, offspring were given the same food and water as their mothers after weaning. The researchers saw the same pattern in the offspring – offspring who were iron deficient and exposed to lead had significantly increased lead levels in their blood and bone compared to lead-exposed offspring fed an iron-normal (control) diet.

Offspring also displayed significantly increased lead levels in parts of the brain - including the hippocampus, which is responsible for learning and memory, and in the prefrontal cortex, which has been associated with planning complex cognitive behaviors. The lab is currently conducting studies in the offspring to determine the behavioral consequences of combined lead exposure and ID in tasks requiring the proper functioning of these brain regions.

Other studies in iron-deficient or lead-exposed children have demonstrated significant decreases in the speed with which auditory signals can travel from the ear to the brain. Auditory signal processing speed is a useful tool often used to diagnose problems with speech perception and language learning in children. To track this effect in their experiment, the lab used a sensitive technique to measure auditory function in the rats’ offspring. Sounds traveled from the ear to the brain significantly slower in adult offspring of females exposed to ID and/or lead compared to offspring of non-lead-exposed females fed an iron-normal diet.

Taken together, these findings underscore the importance of maternal iron levels during pregnancy, particularly for women and children who may also be exposed to lead. Future studies in the lab will continue to measure the impact that lead and ID have on the brain, as well as exploring possible windows of vulnerability during early brain development.

Citations

Center Updates

Healthy Waterways HIA

The EHSC Community Outreach and Engagement Core (COEC) recently completed the first full health impact assessment (HIA) in New York State. HIA is a policy and planning tool that provides decision-makers in non-health related sectors with information about how their proposed plans and policies will likely impact the health of the communities they serve. HIAs assess potential health impacts by studying the effects of proposed plans or policies on “health determinants.” Health determinants are characteristics of the built and social environments where we live, work and play that can influence our health. Non-health policies can often have profound, yet unintended, impacts on health determinants. HIA practitioners use this assessment tool to identify and characterize these impacts, both positive and negative, before decisions are made. HIAs also make recommendations for decision makers that help maximize health benefits of decisions and minimize potential negative impacts. The overall goal of HIA is to ensure that health is considered when all kinds of public decisions are made.

The Healthy Waterways HIA looked at potential health implications of the City of Rochester, NY's Local Waterfront Revitalization Program (LWRP) update. The LWRP is part of the New York State Division of Coastal Resource’s (NYSDCR) statewide coastal management program. These long-term plans guide city, private, and state/federal decisions affecting waterways.

Changes in the waterfront may affect the health of people who live nearby, those who use the waterfront, and the general population in different ways. Healthy Waterways assessed impacts on all three groups, with an emphasis on those whose health is most likely to be affected by changes along the waterfront. These included children, older adults, low-income, and minority residents of waterfront neighborhoods.

Healthy Waterways assessed four health determinants: physical activity, water quality, health-supportive resources, and physical safety. These were identified as likely to impact many of the key health outcomes of local concern: obesity, diabetes, heart...Continued on page 7
Healthy Waterways HIA, continued…

disease, injury and death, respiratory health, mental health and water-borne illness. The study team integrated literature reviews with new and existing data collection and stakeholder interviews to assess potential health impacts.

The Healthy Waterways project team drafted recommendations to protect health through policy, program/project, communication and monitoring based on their assessment findings. The report also covers a set of broad, overarching recommendations for the LWRP and for the adoption of “Health in all Policies” by the City of Rochester. Overarching recommendations for the LWRP included a suggestion to emphasize Rochester’s waterfront as “a healthy place to live, work, and play.” The study team also recommended adding a statement to the LWRP Waterfront Goals that emphasizes the importance of promoting the “health and safety of waterfront neighborhood residents and the population of the greater Rochester area.” Other recommendations included increased waterfront access for the public, improved communication about waterfront services and amenities, and ongoing monitoring of waterfront community health and use of waterfront resources.

Healthy Waterways was the first full HIA conducted in New York State and may provide a model for incorporating HIA in the LWRP process in other areas, or in other kinds of local decisions. The Healthy Waterways report provides information and recommendations to help decision makers and stakeholders understand how to maximize the positive health impacts of water resource related decisions, while minimizing negative effects on the health of Rochester’s communities. Visit the project website to read more about the Healthy Waterways HIA and read the report.

