EOHSI NEWSLETTER

EOHSI
Environmental & Occupational Health Sciences Institute

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Message from the Acting Director
by Kenneth Reuhl

When EOHSI was founded more than 20 years ago, the country was accepting its long legacy of environmental carelessness, negligence and mendacity; of rivers that burned, lax waste management plans, hazardous work environments, and a nascent appreciation of how to assess these issues. Mechanistic understanding of environmental and occupational diseases was rapidly evolving. EOHSI was envisioned as a unique opportunity to bring together scholars from disparate disciplines of environmental and occupational health to address these questions in a multidisciplinary fashion; to fuse exposure, biology, toxicology and policy into a coherent attack on public health issues. In these efforts, EOHSI has been highly successful, and research from the Institute has played a leading role in shaping our understanding of how exposures occur, how they affect health, and in framing the legislation directed at minimizing adverse health effects. The efforts of the Institute and its members are recognized at the state, national and international level.

As EOHSI enters the new century, a different set of challenges confront us. Environmental and occupational threats lie in low dose mixtures, in exposures to agents of uncharacterized nature (e.g., nanoparticles), in purposeful environmental destruction (ecological, biological and chemical terrorism) and a burgeoning population. Maintaining the Institute's leadership in environmental and occupational health research will require members to indentify major priorities, strengths, and to apply the Institute's collective expertise to innovative and cutting-edge research questions, to use the resources of the Institute to foster the development of the next generation of scholars, and above all, to maintain EOHSI's tradition of *research excellence.* As we move into the next year and initiate the search for a permanent director, it is this focus that sustains the mission of the Institute.

Chris, Joanna and Sean

Joanna and Constantine

Radiation Risk to Marine Organisms at Amchitka Island
by Joanna Burger

In the 1960's the Atomic Energy Commission (later the Department of Energy) conducted three underground nuclear tests at Amchitka Island, over the objections of the native Aleut Islanders, the state of Alaska, Canada and many others. After the tests, Amchitka Island reverted to being part of the Alaska Maritime National Wildlife Refuge, but the DOE retained responsibility for the nuclear contamination left behind in underground cavities. When the DOE announced it would clean up surface contamination and terminate responsibility for Amchitka, the Aleuts, the state of Alaska, and the Fish & Wildlife Service required DOE to determine whether there was radiation contamination of the marine environment and subsistence foods. They also expected the DOE to develop a long-term monitoring program so that future generations could be assured of protection from radiation.

DOE agreed to fund the Consortium for Risk Evaluation with Stakeholder Participation (CRESP) an independent multi-university group initiated at EOHSI by Charles Powers and Bernard Goldstein in 1994. Under Powers, CRESP developed and conducted the geophysical and biological study. After the Science Plan was accepted in 2003, Mike Gochfeld and I visited the native villages of Unalaska, Nikolski, and Atka to talk with the Aleut people about the proposed study, particularly their subsistence foods and techniques. Many changes in the plan were made after talking with these stakeholders, including the inclusion of an Aleut fishing/hunting team as an integral part of the collecting expedition. This proved to be extremely valuable.

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Mike and Joanna with bird

In 2004, CRESP conducted a series of expeditions to Amchitka, and I led the biological expedition on a 150-foot trawler to collect many organisms from the marine ecosystem at all levels on the food chain, including algae, sea urchins, mussels, octopus, and many kinds of fish and seabirds. The Aleut science and Western science was melded to collect plants and animals that included subsistence foods and commercial fish species. The impressive traditional knowledge of the Aleuts on the expedition was essential to the safe collecting of a wide range of species.

Once 55 coolers were back at EOHSI, specimens including four species of kelp, sea lettuce, sea urchins, rock jingles, two kinds of mussels, octopus, a dozen species of fish, common eider, eagle, tufted puffin, and pigeon guillemot were prepared for analysis (conducted at Vanderbilt and Idaho National Laboratory). We analyzed for both anthropogenic (bomb-related) isotopes (cesium, strontium) as well as natural uranium isotopes. In all cases, the levels of radionuclides were very low, mostly below detection levels.

