

Your Health

News from the
University of Rochester
Environmental Health
Sciences Center

Fall 2013



The Environment

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Epidemiology and the Environmental Health Sciences Center

What is Environmental Epidemiology?

A primary goal of the EHSC is to facilitate and promote collaboration among varied approaches, disciplines, and methods to inform environmental public health solutions. In this issue of the EHSC newsletter, we focus on environmental epidemiology at Rochester and how it contributes to the mission of the Center. In particular, we focus on the research interests of epidemiologists in the Center and the collaborations they are pursuing with Center researchers from other disciplines.

Epidemiologists study how health outcomes are distributed within and across populations. Epidemiological models are often employed to study risk associations in humans where experimental studies are unethical or impossible to conduct. Epidemiologists rely on statistical models of population data to test hypotheses about what might influence a person's risk for disease. These models may be interpreted independently, or combined with other data such as results from controlled experiments in the lab. Some epidemiological studies also include individual or group-randomized trials that control environmental variables.

Epidemiology can be a means of confirming biological findings, but it can also generate new hypotheses to be tested through lab research. In addition, it can help identify potential associations or pathways by suggesting potential links between exposures and health outcomes. Laboratory studies can then confirm these associations and investigate their causes at a molecular level. Through the EHSC, epidemiologists frequently interact with other kinds of scientists to both determine what questions to examine with population data, as well as to suggest areas for research into causality and mechanism based on patterns identified by their models.

This multidisciplinary interaction is particularly important for environmental epidemiologists who explore dose-response associations between environmental contaminants and health outcomes. The EHSC includes a strong and growing core of environmental epidemiologists, including Drs. Edwin van Wijngaarden, David Rich, and Todd Jusko, all of whom hold primary appointments in the Department of Public Health Sciences.

“Size Matters”

Epidemiological studies typically involve very large populations, often over 1,000 participants. Large sample sizes help epidemiologists identify disease associations based on increased risk. Additionally, epidemiological studies typically do not study hypotheses in a controlled environment. Instead, they must control for potentially confounding variables either statistically or by excluding data points. Larger data sets allow for these corrections while still offering enough “samples” for reasonably accurate estimates of the magnitude of associations.

Epidemiological Studies at the Environmental Health Sciences Center

Lead and cognitive function in older adults: Connecting neurobehavioral and epidemiological research

Although lead has long been known to be a neurotoxicant, research continues to reveal new information about how lead affects the body, including its effect on adults later in life. Recent studies have shown mixed results: some demonstrate adverse effects of lead on aging adults, while others show no association. The potential for multiple scenarios and confounding factors can make these studies difficult to conduct and interpret.

EHSC researchers Dr. Deborah Cory-Slechta (Department of Environmental Medicine) and Dr. Edwin van Wijngaarden are working together to study potential associations between lead and cognitive function in older adults. A 2009 paper published in *NeuroToxicology* summarizes their findings from a pilot study of bone lead and memory. The results demonstrated an association between bone lead levels and memory impairment. Their initial findings suggested that impairment may be related to more recent lead exposure, but the small sample size limited their ability to make firm conclusions.

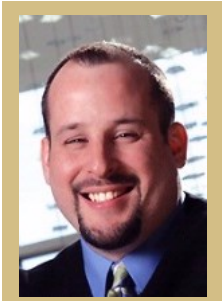
A follow-up study of blood lead levels in older adults, published in *NeuroToxicology* (2011), concludes that concurrent lead exposure in older adults does not appear to have an association with cognitive function. In other words, older adults' brains do not appear to be affected by recent lead exposures. Through another collaborative study, the team is also currently investigating whether there is a relationship between diurnal cortisol patterns (as a marker of hypothalamic-pituitary-adrenal (HPA) axis dysfunction and physiologic stress more broadly) in relation to blood lead levels in adults over age 70. The HPA axis regulates many hormone-based systems in the body, including the stress response system that produces cortisol. Finally, the researchers also work together to study data from the Rochester Lead Cohort. This study addresses the interaction between iron status and lead exposure in relation to children's cognitive development.