Healthy Waterways was supported through a grant from the Health Impact Project - a collaboration of the Robert Wood Johnson Foundation and The Pew Charitable Trusts. The opinions expressed here do not necessarily reflect the views of the Health Impact Project, the Robert Wood Johnson Foundation, or The Pew Charitable Trusts. The authors are solely responsible for this content.
Talking About Talking About Obesogens

Dr. Bruce Blumberg (University of California, Irvine) visited the University of Rochester Medical Center in October 2012 to discuss his work on environmental obesogens. During his visit, the EHSC COEC arranged a meeting with Dr. Blumberg and representatives from the Breast Cancer Coalition of Rochester, Greater Rochester Health Foundation, and Finger Lakes Health Systems Agency who are leaders in local healthy living and obesity prevention efforts. The goal of this conversation was to discuss appropriate outreach strategies for protecting the public from exposure to these chemicals.

Environmental obesogens are endocrine disrupting chemicals that affect the body’s metabolism. For instance, a person exposed to endocrine disruptors may produce more fat cells and store more fat than a person who was not exposed to environmental obesogens during development. The effects of obesogens are permanent. Because of this, diet and exercise interventions for weight loss can be more challenging. Understanding the effects of these chemicals on obesity is especially important in the US, where obesity rates and associated health effects are a major public health concern. According to Dr. Blumberg, there are about 20 known obesogens, including BPA. While it is clear that these chemicals do have an impact on body weight, it is unclear how much obesogens contribute to the obesity epidemic compared to other factors.

Dr. Blumberg’s research focuses on the endocrine disrupting properties of tributyltin (TBT). His work has demonstrated that TBT, when fed to pregnant mice, leads to increased development of fat cells in their offspring. The Blumberg lab also found that this change appears to be permanent for the exposed mice and heritable, lasting at least two generations. They identified two genes that increase fat cell development after TBT exposure. The lab has also identified about 12 more endocrine-disrupting chemicals that appear to have the same effect. Many are fungicides (used primarily in agriculture on fruits and vegetables).

...Continued on page 9
Center Updates

Obesogens, continued…

Dr. Blumberg’s meeting with community leaders focused on the complications of translating research findings on obesogens into public health messages and on developing appropriate messaging for different audiences. For example, those working to promote healthy weight at the community level may find it most effective to continue to work with community members to promote healthy lifestyle interventions, with the understanding that those affected by obesogens may have more challenges in maintaining healthy weight. Those working with mothers to encourage healthy pregnancies can also emphasize reducing exposure to environmental chemicals by cooking fresh or frozen foods and avoiding the use of plastic as much as possible. Researchers and advocates could be encouraged to explore policy tools to reduce exposure to obesogens. Dr. Blumberg emphasized the importance of involving parents in efforts to translate research findings to offer politicians a personal view of obesogen exposures and impacts.

“Aging and Vulnerability to Environmental Chemicals: Age-related Disorders and their Origins in Environmental Exposures”

A recent book, edited by Dr. Bernard Weiss, Professor of Environmental Medicine, highlights the role of exposures to environmental chemicals in speeding the onset of age-related disorders and altering their expression. This volume is designed to guide decision makers in protecting the public from chemical exposures that can alter the aging process. In addition to reviewing existing knowledge about how environmental chemicals influence aging, the book also outlines opportunities for research to better understand chemical effects on aging. This comprehensive overview includes a chapter co-authored by Center member Dr. Edward Puzas, and discusses the potential effects of environmental exposures to BPA, ambient air pollution, heavy metals, persistent organic pollutants (POPs), and polychlorinated biphenyls (PCBs). Health outcomes discussed include age-related disorders such as cognitive dysfunction, Parkinson’s, cardiovascular disease, breast and prostate cancers, kidney and liver diseases, and immune system disorders. More information about “Aging and Vulnerability to Environmental Chemicals: Age-related Disorders and their Origins in Environmental Exposures” can be found online at http://pubs.rsc.org/en/content/ebook/978-1-84973-418-9#!divbookcontent.
Center Updates

EHSC faculty member Dr. Paige Lawrence received the 2012 URMC School of Medicine and Dentistry Mentoring Award

In recognition of the importance of faculty serving as mentors for their junior colleagues, the URMC School of Medicine and Dentistry honors three to four faculty mentors annually. Dr. Paige Lawrence, Professor of Environmental Medicine and Microbiology and Immunology, received the 2012 URMC School of Medicine and Dentistry Mentoring Award for mentoring trainees in basic science. Mentors are highly knowledgeable, well-respected members of their field who commit time and energy to motivate and guide junior investigators in their professional goals. The Spring 2013 Mentoring Conference featured a presentation and panel from award recipients who shared their experiences with research and mentoring. Dr. Yousef Khalifa (Department of Ophthalmology), Dr. Robert A. Bambara (Department of Microbiology and Immunology), and Dr. Jonathan Friedburg (Department of Medicine, Hematology/Oncology) were the other 2012 recipients.