Joanna, crew member and Halibut

In October of 2005, we again visited the Aleut villages to report the results, and to thank the Aleuts for their participation in the collaborative effort to understand the potential for radionuclide exposure from tests. Even though currently there is no cause for concern from radiation at Amchitka, even the DOE believes that the radionuclides may someday seep into the marine environment. The only questions are when and where? If they seep close to shore, there is a wide range of organisms living in the marine environment around Amchitka that could be exposed and could pose a health hazard to people. The only way to ensure that the ecosystem and foods continue to be safe is to monitor the radionuclides levels at regular intervals. CRESP developed a biomonitoring a plan now integrated into the long-term stewardship plan for Amchitka Island. While the underground contamination cannot be cleaned up because it is so far below the ground, early warning would allow for a temporary closure of subsistence hunting and fishing in the areas around Amchitka to prevent exposure. The Unangan peoples have lived in the Aleutians for over 9000 years. It is critical to provide them with the information they need to make informed decisions about their subsistence food.

For more information, the Amchitka Report and the Biomonitoring Plan can be found on the CRESP website, at http://www.cresp.org. A list of papers from the expedition can be found on Dr. Burger's website http://lifesci.rutgers.edu/~burger/start/index.htm.

World Trade Center and Terrorism

by Iris Udasin and Paul Lioy

It has been more than 6 years since 9/11, but health issues concerning the aftermath of the WTC attack and terrorism remain. EOHSI is working on a number of these areas including:

1. Dealing with the long-term health care of workers being led by Dr. Iris Udasin,
2. Developing epidemiological analysis for the long term impact on the general pubic being investigated by Drs. Wartenberg, Kipen, Laumbach and Georgopoulos,
3. Examining and developing better ways to reduce exposures and risks immediately after an attack. This includes the CounterAct Center directed by Dr. J. Laskin and D. Gerecke and the Prospective Human Exposure studies being conducted by Drs. Lioy, Isukapalli and Georgopoulos within the Exposure and Dose Modeling Center.

As the EOHSI principal investigator for the World Trade Center (WTC) Medical Monitoring and Treatment Program, Iris Udasin recently provided testimony to the House of Representatives. She described her clinical experience in the treatment of these patients who have complicated illnesses and described the need for continued monitoring. She noted that WTC patients have complicated medical conditions such as asthma, bronchitis, sinusitis, laryngitis, rhinitis, and gastro-esophageal reflux. The patients have unusual presentations that make these conditions difficult to diagnose, requiring more physician time than is usually allotted by primary care physicians.

Highlighting Jason Richardson

Investigating Attention-Deficit Hyperactivity Disorder (ADHD)

Attention-deficit hyperactivity disorder (ADHD) is a clinically heterogeneous disorder characterized by core features of impulsivity, hyperactivity, and attention deficits that is estimated to affect 8-12% of school-aged children worldwide. While ADHD is a complex disorder with significant genetic contributions, no single gene has been linked to a significant percentage of cases, suggesting that environmental factors or gene-environment interactions may contribute to the etiology or clinical manifestation of ADHD. Recent data from my laboratory have demonstrated that mice exposed during development to low levels of the pyrethroid pesticide deltamethrin exhibit symptoms similar to those observed in children with ADHD, including elevated dopamine transporter levels, hyperactivity, and a paradoxical calming response to psychostimulants. Furthermore, mice developmentally exposed to deltamethrin exhibit impulsive-like behaviors on a fixed ratio waiting for reward paradigm that are reversed with methylphenidate (Ritalin®) treatment. To determine

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whether our laboratory findings were supported by observations in the human population, we carried out a cross-sectional study of pyrethroid pesticides as a risk factor of ADHD on U.S. children between the ages of 6 and 15 years. Data for this analysis was obtained from the 1999-2002 rounds of the National Health and Nutrition Examination Survey (NHANES) using parent-reported diagnosis of ADHD and urinary levels of 3-phenoxybenzoic acid, a metabolite of pyrethroid pesticides including deltamethrin, as a measure of exposure. Parents of children aged 6-15 with detectable levels of pyrethroid metabolites in their urine were more than twice as likely to report that a doctor or health professional had told them their child had ADHD. The parallels between mice developmentally exposed to deltamethrin and individuals with ADHD (not parent-reported diagnosis) reinforce the epidemiological data suggesting that developmental pesticide exposure may be a risk factor for ADHD. The epidemiological portion of these studies was conducted in collaboration with Dr. Stuart Shalat of EOHSI. The impulsive behavior experiments were conducted in collaboration with Dr. Deborah Cory-Slechta, now at the University of Rochester Medical School.