These collaborative efforts are born out of shared interests between the scientists. For example, their recent findings on lead and cognitive function suggest that focusing research on the effect of early life (rather than concurrent) exposures may lead to clues for cognitive decline later in life. Work in the Cory-Slechta lab now aims to further determine the mechanisms by which chronic, low-level exposure to lead affects cognitive function in childhood and later in life.



Epidemiological Studies at the Environmental Health Sciences Center

Understanding the influence of air pollution on cardiac health



Dr. David Rich

Dr. David Rich is globally recognized for his work on air pollution and health. He recently published a series of papers highlighting the negative impacts of air pollution on biomarkers of cardiovascular health in young adults in China before, during, and after the mass effort to reduce air pollution for the Beijing Olympics. This study allowed Dr. Rich to confirm the importance of the inflammatory and coagulation/thrombosis – clotting of blood in the circulatory system – mechanisms, both important biomarkers for cardiovascular health.

A 2012 paper published in *Environmental Health Perspectives* summarized the findings of a study led by Dr. Mark Utell (Department of Medicine, Pulmonary Diseases and Critical Care), in which Dr. Rich collaborated with center members Dr. Wojciech Zareba (Department of Medicine, Cardiology), Dr. David Oakes (Department of Biostatistics and Computational Biology), Dr. Mark Frampton (Department of Medicine, Pulmonary Diseases and Critical Care), and long-time collaborator Dr. Phil Hopke from Clarkson University (Department of Chemical and Biomolecular Engineering). The study built on Dr. Rich's air pollution work, hypothesizing that exposure to air pollution negatively impacted inflammatory and autonomic function biomarkers in patients undergoing cardiac re-habilitation. Their study found adverse effects associated with increased levels of ultrafine particles (10-100 nm), accumulation mode particles (100-500 nm), and fine particles ($PM_{2.5}$; $\leq 2.5 \mu m$) in subjects, increasing their short-term risk of cardiovascular events.

Dr. Rich also studies links between air pollution and reproductive health. Again using the Beijing Olympics data, he found that babies born during the 2008 Beijing Olympics – when air pollution significantly declined – had higher birth weights than babies born in 2007 or 2009 when air pollution levels were much higher.

Dr. Rich's interests in the impacts of air pollution on health also have local applications: he is currently collaborating with Dr. Jill Halterman (Department of Pediatrics) on a translational pilot project to test the effectiveness of air filtration systems in improving air quality in the homes of smokers with premature infants recently discharged from the neonatal intensive care unit in Rochester.

Combining the strengths of environmental epidemiology and immunotoxicology to assess effects of PCBs on the developing immune system

New center member Dr. Todd Jusko collaborates with Dr. Paige Lawrence (Department of Environmental Medicine) and other investigators to study the potential effects of

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Epidemiological Studies at the Environmental Health Sciences Center

PCBs and the developing immune system, continued....

polychlorinated biphenyls (PCBs) on the developing immune system. This work builds on Dr. Jusko's background in children's environmental epidemiology and Dr. Lawrence's background in immunology and toxicology. Collaborative efforts across research methodologies add significant value to the study team's findings, for example by improving study design across multiple elements. For instance, Dr. Jusko is able to optimize study design to reduce bias and confounding based on modern epidemiologic approaches. Additionally, Dr. Jusko's statistical knowledge allows the application of appropriate statistical methods to deal with correlated data because of repeated measurements on the same individual. Dr. Lawrence, who studies the effects of environmental chemicals on the immune system in animal models and the biological mechanisms responsible for these changes, contributes to interpretation of findings from a biological perspective and advises on biomarkers of study. For example, the team worked with Dr. Lawrence to select appropriate endpoints to evaluate, such as T-cell-dependent antibody responses.



