Protecting Children's Health for a Lifetime:

Environmental Health Research Meets Clinical Practice and Public Policy

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Proceedings

October 29 - 30, 2013

Omni Shoreham Hotel
2500 Calvert Street, NW
Washington, D.C. 20008

EPA United States Environmental Protection Agency

NIH National Institute of Environmental Health Sciences

PEHSU Pediatric Environmental Health Specialty Units

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The National Center for Environmental Research (NCER), Office of Research and Development was responsible for the preparation of this meeting report. Nica Louie served as the Task Assignment Manager, providing overall direction and technical assistance, and is a contributing author/reviewer. The proceedings were prepared by the Scientific Consulting Group (SCG) under contract with the U.S. EPA (contract number EP-C-08-010). The document serves as a general record of presentations and discussions during the meeting and captures the main points while highlighting discussions. It is not a complete record of all details discussed, nor does it interpret or elaborate upon matters that were incomplete or unclear. Statements represent the individual views of the workshop participants; except as specifically noted, none of the statements represent analyses by or positions of EPA.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
NATIONAL INSTITUTES OF HEALTH
WASHINGTON, D.C.

OFFICE OF
RESEARCH AND DEVELOPMENT

DIVISION OF EXTRAMUARAL
RESEARCH AND TRAINING

October 28, 2013

Dear Conference Participants:

We are delighted to welcome you to the EPA/NIEHS Children's Environmental Health and Disease Prevention Research Centers conference. We are celebrating 15 years of innovative and outstanding accomplishments of this highly significant research program. In 1998, EPA and NIEHS established the Children's Centers and today they continue to produce high-quality research results that are being translated into policy and practice. As we gather during Children's Health Month, this year is very special because we are joined by clinicians from the Pediatric Environmental Health Specialty Units to discuss current findings and lay the groundwork for future progress.

We are excited about the opportunity to host this conference since events like this hold significant value for both agencies. They afford us a tremendous opportunity to learn from key findings and developments in the work of our grantees, to discuss ways to translate research into policy, to identify how best to communicate research findings effectively to the public, and to highlight the diverse and emerging research topics of concern affecting children in communities across the United States and beyond. Also importantly, this conference provides a forum for innovative discussion and incubation of ideas amongst all participants whether representing extramural or intramural scientists, clinicians, community partners, policy makers and public health practitioners.

As you will discover, we have prepared an agenda that is fast-paced and comprehensive – featuring a highly accomplished and multi-disciplinary group of presenters. Over the next two days, we hope to highlight the importance of fostering collaborative and community-engaged research among basic, clinical, and behavioral scientists and local communities. The meeting program focuses on understanding complex interactions between the environment, genetics and epigenetics, from preconception to young adulthood and beyond as they relate to a host of children's health outcomes. Our Children's Centers program remains strong and timely because of you – since you share our agencies' priorities to protect children from potentially harmful environmental exposures now and in the future.

So once again, welcome and enjoy!

Sincerely,

James H. Johnson, Jr., Ph.D.
Director
National Center for Environmental Research, EPA

Gwen W. Collman, Ph.D.
Director
Division of Extramural Research & Training, NIEHS

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AGENDA

Meeting Goals

- Share reproductive and children's environmental health research and clinical findings and discuss implications for improving public health, clinical practice and public policy
- Learn about cutting-edge issues from the clinic, basic research and the community
- Share findings on how research translation and community engagement can improve the lives of children and families around issues of environmental health
- Identify key environmental health disparities and related factors that adversely affect children's health and development
- Seek collaborations between children's environmental health researchers, health care providers and the community

Meeting Objectives

- Expand understanding and investigate opportunities for research on various environmental topics and chemicals affecting children's health
- Share success stories and highlight challenges, strengths and lessons learned

October 29, 2013

7:30 a.m.	**Registration**
8:30 – 9:00 a.m.	**Welcome and Opening Remarks** *Lek Kadeli, Principal Deputy Assistant Administrator* *U.S. Environmental Protection Agency (EPA), Office of Research and Development (ORD)* *Gina McCarthy, EPA Administrator* *U.S. Environmental Protection Agency* *Linda Birnbaum, Ph.D., Director* *National Institute of Environmental Health Sciences (NIEHS)*
9:00 – 10:15 a.m.	**Session 1: Hot Topics in Food Safety and Children's Health** *Moderator: Brenda Eskenazi, Ph.D., M.A.* Children are exposed to contaminants in food that may affect their health and development. This session focuses on some specific contaminants that are of increasing concern to scientists, policy makers and the community. The goals of this session are to: 1) Provide an overview of what is known about the presence of arsenic and pesticides in food, current regulatory initiatives and risk communication challenges; 2) Present the state of the science of children's health and food exposure to pesticides, Bisphenol A (BPA) and arsenic; and 3) Stimulate audience questions and discussion with our presenters in a concluding panel.