National Children's Study: EOHSI's Role in this 20-Year Study

by Paul Lioy

Prospective, multi-year epidemiologic studies have proven highly effective in identifying preventable risk factors for chronic disease. To identify environmental risk factors for chronic disease in children, the U.S. Congress directed the National Institute of Child Health and Human Development (NICHD) through the Children's Health Act of 2000, to undertake the National Children's Study, a prospective study of a nationally-representative cohort of 100,000 U.S.-born children to be followed from pregnancy to age twenty-one years. NICHD is conducting the Study in collaboration with the Environmental Protection Agency, the Centers for Disease Control and Prevention, and the National Institute of Environmental Health Sciences. Environmental risk factors, including chemical, physical, biological and psychosocial factors, will be assessed on multiple levels. Recruitment is planned at 105 sites (seven Vanguard Centers) across the U.S., beginning in 2006. Drs. Lioy, Weisel, Shalat, and Georgopoulos of EOHSI are currently part of the Queens Vanguard Center, and are the lead consortium organization on environmental exposure issues and sampling and modeling. Banks of biological and environmental samples will be established. Genetic material will be collected on each of 1250 mothers and their children and banked to permit study of gene-environment interactions and individual susceptibility factors. We anticipate that the National Children's Study will provide invaluable information on preventable risk factors for chronic diseases such as asthma, certain birth defects, neurobehavioral syndromes (dyslexia, attention deficit hyperactivity disorder, autism and schizophrenia) and obesity. At the end of September 2007 the Consortium was selected to add five more counties. This separate contract, called the New York/New Jersey NCS Center, will include the Boroughs of Manhattan, Brooklyn and Nassau in New York, and Passaic and Middlesex Counties in New Jersey. The latter mark the first New Jersey counties to be part of a national cohort examining children's health over the next 20 years. Dr. Lioy's Exposure Science Division will continue to lead the exposure part of the Consortium, and Dr. George Rhoads of the UMDNJ School of Public Health is a principal investigator for all NJ counties.

NEWS FROM EOHSI CENTERS

UMDNJ's Environmental Bioinformatics and Computational Toxicology Center (ebCTC)

by Panos Georgopoulos

On November 2, 2005, the USEPA announced an award of $9 million to establish two cutting-edge environmental bioinformatics research centers at the University of North Carolina at Chapel Hill and the University of Medicine and Dentistry of New Jersey. The USEPA's official announcement further stated that these "centers represent a major component of EPA's computational toxicology program that is using computer models to study the relationship between environmental contaminants and their potential adverse effects." UMDNJ's Environmental Bioinformatics and Computational Toxicology Center (ebCTC), under the direction of Professors William Welsh and Panos Georgopoulos, constitutes a research partnership with Rutgers University, Princeton University, and USFDA's Center for Toxicoinformatics. Researchers within ebCTC employing bioinformatics-related methods and technologies to pursue a multi-disciplinary environmental systems toxicology research approach. The objective of this effort is the development and application of a novel, consistent and integrative framework for mechanistic assessment of human health risks associated with exposures to environmental stressors.

This framework is based on the concept of coupled bionetworks that span multiple scales of biological space (genomic, cytomic, histomic, physiomic) and on the study of their hierarchical structures and functional states, as those are perturbed by behavioral and environmental influences. At any given time, human health state reflects the dynamics of coupled signaling, regulatory and metabolic bionetworks, which are potentially influenced by developmental and aging processes, as these interact with − or are perturbed by − extragenomic factors, such as the presence of xenobiotics. Systematic study of bionetworks at each scale involves identification and quantitative characterization of (i) network components (nodes), (ii) network interactions (links) and (iii) network dynamics (states). For example, components of transcriptional regulatory networks are binding sites, transcription factor molecules, riboswitches, etc., while network links include DNA-protein, protein-protein and metabolite-RNA interactions. Computational chemistry methods (e.g. QSARs)

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are also being developed and utilized to quantitatively characterizate molecular components and interactions at a local (e.g. ligand-receptor) scale. Deterministic and stochastic system process analysis and optimization techniques are applied towards elucidation of larger network structures (e.g.interlinked signaling, regulatory and metabolic pathways). The latter process relies on interpretation of data from network perturbation experiments, that may include consideration of genetic perturbations (polymorphisms, gene knockouts, gene silencing, etc.), environmental perturbations (toxicant dosage, nutrient availability, etc.) and disease state (pathological vs. normal). Outcomes of this interpretation provide information that aims to improve understanding of (a) molecular mechanisms of toxic responses, (b) differences in responses between humans and model species (improved cross-species extrapolation), and (c) interindividual variability in responses (improved consideration of genetic susceptibility to environmental disease). We believe that considering individual-specific toxicoinformatic data, within a systems toxicology framework, will allow development of more accurate, and eventually even "personalized," risk assessments.