The potential neurotoxicity of PCBs is well studied in human populations, but by comparison, very little is known about PCBs and the developing immune system. To begin to address these knowledge gaps, Drs. Jusko and Lawrence study a cohort of children born in eastern Slovakia with high PCB concentrations in their blood. The median maternal PCB-153 concentration in the Slovak cohort is approximately 150 ng/g lipid. In the United States, 2003-2004 concentrations in pregnant women were approximately 8 ng/g lipid (PCB-153 is a common type of PCB detectible in most people's blood). Collaborative papers published in *Environmental Research* (2010) and *Journal of Immunotoxicology* (2011) report the team's findings: Their 2010 findings revealed no association between prenatal PCB exposure and post-vaccination antibody response at 6-months; results published in 2011 also identified no association between pre- and early post-natal PCB exposures and signs of a compromised immune system (in this case, immunoglobulin concentrations) at 6-months of age. Building on this work, Dr. Jusko assessed potential pathways affected by early life PCB exposures, this time assessing potential associations between thymus volume at birth, 6-, and 16-months of age and early life PCB exposure. The thymus is important for T-cell development in infants. Findings published by Jusko and colleagues in 2012 in *Environmental Health Perspectives* suggest that neonatal exposure to PCBs may have an impact on thymus volume, and that thymus volumes later in infancy may be influenced by concurrent, postnatal exposure. Future planned collaborative work between Drs. Jusko and Lawrence includes the examination of perfluorinated compounds (PFCs) in breast milk and immune outcomes, and whether PCBs themselves affect the quality of maternal breast milk.

Environmental Health Sciences Center Updates

Giving communities a voice in fracking research: A collaboration among Community Outreach and Engagement Cores

By Kathleen Gray (UNC), Erin Haynes (Cincinnati), and Katrina Korfmacher (URMC)



Dr. Katrina Korfmacher, URMC



Dr. Kathleen Gray, UNC



Dr. Erin Haynes, UC

Shale gas extraction (often referred to as hydraulic fracturing, or “fracking”) is a hot topic nationally, especially in states like North Carolina, New York and Ohio that sit on extensive, gas-rich shale formations deep underground. The effects of this rapidly growing industry include not only the drilling/fracking itself, but also transportation, compressor stations and other operations involved in extracting natural gas from these shale formations.

Scientific research is underway to understand the potential health and environmental impacts of shale gas extraction on the surrounding communities. Community engagement experts agree that community input in research planning is a critical first step in ensuring that research meets community needs and informs decisions. Therefore, the Community Outreach and Engagement Cores of three NIEHS Centers (Rochester, Cincinnati, and North Carolina) decided to collaborate on a project to identify what types of research and information communities in their states want about potential health effects of hydrofracking.

Fracking has already started in Ohio; North Carolina and New York have not yet permitted hydrofracking. While several research studies have been funded to assess the potential health impacts of shale gas extraction, none have studied the informational needs of impacted communities. The NIEHS-funded supplement project by the three COECs aimed to answer this question.

The project team interviewed 48 citizen landowners, public health, environment and outreach/education professionals, and government officials in the three states. They asked what health concerns interviewees have related to these operations entering their communities, and what research they need to address their concerns and inform sound decision-making. Study leaders also asked where these individuals currently get their information about potential health impacts of shale gas extraction, and what sources they do, or don’t, find credible.

The COECs presented their results on November 4th at the American Public Health Association’s national meeting in Boston. Their hope is that findings will be valuable for agencies, researchers, and communities grappling with the many uncertainties and decisions being made about hydrofracking in their areas.

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Environmental Health Sciences Center Updates

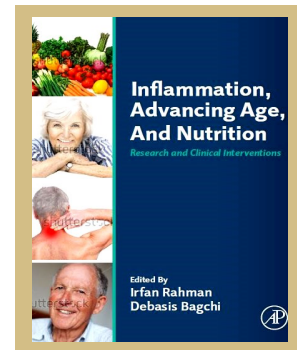
Giving communities a voice in fracking research, continued...

Collaboration in this study allowed the researchers to leverage relationships in their own local communities to include the perspectives of community members in three different states, and explore these issues in much greater depth with a local context. This collaboration allowed the project team to identify key cultural, political, economic, land use and historical differences in the three states.

A second NIEHS supplement was awarded in 2013 to the University of Pennsylvania COEC which will collaborate with UR, UNC and Cincinnati to identify factors that affect risk perception among people living in proximity to fracking, and how these factors compare for those living in areas where fracking is likely to occur in the future.