	BPA and Children's Health: Updates on Food Packaging Exposure and Health Effects *Lesliam Quirós-Alcalá, Ph.D.* *University of California, Berkeley*	BPA has been found in plastics and food can liners. This presentation discusses human exposure to BPA and the potential health effects that have been described in children.
	Pesticides and Children: State of the Science of Exposure Assessment and Health Effects *Brenda Eskenazi, Ph.D., M.A.* *University of California, Berkeley*	This presentation focuses on trends in pesticide use in agriculture and the levels of exposures to various pesticides in pregnant women and children. It includes a brief review of some recent findings on health effects in children from pesticides.
	Arsenic in Food and Children's Health: Updates on Exposure Assessment and Health Effects Research *Kathryn Cottingham, Ph.D.* *Dartmouth College*	Relatively little is known about the possible effects of low-level arsenic exposures, especially during childhood, via food and water. This presentation summarizes exposure estimates for the New Hampshire Birth Cohort and describes plans to assess potential health effects in this population.
	Overview and Role of Improving Food Safety Through Strategic Science, Communication and Advocacy *Michael Crupain, M.D., M.P.H.* *Urvashi Rangan, Ph.D.* *Food Safety and Sustainability Center, Consumer Reports*	Consuming foods contaminated with heavy metals, pesticides and other chemicals such as BPA can increase health risks. This presentation focuses on how scientists can engage policy makers and the public to help reduce exposure.
	Panel	Question-and-Answer
10:15 –10:35 a.m.	**Tribute—Professor Patricia Buffler** Internationally renowned researcher in childhood leukemia and environmental health at the University of California, Berkeley's School of Public Health	
10:35 – 10:55 a.m.	**Break**	
10:55 a.m. – 12:05 p.m.	**Session 2: Air Pollution Update: Unraveling the Science, Making a Difference** *Moderator: Catherine Karr, M.D., Ph.D.* Understanding the adverse impacts of air pollutants on children's health and ensuring the translation of this evidence to clinicians and communities has matured through the EPA/NIEHS Children's Environmental Health and Disease Prevention Research Centers (CEHC) program and the Pediatric Environmental Health Specialty Units (PEHSU) program. This session provides some highlights of recent epidemiological studies that are advancing our understanding of indoor and outdoor factors, effects on the brain as well as airways, and consideration of cumulative exposure and lifespan implications. In addition, examples of moving forward from the etiologic science toward intervention strategies and effective outreach and translation strategies are presented.	

	Airborne Endotoxins and Asthma Morbidity in the Inner City: Friend or Foe? *Elizabeth Matsui, M.D., M.H.S.* *The Johns Hopkins University*	Co-exposure to both endotoxins and certain pollutants can modify the effects of endotoxins on markers of airway inflammation. However, it is unknown whether pollutant exposure modifies the effect of endotoxins on asthma symptoms and/or morbidity, particularly in "real world" settings. The goal of this presentation is to share findings from an analysis of endotoxin, pollutant, and asthma outcome data from a prospective cohort study that looks at how endotoxin and pollutant exposure may affect asthma among a population of urban, predominantly black children with persistent asthma.
	Early Life Traffic Pollution Exposure and Behavior at School Age *Nicholas Newman, D.O., M.S.* *University of Cincinnati* *Cincinnati Children's Hospital*	Findings from an ongoing birth cohort study will be presented. This study demonstrates associations between traffic-related air pollution exposure in the first year of life and ADHD-related symptoms when the children reached seven years of age. Additionally, there is evidence of effect modification between traffic-related air pollution exposure and maternal education.
	The Impact of Prenatal and Cumulative Exposure to Air Pollutants on Neurodevelopment *Frederica Perera, Dr.P.H., Ph.D.* *Columbia University*	This presentation focuses on findings from an ongoing birth cohort study. This study has found that there are associations between prenatal and cumulative exposure to combustion-related air pollutants and polycyclic aromatic hydrocarbons (PAH) with adverse neurodevelopmental effects in children. It also includes evidence of interactions between environmental exposures and psychosocial stress.
	Air Cleaner Interventions in Asthma—State of the Evidence *Greg Diette, M.D., M.H.S.* *The Johns Hopkins University*	Air cleaners have been touted as a potential strategy for environmental management of asthma. Intervention trials have varied in approach and findings. This presentation provides an up-to-date critical review of air cleaners and asthma research.
	Translating the Link Between Air Quality and Health Through Community Engagement and Partnerships *Lisa Cicutto, Ph.D., R.N.* *National Jewish Health*	This presentation briefly describes the development and implementation of the Denver center's website, Clean Air Projects (www.capk-12.org). The important partnerships and roles of the Community Advisory Board and community organizations will be stressed and discussed.
12:05 – 1:05 p.m.	**Lunch/Network**	