NIEHS Center – Thoughts from the New Director

by Helmut Zarbl

It's difficult to believe that it has been almost a year since I left the Fred Hutchinson Cancer Research Center in Seattle to join the faculty at UMDNJ and EOHSI. As with any move there have been many challenges, but these were largely overshadowed by the numerous leadership and research opportunities afforded to me by becoming a member of the EOHSI family. I was both honored and humbled when my colleagues selected me to serve as the new director of the NIEHS Center. I am in the process of writing the renewal application for the grant that funds the Center, a process that I am enjoying immensely as it is affording me the opportunity to learn the details of all the exciting research going on at EOHSI. As the former Director of the Toxicogenomics Research Consortium in Seattle, I hope integrate my own vision of interdisciplinary research into the Center in a way that will also leverage the mission of EOHSI to improve environmental health.

My own research is also benefitting tremendously from my interactions with new colleagues and the advanced and often unique infrastructure provided researchers by EOHSI. My own areas of expertise include the use of biochemical, genetic and genomic approaches to understand the molecular mechanisms underlying of toxicity, mutagenesis, and the differential susceptibility to carcinogenesis following exposure to environmental toxicants and carcinogens. The state of the art infrastructure built at EOHSI over the past several years has made it possible for my group to hit the ground running and continue our research in toxicogenomics and toxicogenetics. New colleagues and resources such as EOHSI's controlled exposure facility have provided new opportunities for research in exposure assessment, translational research, and also inspired me to invent a novel approaches for biomarker discovery and a new microarray platform for biomarker screening. All in all, I would say that my move to EOHSI has been an excellent career move that has both invigorated by research and provided welcomed new challenges and opportunities. I look forward to the coming years.

Airline Cabin Environmental Research Center

by Clifford Weisel

UMDNJ is one of seven core institutes of the Airliner Cabin Environmental Research – FAA Center of Excellence (ACER-COE). The other institutes are Auburn University, Purdue University, Harvard University, Boise State University, Kansas State University, and the University of California at Berkley. The UMDNJ effort, centered in EOHSI, is led by Professors Clifford Weisel and Charles Weschler, both members of the Exposure Science Division. The ACER-COE team focuses on the health and the security issues related to the passenger and crew within an airplane cabin. Our research projects within ACER-COE are: exposure to ozone and secondary oxidation products formed within aircraft and subsequent health effects, exposure of the crew and passengers to pesticides, and identification of whether engine oil or its pyrolysis products leak into the airplane cabin air resulting in reportable incidents. The ozone research has identified a number of carbonyl compounds that are eye and respiratory irritants. The carbonyl compounds from reactions of ozone with emissions from people and cleaning agents used in aircraft. Increases in the numbers of symptoms linked to the production of these compounds have been found by Charlie Weschler and colleagues while he was a visiting professor at the Danish Technical Institute using their ground-based simulated airplane (Wisthaler A. Tamas G. Wyon DP. Strom-Tejsen P. Space D. Beauchamp J. Hansel A. Mark TD. Weschler CJ. Products of ozone-initiated chemistry in a simulated aircraft environment. *Environmental Science & Technology. 39(13):4823-32, 2005*). We are planning to continue these studies in the Controlled Environmental Facility at EOHSI to identify the specific agents responsible for the symptoms. A new pesticide wipe sampler has been developed at EOHSI for use on aircraft to determine dermal exposures from seats, panels and arm rests. This sampler will be used on flights as part of a grant received jointly with Battelle from ASHREA (American Society of Heating, Refrigeration, Air-Conditioning Engineers) to characterize the air quality within domestic and international passenger airplanes and links to the health of passengers. The center is expanding to become a Center for Research in the Intermodal Transport Environment (RITE). More information at the FAA-COE can be found at www.acer-coe.org .

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