New book focuses on the prevention of early aging and how to mitigate its effects

Myriad factors influence the onset of early aging, including environmental exposures that increase inflammation. A new book co-edited by Dr. Irfan Rahman (Department of Environmental Medicine), *Inflammation, Advancing Age and Nutrition: Research and Clinical Interventions* (Elsevier and Academic Press publication 2014 ISBN 978-0012-397803-5), helps readers understand the integrated impacts of these factors and offers recommendations for lifestyle changes that can prevent or mitigate the effects. Specifically, it examines how interventions such as everyday diet and medication can reverse inflammation, cancer and premature aging.



Special issue of *Environmental Immunology and Toxicology*

Dr. Steve Georas (Department of Medicine, Pulmonary Diseases and Critical Care) co-edited the July/August 2013 issue of the *Journal of Environmental Immunology and Toxicology*. This special issue focuses on "environmental exposures and innate immunity in the lung." In this issue of the journal, five articles address different aspects of how the lung innate immune system senses and responds to different environmental exposures including inhaled toxicants. The full issue is available online at <http://www.stmconnect.com/jeit/content/1/3.toc>.

Environmental Health Sciences Center Updates

Identifying a mechanism by which environmental obesogens influence weight gain



Dr. Richard Phipps

Dr. Richard Phipps, Department of Environmental Medicine, was awarded a two-year R21 from NIEHS to study the mechanisms by which environmental obesogens – endocrine disrupting chemicals that affect the body’s metabolism – influence weight gain. One mechanism by which obesogens may function is to reprogram the epigenetic code, thus affecting the rate of adipogenesis, or development of fat cells. Past studies from the Phipps Laboratory have shown that depletion of the Thy1 protein increases adipogenesis while over- expression of Thy1 impairs adipogenesis. The characteristics of Thy1 mean that it can be controlled epigenetically, and may be a key target of obesogens. Developmental exposure to obesogens may therefore reprogram Thy1 expression levels and modify physiology long after exposure. For this new study, “Environmental Obesogens Reduce Thy1 Expression and Promote Obesity,” Dr. Phipps hypothesizes that environmental obesogens alter Thy1 expression to increase adipogenesis and obesity. The results of these studies will show for the first time whether Thy1 expression is reduced by environmental obesogens, and that this reduction is key to the mechanism whereby obesogens increase adipogenesis and obesity.

Symposium Honored the Legacy of Dr. Patricia M. Rodier

Dr. Patricia Martin Rodier, Professor of Obstetrics and Gynecology at the University of Rochester School of Medicine and Dentistry, passed away in May, 2012. Dr. Rodier trained and collaborated with scientists from around the world, including many EHSC faculty. Her research focused on how alterations to brain development affect behavior, which helped lay the groundwork for identifying windows of susceptibility to environmental contaminants such as heavy metals, as well as anesthetics, alcohol, and hormones. Colleagues and former students hosted a symposium in June to honor Dr. Rodier and her legacy.



Dr. Patricia M Rodier

Environmental Health Sciences Center Updates

Recent study confirms effects of tobacco smoke on circadian rhythm

A recently completed study led by Dr. Irfan Rahman found that exposure to tobacco smoke elicits a physiological response similar to jet lag. In addition to being regulated by a specific region in the brain, circadian rhythms are also regulated by a number of peripheral “clocks” throughout other organs, including the liver, heart and lungs. The study team’s mouse model identified the mechanism by which tobacco smoke affected the “clock” gene found in the lung. This change results in inflammation, and can lead to a jet lag-like effect for up to 30 days. This study, funded by NIH/NHLBI, is published in the September 2013 issue of *FASEB Journal*.



Dr. Irfan Rahman and lab members

Investigating the transgenerational effects of dioxin

Dr. B. Paige Lawrence (Department of Environmental Medicine) was awarded a 5-year R01 from NIEHS to look into how exposure to TCDD (dioxin) affects immune responses to influenza infection across generations. Few studies of transgenerational inheritance of the effects of environmental exposures have considered the immune system.