1:05 – 1:30 p.m.	**Keynote** *Sandra Steingraber, Ph.D.* *Ecologist, Author and Cancer Survivor*	An acclaimed ecologist and author, Dr. Steingraber explores the links between human health, rights and the environment. Her personal and scientific exploration into these issues offers insight into how our Nation can better protect our environment. Inspired by the 19th century abolitionist, Elijah Lovejoy, Dr. Steingraber calls for heroism in the face of the environmental crisis. Her published books include *Living Downstream: An Ecologist's Personal Investigation of Cancer and the Environment*, *Having Faith: An Ecologist's Journey to Motherhood*, and *Raising Elijah: Protecting Children in an Age of Environmental Crisis*.
1:30 – 2:15 p.m.	**Children's Environmental Health Research—Past, Present and the Future** *James H. Johnson, Jr., Ph.D., Director* *National Center for Environmental Research* *U.S. EPA/ORD* *Ramona Trovato, Associate Assistant Administrator* *U.S. EPA/ORD* *Ken Olden, Ph.D., Sc.D., L.H.D., Former NIEHS Director* *National Center for Environmental Assessment* *U.S. EPA/ORD* *Gwen W. Collman, Ph.D., Director* *Division of Extramural Research and Training* *NIEHS*	
2:15 – 3:30 p.m.	**Session 3: Risks to Children's Health: Chemicals in Consumer Products** *Moderators: Kim Harley, Ph.D., and Maida Galvez, M.D., M.P.H.* Increasing concern has been paid to children's exposure to chemicals found in common consumer products. Household items of concern include: furniture and electronics (containing flame retardants); cosmetics and personal care products (containing phthalates, triclosan and other phenols); food storage containers (containing BPA); and children's toys (containing phthalates and metals). This session focuses on recent epidemiologic studies that are advancing our knowledge of the health effects of these chemicals and examining trends and changes in exposure over time. Attendees also will learn methods for communicating with patients about risks and lowering exposure and information on current policy and regulations.	
	Health Effects of Chemicals in Consumer Products: Flame Retardants *Kim Harley, Ph.D.* *University of California, Berkeley*	This presentation summarizes recent findings from the CHAMACOS birth cohort study and other studies on the effects of PBDE flame retardants on thyroid hormone function, neurodevelopment, and obesity. Additionally, we will examine what is known about the new flame retardant chemicals being used as replacements for PBDEs.

	Chemicals in Consumer Products: Trends in Exposure and New Chemicals of Interest *Antonia Calafat, Ph.D.* *National Center for Environmental Health, U.S. Centers for Disease Control and Prevention (CDC)*	Synthetic chemicals, such as phthalates or bisphenol A (plasticizers), parabens (preservatives), triclosan (antimicrobial agent) and benzophenone-3 (sunscreen agent) can be used in personal care products, medications, paints, adhesives and in some medical products. Because several of these chemicals have demonstrated toxicity in experimental animals, alternative chemicals are entering the consumers market. Biomonitoring can be used to assess human exposure to the replaced, as well as to the replacement, chemicals and to evaluate exposure trends.
	Chemicals in Consumer Products: An Overview of Clinical Questions to the PEHSU *Maida Galvez, M.D., M.P.H.* *Icahn School of Medicine at Mount Sinai*	Families today are deluged with headlines about environmental threats to children's health present in consumer products, including children's toys, furnishings and personal care products. They often turn to their physicians for answers. However, health care providers often lag behind their patients with respect to knowledge about environmental chemicals. This presentation focuses on examples and experience from the PEHSU National Network in translating emerging science on chemicals in consumer products to action.
	Chemicals Management Policy: Where Do Consumer Products Fit? *Jerome A. Paulson, M.D.* *The George Washington University*	This presentation looks at some of the laws and regulations that attempt to protect the public by managing (or not) the health threats of chemicals contained in consumer products.
	Panel	Question-and-Answer
3:30 – 3:50 p.m.	**Break**	
3:50 – 4:20 p.m.	**Highlight—15 Years of the CEHC Program** *Brenda Eskenazi, Ph.D., M.A.* *University of California, Berkeley* *Frederica Perera, Dr.P.H., Ph.D.* *Columbia University* *Elizabeth Matsui, M.D., M.H.S.* *The Johns Hopkins University*	

4:20 – 5:35 p.m.	**Session 4: New Findings and Tools for Understanding the Effects of Early Exposures on Brain Function** *Moderator: Elaine Faustman, Ph.D.* A tremendous increase in the availability and application of brain imaging and functioning has opened many opportunities to better understand early brain development and how this can be impacted by environmental influences. The purpose of this session is to understand new techniques in brain imaging and how they relate to functional and diagnostic changes. Human evidence across examples of developmental neurotoxicants will be presented, using case studies. Immune system function also has proven that these pathways may contribute to and be impacted during neurodevelopmental disorders. This session ends with a panel discussion that identifies new opportunities for application as well as discussion on how these novel methods will impact clinical practice.
	What Can Brain Imaging Tell Us: The Case of Organophosphate Insecticides *Virginia Rauh, Sc.D.* *Columbia University*	Recent work suggests that prenatal exposure to organophosphate insecticides is associated with deficits in birth weight, early cognition and behavior problems in childhood. This presentation focuses on advances in neuroimaging that provide a window into the structural brain disturbances that underlie these impairments.
	Environmental Toxicant Exposure and Immunological Susceptibility: The Case of Autism *Judy Van de Water, Ph.D.* *University of California, Davis*	Characterization of the relationship between the immune and neuronal systems and their synergy with respect to environmental exposure is key to understanding the mechanisms through which toxicants can alter neurodevelopment, resulting in disorders such as autism. Emerging science concerning the role of environmental toxicant exposure in immune dysregulation in autism spectrum disorder (ASD) suggests that children with ASD have a differential ex vivo response to the toxicant BDE-49 as compared to typically developing control children.
	The Impact of Early Environmental Exposures to Lead on Adult Neurodevelopmental Status: Neuroradiological and Behavioral Assessments *Kim Dietrich, Ph.D., M.A.* *University of Cincinnati College of Medicine*	Many of the most important effects of early environmental exposures are only revealed in the fullness of time. Adult outcomes of urban inner-city subjects exposed to lead as infants and children are indexed using advanced neuroradiological and behavioral assessment tools. The current status of adult subjects enrolled in the Cincinnati Lead Study will be presented, including Magnetic Resonance Imaging (vMRI, fMRI, MRS, DTI) and behavioral adjustment studies as they reach their early 30s.