New Directions for EHSC Researcher Dr. Richard Phipps

Dr. Richard Phipps received four new funding awards spanning the next five years. One project, funded by NIH/NICD, aims to develop an understanding of the vulvodynia pain mechanism. An NIH/NAID award will fund research to develop new safe substances that enhance antibody production. Funding through NIH/NEI will allow the Phipps lab to study anti-scarring agents in the ocular orbit. Lastly, an NIH/NIEHS funded project will investigate the molecular mechanisms by which obesogens drive fat cell development.

URMC Faculty Recognized for Environmental Health Research

Dr. Hongwei Yao, a Research Assistant Professor in the Department of Environmental Medicine, was chosen by the American Lung Association (ALA) as a recipient of the Biomedical Research Grant award. The ALA offers these funding awards to junior investigators researching the mechanisms of lung disease and general lung biology. Dr. Yao’s work aims to understand how environmental and epigenetic factors interact to cause lung damage. His future research interests include oxidative stress-induced inflammation and injury. This biomedical research grant will fund a new study to investigate how Sirtuin1, an anti-aging protein, regulates the gradual depletion of telomeres as lung cells age. Telomeres protect genetic information during cell division, but gradually break down over time as cells divide. The interaction of Sirtuin 1 with this process may have implications for Chronic Obstructive Pulmonary Disease in aging adults.
Student Awards

Several students and postdoctoral fellows associated with the EHSC were presented with awards this spring:

* Joshua Allen received the Robert N. Infurna Award for Best Scientific Publication by a graduate student and is the Student Representative for the 2012-2013 Society of Toxicology (SOT) Communications Committee
* Brittany Baisch was awarded 2nd place for multi-cellular/organismal category at the Graduate Student Society poster session, April 2013
* Eric Beier achieved 1st place for the Stem Cell Specialty Section Student Award
* Amanda Croasdell received the MacGregor Award for Best Poster at the annual Toxicology Retreat this year, and was offered a PhRMA Foundation Predoctoral Fellowship in Pharmacology/Toxicology
* Daniel P. Dever received the William F. Neuman Award for Exemplary Scholarship and Citizenship
* Bethany Winans was awarded the 1st place Graduate Student Poster Award in the SOT Reproductive and Developmental Toxicology Specialty Section
* David McMillan won the Harold C. Hodge award for especially meritorious research
* Emily Kelly was awarded Best Presentation at the May 2013 Toxicology Training Program Retreat
* Lisa Prince was awarded Best Poster by a 1st Year at the Toxicology Retreat
* Sesquile Ramon was awarded first place for his Genetics Day poster
* Anirban Roy received the Robert N. Infurna Award for Best Scientific Publication by a postdoctoral fellow.
* Allison Greminger, Bethany Winans, Daniel Dever, and Sadie Gorman received Society of Toxicology Travel Awards
* Christiaan King received an American Society of Gene and Cell Therapy Travel Award
* Sage Begolly received a Scholars-in-Training (SIT) Travel Award to the Radiation Research Society Annual Meeting
* Katie Lannan received a Graduate Women in Science travel award from the University of Rochester.
* Amanda Croasdell, His-Min (Jim) Hsiao, and Katie Lannan were accepted into the summer 2013 NIH Clinical and Translational Research Course for PhD students.
Welcome new Center Members

New Toxicology Training Students:

* Tyler Beach
  (SUNY College of Environmental Science Forestry, Roberts Wesleyan College; Tyler has also been a science teacher at Greece Athena High School since 2001).