Past research has shown that TCDD disrupts immune system response to influenza A infections in exposed mice, and pilot data suggests an effect on T-cell development in offspring of exposed mice, perhaps due to changes in DNA methylation, which alters gene expression. Other studies have demonstrated effects of TCDD on the third generation in other organ systems. This study adds to the growing body of evidence by investigating transgenerational effects on T-cell function in third generation offspring. The researchers aim to define the dose at which effects are seen, identify a developmental window of susceptibility, establish the nature of changes to immune function across generations, determine whether gender differences influence the effects, and investigate the mechanism by which immune system impacts are transferred across generations.

The award also supports University of Rochester collaborators Dr. Steven Gill (Department of Microbiology and Immunology) and Dr. Sally Thurston (Department of Environmental Medicine).

Environmental Health Sciences Center Updates Recognitions and Awards

How does use of e-cigarettes compare to conventional smoking?

Dr. Irfan Rahman (Department of Environmental Medicine) has joined Dr. Risa Robinson (RIT Mechanical Engineering Department) in an electronic cigarette study. The use of e-cigarettes has increased dramatically over the past few years, however the comparative health effects of these types of cigarettes are not well understood. Through an NIH FDA R21 funding award, the researchers propose to establish comparative nicotine emissions and dosages between e-cigarettes and cigarettes, and to evaluate whether or not these doses result in toxicological responses in vivo in mice. They hypothesize that electronic cigarette users are exposed to lower amounts of nicotine compared to conventional cigarettes, but that these exposure levels will cause toxic oxidative and inflammatory responses in vivo, and addiction comparable to that seen from smoking. Over the next two years, they will examine differences among e-cigarettes by manufacturer and user behavior and measure oxidative damage and inflammatory effects in mice. Not only will results from this study inform efforts by the FDA to regulate e-cigarettes, it may also help consumers make more informed decisions about the use of e-cigarettes as a tobacco replacement.



Dr. Richard Miller recognized by the Teratology Society

In June, Dr. Richard K. Miller (Department of Obstetrics and Gynecology) received the 4th Teratology Society Distinguished Service Award at the 53rd Annual Meeting in Tucson, AZ. Recipients of this award are long-time members of the Society who demonstrate leadership in their discipline, and have offered service to the Society.

A former graduate student in the Miller Laboratory was also recognized for her excellence by the Teratology Society. Dr. Tacey White (class of 1991), Managing Scientist for Toxicology and Mechanistic Biology at Exponent Health Sciences, was recently elected to Vice President of the Teratology Society. She will serve as President in 2015-16.

Graduate Student Awards

Sesquile Ramon (Phipps Lab)

- » Melville A. Hare Award, Distinction in Research in Microbiology and Immunology, University of Rochester, 2013

His-Min (Jim) Hsiao (Phipps Lab)

- » Medical Faculty Council University of Rochester School of Medicine and Dentistry Trainee/Student Travel Award, University of Rochester, 2013

Welcome to the Environmental Health Sciences Center

Jill Halterman

Jill S. Halterman, MD, MPH, is Professor of Pediatrics and also serves as Associate Chair for Clinical Research for the Department of Pediatrics. Dr. Halterman's research aims to better understand and improve care for low-income children with asthma. She has conducted several randomized trials in community settings in partnership with Rochester City School District school nurses and in primary care offices to improve asthma care delivery and reduce morbidity. She is currently collaborating with Center member Dr. David Rich through an EHSC Pilot Project to test a novel in-home air filtration device to reduce smoke exposure among vulnerable premature infants, in order to prevent respiratory morbidity. The scientific merit of her work has been acknowledged through multiple peer-reviewed publications, substantial extramural funding (including a recent competing continuation award for her school-based asthma work), inclusion of references from several of her publications in the 2007 national guidelines for asthma put forth by the National Heart Lung and Blood Institute (NHLBI), and participation in an asthma outcomes workshop sponsored by the NHLBI. She looks forward to developing collaborative research opportunities through the EHSC related to environmental exposures and childhood asthma.