	Translation and Communication of Emerging Methods and Opportunities to Impact Clinical and Research Practice **Discussant:** Elaine Faustman, Ph.D. **Panel:** Virginia Rauh, Sc.D.; Judy Van de Water, Ph.D.; Kim Dietrich, Ph.D., M.A.; Kimberly Gray, Ph.D.; Leslie Rubin, M.D.; and Elaine Faustman, Ph.D.	Translation and communication of emerging methods and opportunities to impact clinical and research practice.
5:35 – 6:00 p.m.	**Keynote** **Could You Make Your Children's Health Research Understandable Even to Children?** *Randy Olson, Ph.D.*	The answer is, "yes," according to scientist-turned-filmmaker Dr. Randy Olson, author of *Don't Be Such a Scientist: Talking Substance in an Age of Style*. He has a new way for you to present your research to the general public, and even to children (provided they have Ph.D.s—no, just kidding). It's called the WSP Model, which stands for one Word, one Sentence and one Paragraph. But wait—there's more! At the core of the model are two templates—the ABT (And, But, Therefore) and the Logline. Most importantly, he and his colleague Dorie Barton have put this model into the CONNECTION STORYMAKER app, where you can put it to work for your own communications needs. In this session, they will show you how this new model provides a pathway to telling stories that are concise, clear and compelling—even to children (provided they have Master's degrees—no, just kidding again).
6:00 – 7:00 p.m.	**Poster/Networking Session**	

October 30, 2013

8:00 a.m.	**Registration**	
8:30 – 9:45 a.m.	**Session 5: Next Steps for Collaboration Between the Children's Environmental Health Centers and the Pediatric Environmental Health Specialty Units** *Moderator: Pam Maxson, Ph.D.* This session will highlight how effective collaborations that capitalize on research, clinical, NGO and governmental expertise can lead to important gains for the CEHCs, PEHSUs and the environmental health field. The presentation will give some concrete examples of current successful partnerships and ideas for future partnerships. The remainder of the session will be used for group dialogue and brainstorming on potential collaborations in the near future.	
	Session Overview *Pam Maxson, Ph.D.* *Duke University*	Introductory Remarks

	Why We Should Collaborate? *Patrice Sutton, M.P.H.* *University of California, San Francisco*	This presentation highlights the importance of collaboration and partnerships for researchers, clinicians and the field of pediatric environmental health.
	Overarching Ways to Collaborate *Susan Buchanan, M.D., M.P.H.* *University of Illinois*	This presentation focuses on systems-based ways for the PEHSUs and CEHCs to collaborate.
	Specific Ideas and Examples for Collaboration *Sheela Sathyanarayana, M.D., M.P.H.* *University of Washington*	This presentation focuses on examples of current collaborations and ideas for future collaborations.
9:45 – 10:55 a.m.	**Session 6: Social Context of Environmental Exposures** *Moderator: Marie Lynn Miranda, Ph.D.* This session examines the social context of environmental exposures in children's environmental health. Animal models are used as a means to understanding combined social and environmental stress. The session includes, discussions on the progress made in modeling issues that children face, in assessing risk, and incorporating knowledge from the animal models into epidemiological work.	
	Prenatal Stress and Neurotoxic Metals: If One is Bad, Then Two Must Be…? *Deborah Cory-Slechta, Ph.D.* *University of Rochester Medical School*	This presentation describes cumulative central nervous system toxicity in rodents that results from combined exposures of prenatal stress with lead or methylmercury, risk factors that are co-occurring in the human environment, and that share biological substrates and produce common adverse outcomes.
	Maternal Stress and Pollution: Rewiring Brain in Offspring *Richard L. Auten, M.D.* *Duke University Medical Center*	This presentation provides research findings which confirm that combined respiratory exposure to diesel particles and social stress during pregnancy increase the vulnerability of offspring to impaired postnatal brain development.
	An Ecological Approach to Human Health Studies and Health Promotion *Mark Miller, M.D., M.P.H.* *University of California, San Francisco, PEHSU*	Addressing social and cumulative impacts may be a powerful way of building collaborative efforts among traditionally disparate groups. Opportunities for researchers, clinicians and policy makers include development of studies that reflect "real world" conditions, as well as evaluating practical interventions that work across sectors.
	Panel	Question-and-Answer
10:55 – 11:20 a.m.	**Break**	
11:20 – 11:30 a.m.	**Highlight – 15 Years of the CEHC Program** University of Washington	