* Denise Herr
  (Duquesne University)

* Brian Palmer
  (St. Lawrence University)

* Christina Post
  (University of Massachusetts, Boston)

New EHSC Faculty:

Dr. Emily Barrett, Assistant Professor of Obstetrics and Gynecology, received her PhD in Biological Anthropology from Harvard University, where she studied how ecological factors affect the female reproductive system. Her current research builds on this, looking at how exposure to stress and endocrine disruptors (particularly phthalates) affect the reproductive health of pregnant women and their children. Dr. Barrett is currently the Director for NIH-funded The Infant Development and the Environment Study (TIDES) as well as a scholar in URMC’s K-12 Women’s Health and the Environment over the Entire Lifespan (WHEEL) program. She looks forward to collaborating with Center researchers on projects related to environmental epidemiology and women’s health.

...Continued on page 13
Welcome new Center Members

New EHSC Faculty, continued….

Dr. Danielle Benoit joined the University of Rochester in 2010 as the James P. Wilmot Distinguished Assistant Professor within the Department of Biomedical Engineering with secondary appointments in Chemical Engineering and the Center for Musculoskeletal Research. Dr. Benoit is one of three trainees in the URMC’s Women’s Health and the Environment over the Entire Lifespan (WHEEL) program. She is enthusiastic to continue current collaborations and foster new ones in therapeutic strategies to combat lead-associated bone toxicology through her recent appointment in the Environmental Health Sciences Center. Her research specializes in the rational design of polymeric materials for regenerative medicine and drug delivery applications. Her work has provided insights into the translation of tissue engineering strategies for bone allograft repair, development of pH-responsive nanoparticles for nucleic acid and small molecule delivery, and novel targeting strategies for bone-specific delivery of therapeutics. She received her undergraduate degree in Biological Engineering from the University of Maine and M.S. and Ph.D. in Chemical Engineering from the University of Colorado. She then trained at the University of Washington where she was a Damon Runyon Cancer Research Foundation Postdoctoral Fellow.

Dr. Lisa DeLouise is an Associate Professor in the Departments of Dermatology, Biomedical Engineering, and Material Chemistry. She has established a cross-disciplinary research program focused on investigating the environmental health and safety effects of nanomaterial skin exposure. Her research seeks to elucidate factors that impact nanomaterial skin penetration and systemic translocation. In particular she is interested in understanding how ultraviolet radiation (UVR) and nanomaterial exposure may alter skin immune function. Skin is the largest organ of the body and a main route to allergen sensitization. Understanding how the physiochemical properties of the nanomaterials (composition, charge, size) can affect generation of contact hypersensitivity in relation to developing immuno-tolerance from UVR skin exposure are clinically relevant from toxicology and immunotherapeutic perspectives. As a new member of the EHSC, Dr. DeLouise looks forward to leveraging the diverse expertise of EHSC faculty to problem solve and forge new collaborations. Dr. DeLouise is also interested in acting as a mentor for emerging students in the field of nanotoxicology and nanodermatology.

...Continued on page 14
Welcome new Center Members

New EHSC Faculty, continued….

Dr. Todd Jusko was recently appointed as Assistant Professor in the Departments of Public Health Sciences and Environmental Medicine. He received his PhD in Epidemiology at the University of Washington. Most recently, he came from NIEHS as a postdoctoral fellow in the Biomarker-Based Epidemiology Group. Broadly, Dr. Jusko's research interests include the environmental determinants of children's health, but he is specifically interested in the potential impact environmental chemicals have on the developing immune system. He hopes cross-disciplinary collaborations with investigators in Environmental Medicine and Immunology will facilitate the design of high quality studies to answer questions about potential developmental immunotoxicity in humans.

Dr. Tanzy Love joined the University of Rochester in June 2008 as a post-doc working in Biostatistics on the Seychelles Child Development Study (SCDS). Dr. Love has been a faculty member since June 2010 and joined the EHSC this spring. Her work in the SCDS has involved finding sub-populations susceptible to high prenatal fish consumption, clustering dietary profiles, and analyzing the data from the audiology and genetics aims of the study. She also has the role of biostatistical core to the Center for Medical Countermeasures against Radiation.
Dr. Andrew Doniger retired in May 2013 after 23 years as Director of the Monroe County Department of Public Health. Dr. Doniger served as our Community Advisory Board chair since its formation in the late 1990’s. His commitment to reducing exposure to environmental health hazards for Monroe County residents helped the COEC and other local organizations improve the health and lives of many, including through preventing childhood lead poisoning and improving home environmental health. We thank Dr. Doniger for his commitment to improving environmental health for all, and wish him a long and happy retirement.