11:30 a.m. – 12:30 p.m.	**Session 7: The Clinical and Translational Implications of Epigenetics in Children's Environmental Health** *Moderator: Joe Wiemels, Ph.D.* Epigenetics is a "hot" topic in basic research, but the field's impact on public health is yet to be determined. This session reviews the foundations of epigenetic programming in humans during development and how perturbations in this process impact children. Epigenetics provides researchers with a whole new set of biomarkers for identifying both exposures and disease, and will likely lead to new tools for population and clinical research. Ultimately, the power of manipulating epigenetic processes will be realized in the clinic, leading to new therapeutics. Following an overview of the field, we will first learn about how environmental chemicals (BPA and lead) directly impact epigenetic processes using an animal model, and then discuss the use of epigenetics in understanding mechanisms of environmental agents in disease causation in a longstanding cohort with precise and multiple exposure metrics.	
	The Role of Epigenetics in the Spectrum of Human Health: From Basic Development Processes to Population Research and Therapeutics *Joe Wiemels, Ph.D.* *University of California, Berkeley*	An introduction to epigenetics research and its potential impact on biomedical research and clinical practices.
	How Early BPA, Lead and Phthalates Exposures Alter the Epigenome and Health Outcomes Later in Life *Dana Dolinoy, Ph.D.* *University of Michigan*	Environmental exposures during early development induce changes to the epigenome, resulting in potentially harmful phenotypic effects, including metabolic disease, cancer and neurological disorders. Utilizing a multipronged approach with an *in vivo* mouse model, human clinical samples, and an ongoing 15-year longitudinal epidemiological study, the overall goal of this presentation is to elucidate the impact of perinatal BPA, phthalates and lead exposures on metabolic homeostasis and DNA methylation, and the interplay between the two.
	Mechanistic Pathways Between Environmental Exposures and Epigenetic Changes *Frederica Perera, Ph.D., Dr.P.H.* *Columbia University*	This presentation focuses on applying epidemiology to understand the mechanisms whereby environmental exposures cause epigenetic changes that affect human health.
	Panel	Question and Answer

12:30 – 12:55 p.m.	**Keynote** **Protecting ALL Children's Health: Recognizing and Mitigating the Effects of Chronic Exposure to Adversity** *Gail Christopher, D.N.* *Kellogg Foundation*	Promoting the health and well-being of our Nation's vulnerable children requires the social determinants of health (SDoH) framework. In the United States, the SDoH framework must include a racial equity and racial healing lens. This talk will explore programs that are using innovative approaches to mobilize and support communities in their efforts to protect children and enhance their well-being.
12:55 – 1:00 p.m.	**Closing Remarks**	
1:00 p.m.	**Adjournment**	

Protecting Children's Health for a Lifetime: Environmental Health Research Meets Clinical Practice and Public Policy

Omni Shoreham Hotel, 2500 Calvert Street, NW, Washington, D.C.

Tuesday, October 29 – Wednesday, October 30, 2013

MEETING SUMMARY

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TUESDAY, OCTOBER 29, 2013

Welcome and Opening Remarks

Lek Kadeli, Principal Deputy Assistant Administrator, Office of Research and Development (ORD), U.S. Environmental Protection Agency (EPA)

Gina McCarthy, Administrator, EPA

Linda Birnbaum, Ph.D., D.A.B.T., A.T.S. Director, National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH)

Mr. Lek Kadeli, the Principal Deputy Assistant Administrator for EPA's Office of Research and Development (ORD) welcomed the meeting participants to the Children's Centers annual conference. He began his address by recognizing Children's Health Month as well as the opportunity to celebrate the 15th anniversary of the Children's Environmental Health and Disease Prevention Research Centers (CEHC, Children's Centers). Mr. Kadeli noted that this EPA and NIEHS partnership has both grown in strength and helped establish the foundation for children's environmental health research. He noted that progress made by the Children's Centers has increased knowledge about how environmental, genetic, and epigenetic components may be linked to conditions common in children, such as asthma and neurodevelopmental deficits. Mr. Kadeli emphasized the need for leveraging resources, establishing partnerships, and developing a collaborative network in order to further improve children's health. He recognize the Pediatric Environmental Health Specialty Units (PEHSUs) which are jointly funded by EPA and the Agency for Toxic Substances and Disease Registry (ATSDR) and can help translate the findings of the Children's Centers and others for use by clinicians and the general public. Mr. Kadeli reflected on the opportunity provided by this conference to explore connections between research findings, clinical practice, and community outreach. These connections are vital to protecting children from harmful environmental exposures. Mr. Kadeli introduced EPA Administrator, Gina McCarthy and invited her to address those gathered. Administrator McCarthy warmly greeted meeting participants and expressed appreciation to everyone working on children's environmental health issues within EPA, NIEHS, the research community and the public. The Administrator recognized those present at the

meeting for the work that they do - whether physicians, nurses, other health care providers, scientists, NGO's, parents and family members. She said that those present are driving the EPA and the Federal Government to do better work to try and identify the real challenges that face our children. While honored to be working towards this goal as the EPA Administrator, she is also the mother of three children. EPA is essentially a public health organization with tools that can drive protection of public healthEPA is a public health organization that relies on partnerships with the scientific research community to obtain information that can inform health policy. Successes such as the 92 percent drop of the median concentration of lead in blood in 5-yearold children between 1976 and 2010 resulted from efforts to remove lead from gasoline and paint. Other successes have been achieved in policies related to water, land cleanup and air issues. The Clean Air Act (CAA) is among the most successful public health statutes ever passed in the United States and has proven to save lives and money. EPA has addressed significant air issues (e.g., particulate matter [PM], sulfur dioxide, mercury exposure), however many challenges remain. Information on indoor air quality, asthma and other topics are still needed and should be delivered in a way that allows families and communities to improve their lives. Climate change poses significant challenges to health and the environment, as increases in the ozone are expected to exacerbate asthma and result in more wildfires and storms. EPA has invested $50 million in developing partnerships and looks to the academic community for research and guidance in applying the knowledge gained. Administrator McCarthy said that the heart of her message to meeting participants is that EPA is their partner in protecting public health. She highlighted the importance of the 15 year partnership between EPA and NIEHS with an investment of over $150 million into more than 20 Children's Centers. This program has created leaders in the field of childrens environmental health who have collaborated to translate their research into actions. The Administrator concluded her address by saying that EPA and its partners need to run faster in this mission, and she thanked participants and the research community for their willingness to be in a sprint for this marathon, applying their practical knowledge, enthusiasm and relationships to move ahead. EPA remains a strong ally in this endeavor.

Dr. Linda Birnbaum, NIEHS Director, reviewed key milestones in the history of NIEHS/EPA-supported children's environmental health research, starting with the Pediatric Environmental Research Workshop in 1993 and the establishment of the joint CEHC Program in 1998 in response to Executive Order 13045 to protect children from environmental health risks. The Program was expanded over the years and totals 14 Centers in 2013. NIEHS funds more than 300 other child health-related grants as well. Dr. Birnbaum expressed the Institute's commitment to continue funding the Children's Centers program despite the constrained fiscal environment. NIEHS support for children's health funding totaled $112 million in the 2012 fiscal year, of which approximately $20 million supported the Centers. There is broad interest in looking beyond easy measurements and considering functional outcomes in areas that affect children, including at conception, *in utero* and during childhood/development.

The CEHC Program goals are to better understand the environmental factors affecting children's health and turn research into treatment and interventions through establishing a national network of multidisciplinary teams that involve communities at the outset. She noted that innovative approaches are needed to address key research challenges, including low-level

exposures; the vulnerability of children (i.e., higher risks); and the complex and combined nature of exposures. Community outreach and translation activities are a key component of the Children's Center's program addressing the need to translate science to help communities, physicians and policymakers reach the target audiences, including nurses, health educators, children health advocates and professional societies as well as local and state governments. The PEHSUs play a key role in disseminating information to providers, serving as a resource for physicians, as well as in community practice. Dr. Birnbaum cited several studies where scientific evidence has led to policy changes. The studies showed the relationship between prenatal exposure to organophosphate (OP) and a seven point IQ deficit in children. These studies resulted in two landmark bills in New York City to reduce exposure to pesticides at the household level. The translation of research into policy is needed to protect children worldwide as borders cannot contain contamination; science underpins policy and action, and collaborative research strengthens the knowledge base and can elevate environmental health issues to impact global policies.

Dr. Birnbaum informed participants that earlier this year the World Health Organization (WHO) re-established NIEHS as a partner in the Children's Environmental Health Sciences Collaborating Centers. Joint areas of interest include: cook stoves, the fetal basis of adult diseases, climate change and human health, e-waste, and training and education. Recent activities have included a workshop on e-waste and child health and a consortium conference. The Fourth International Conference on Children's Environmental Health is planned for 2015 in Bangkok and will focus on e-waste. Goals for the next generation of Children's Centers include supporting the Centers' network, strengthening basic science, retaining the emphasis on dissemination and translation, continuing training opportunities and supporting existing and developing new community partnerships. New areas and approaches include epigenetics as well as the microbiome, "omic's" approach, exposome and pathway analysis and the development of new technologies, biomarkers of disease and exposure, and environmental sensors.

SESSION 1: HOT TOPICS IN FOOD SAFETY AND CHILDREN'S HEALTH

Moderator: Brenda Eskenazi, Ph.D., University of California (UC), Berkeley

BPA and Children's Health: Updates on Food Packaging Exposure and Health Effects

Lesliam Quirós-Alcalá, Ph.D., UC Berkeley

Bisphenol A (BPA) is a high-volume production chemical present in many consumer products, with an estimated six billion pounds produced each year. Food is thought to be the dominant source of human exposure, but other routes of exposure are also plausible. Researchers are concerned about BPA exposures because BPA is an endocrine disruptor that can leach into food and water. Human exposure is nearly ubiquitous; BPA is found in 93 percent of the U.S. general population and in 96 percent of U.S. pregnant women. A 2008 National Toxicology Program Report has also expressed concerns that BPA could affect human development.

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) studied the effects of BPA exposure in a cohort of 601 pregnant women in Salinas Valley, California. CHAMACOS also followed the children from pregnancy through age 12, with special focus at prenatal, 5 years and 9 years of age. The women were receiving prenatal care at community

clinics, were less than 20 weeks gestation when entering the study, were at least 18 years old and were receiving state government assistance. The mothers primarily were born in Mexico (85%); living within 200 percent of the poverty line (96%); had a sixth grade education or less (44%); worked in agriculture during pregnancy (44%); and had other agricultural workers in their household (84%). The study assessed the levels and predictors of BPA exposure and considered the association of prenatal and/or childhood BPA exposures with thyroid hormone levels, behavior and obesity. Higher BPA concentrations were seen in mothers who had lived longer in the United States and had a higher soda and hamburger consumption. In addition, higher BPA concentrations were found in children (age 9) who were obese, had higher soda consumption, and consumed school lunches. Prenatal BPA exposure may be associated with decreased thyroid hormone, T4, in mothers, decreased thyroid stimulating hormone (TSH) in boys, increased internalizing behavior problems in boys and decreased body mass index (BMI) in girls, particularly at younger ages and prepuberty. Childhood BPA exposure may be associated with internalizing behavior problems in both boys and girls as well as attention deficit/hyperactivity disorder (ADHD) in girls. A number of BPA substitutes have been developed, but they have been found to be structurally similar to BPA and could pose similar health problems.

Pesticides and Children: State of the Science of Exposure Assessment and Health Effects
Brenda Eskenazi, Ph.D., UC Berkeley

The Food Quality Protection Act of 1996 charged EPA to determine the safe levels of pesticide residues in food. California is the leading agricultural state in the United States, and Salinas Valley is the "salad bowl" of the Nation. CHAMACOS is a longitudinal birth cohort study that enrolled women in 1999–2000. Pesticides studied in the cohort included OPs, pyrethroids, methyl bromide and fungicides. OPs are acute neurotoxins that depress acetylcholine, cause over-excitation of the central nervous system, and were widely used in homes before mid-2000s. Chlorpyrifos (CPF) was removed from home use in 2001 and diazinon in 2004. OPs account for approximately 35 percent of all insecticides used, mostly in California. OPs degrade quickly and are excreted in urine as dialkyl phosphate (DAP) metabolites and many measure DAPs as a measure of exposure, although they do have limitations. DAPs fall into two classes: dimethyl and diethyl reflecting the OPs from which they devolve.

Research found that CHAMACOS participants had OP metabolites higher than U.S. averages. Nearby agricultural use of CPF was associated with home dust levels, and some OP pesticides were seen in breast milk. In addition, studies showed that mothers' OP pesticide levels during pregnancy were associated with shortened gestation, abnormal neonatal reflexes, decreased mental development at age 2, poorer verbal abilities, autism-like behaviors and attention problems in school-age children. Other studies also have reported an association between OP pesticides and IQ in school-age children.

A study by the Columbia Center for Children's Environmental Health (CCCEH) found a correlation of brain surface measures with CPF exposure levels. Additional research by CERCH examined whether the susceptibility to OPs varies by individual and determined that the level and efficiency of paraoxonase, an enzyme that detoxifies OPs in the body, depends on genetics

and age. This enzyme is coded by the PON1 gene. We have seen associations suggesting that PON1 may modify the relationship of DAPs and mental development.

Other types of pesticides have been found to have deleterious health associations. CHAMACOS detected pyrethroids in dust and breast milk in both farmworker and urban homes. A general metabolite of pyrethroids that has been related in the literature to cognitive and behavioral development in children. Pregnant women living close to strawberry fields where the fungicide methyl bromide is applied experienced lower birthweight. CHAMACOS also looked at maneb and mancozeb, which are fungicides applied to lettuce and are 21 percent manganese by weight. Manganese is an essential nutrient at low doses but a neurotoxicant at high doses. Manganese prenatal tooth concentration can be measured via growth rings in teeth, similar to tree growth rings. It was associated with agricultural work, soil type at the residence and manganese dust loading.

Dr. Brenda Eskenazi highlighted areas for future work. In Costa Rica, manganese-containing fungicides are applied by air, and much higher levels will likely be seen than those in the CHAMACOS study, where it is applied by tractor. During the past 20 years in California, the agricultural use of OPs has decreased, and the certified organic cropland increased. Challenges remain, however, and the Berkeley Food Institute has been established to address food insecurity and other complex issues faced by CHAMACOS children and their families.

Arsenic in Food and Children's Health: Updates on Exposure Assessment and Health Effects Research

Kathryn Cottingham, Ph.D., Dartmouth College

Evidence is emerging about the impact of high levels of arsenic exposure on children's health, including pulmonary, immunological, growth and neurodevelopmental effects. Chronic effects of low-dose exposure have not been studied but also are of concern to researchers. Children are exposed to arsenic in numerous ways, such as private (well) water, which is not regulated, as well as various foods. The health effects of dietary arsenic, however, have not been well studied. There are significant differences between organic and inorganic arsenic and rice and other commonly available foods contain both types, posing challenges to health researchers. Inorganic arsenic is known to be highly toxic. In 2009, the European Food Safety Authority reported that exposure to inorganic arsenic via diet could be two to three times higher for infants and young children than for adults.

Dr. Kathryn Cottingham described the Dartmouth Children's Center Project 2 that used a prospective birth cohort to predict pregnant women and children's potential exposure to arsenic via food and water and to compare to measured biomarkers of exposure. The cohort's geographic region is an area with many private well users, and more than 1,000 mother/children pairs were recruited. During pregnancy, the researchers found that predicted urinary arsenic concentrations were equal for eating one-half cup of cooked rice and drinking 1 liter of water at the current USEPA maximum contaminant level (10 µg/L). During early infancy, predicted arsenic exposure and infant urinary arsenic concentrations are both low, with breast-fed infants less exposed than formula-fed infants. Rice cereal is the first of many foods high in arsenic that will increase exposure, including inorganic arsenic levels up to four

times higher than in infant formula. In addition, "hidden" rice in packaged foods likely will be an issue as diets increase in complexity.

Overview and Role of Improving Food Safety through Strategic Science, Communication and Advocacy

Michael Crupain, M.D., and Urvashi Rangan, Ph.D., Food Safety and Sustainability Center, Consumer Reports

The mission of *Consumer Reports* is to work for a fair, just and safe marketplace for all consumers and to empower consumers to protect themselves. This includes food safety. The *Consumer Reports'* Consumer Safety and Sustainability Group (CSSG) conduct strategic science, that is, a systemic study of issues critical to public health. The process involves defining the public health problem; measuring the magnitude of the problem; identifying key determinants (e.g., political, social, biological, environmental) and stakeholders; designing and implementing interventions (e.g., policy, advocacy, education); and developing and executing a communication strategy. This process was used in an examination of increased exposure to inorganic arsenic among adults and children consuming rice in the United States from 1991–2012.

The magnitude of the problem was shown through review of biomonitoring studies (e.g., National Health and Nutrition Examination Survey [NHANES]), government reports, and a *Consumer Reports* study that found relatively high levels of arsenic in rice and rice products. The CSSG conducted a risk assessment, for combined risk of lung and bladder cancer, focused on arsenic levels in rice as a basis for advice to consumers on ways to reduce health risks from arsenic exposure. Key determinants included several environmental, cultural, agricultural and political factors: arsenic is used as a pesticide; some cultures consume greater quantities of rice; arsenic is traditionally fed to chickens, and chicken manure is used as fertilizer on rice fields; and there are no limits for arsenic levels in food. Government agencies, rice consumers and growers, schools, and restaurants are among the numerous stakeholders to consider. Optimal interventions to protect public health include setting limits for the arsenic levels permitted in rice, educating consumers, banning arsenic in rice production, and increasing support for arsenic abatement research.

The CSSG's communication strategy about the findings of arsenic exposure in rice included identifying the information needs of stakeholders and anticipating barriers as well as preparing "talking points" to ensure that the message is clear and consistent, tailored to the specific audience and presented in a way that does not overwhelm anyone receiving the message. In addition, focus groups could facilitate a clear message, and the message should be kept in context for the media to avoid misunderstanding or misrepresenting it. For example, for the goal to educate and motivate the U.S. Food and Drug Administration (FDA) to set a limit for arsenic in rice, the communication strategy included publishing a report about the problem of arsenic in rice, how it happens, what the risk is, and how consumers can take action. Prior to publication, however, press releases were prepared with special attention to the sequence of the information and tone in quotations, specific media were contacted and an infographic was created for social media. CSSG engaged key stakeholders by briefing lawmakers, helping to

draft legislation, briefing medical and academic organizations to help answer questions about arsenic exposure, and holding many meetings with FDA and other government agencies. A concerted effort was made to communicate a consistent message throughout these activities. Work continues in developing guidance on the benefits of varied diets as well as vulnerable population guidance. The outcome is that the FDA is continuing to study arsenic levels in rice and considering actions. Also FDA has removed approval for 3 out of 4 arsenic drugs approved for use in food animal production.

Panel

Questions and Answers

Dr. Birnbaum asked about confidence in the accuracy of using spot urine tests in pregnant women to measure BPA exposure, and she suggested that the topic of how best to measure BPA would benefit from further discussion by the research community. Integrated exposure might best be obtained from multiple 24-hour urine collections. She also noted that dust is a significant source of exposure. Dr. Lesliam Quirós-Alcalá acknowledged these as challenging areas, and Dr. Eskenazi confirmed the lack of good exposure biomarkers for urine measurements in pesticide studies. Another participant emphasized the importance of variability and contributing factors in OP exposure, citing research that shows close correlation to the parent compounds in blood and advocating for repeat measurements to capture episodic data and better understand the full range of exposures.

Dr. Mateusz (Matt) Karwowski, Boston Children's Hospital and PEHSU Region 1, asked whether Dr. Quirós-Alcalá's research group had examined combined effects of prenatal and early childhood BPA exposure. Dr. Kim Harley, UC Berkeley, replied that limited measures for exposure were included.
Dr. Katharine Hammond, UC Berkeley, commented that better exposure methods are needed but reminded participants that because the randomness classification of exposure presents biases, underestimation occurs.

Dr. Ed Levin, Duke University, asked about interactions with drugs, such as ADHD therapies and abuse of drugs. Dr. Eskenazi indicated that reported drug use, smoking and drinking are minimal in the CHAMACOS study, but these issues will be areas for the study to watch as the children age.

A participant considered intra/inter-individual variability and wondered whether repeated individual measurements during pregnancy or postnatal periods have shown associations between exposures and the consistency in the ordinal ranking of children. The response was that brain correlations remain at a low level.

TRIBUTE—PROFESSOR PATRICIA BUFFLER

Colleagues and friends paid tribute to Dr. Patricia Buffler, EPA/NIEHS Children's Center Director, UC Berkley, an internationally renowned researcher in childhood leukemia and environmental health who passed away in 2013. Dr. Buffler's contributions to children's environmental health and biomedical research were described, including leukemia research, cancer prevention, data sharing and research in the global environment. Dr. Gwen Collman (NIEHS), Dr. Joe Wiemels

(UC San Francisco), Dr. Catherine Metayer (UC Berkeley), Dr. Deborah Cory-Slechta (University of Rochester Medical Center) and Dr. Brenda Eskenazi (UC Berkeley) shared their remembrances about Dr. Buffler's vision, enthusiasm, optimism, mentorship and mediation abilities. Dr. Buffler loved people, celebrated life, and had a sense of both aesthetic beauty and fun. She will be remembered and missed for her graciousness, generosity and commitment to health science research.

SESSION 2: AIR POLLUTION UPDATE: UNRAVELING THE SCIENCE, MAKING A DIFFERENCE

Moderator: Catherine Carr, M.D., Ph.D., University of Washington

Airborne Endotoxins and Asthma Morbidity in the Inner-City: Friend or Foe?

Elizabeth Matsui, M.D., The Johns Hopkins University

Endotoxin is a component of Gram-negative bacteria that interacts with the human immune system through toll-like receptor 4 (TLR4) to produce an inflammatory response. It has been associated with adverse health outcomes in occupational settings and wheeze in US children but has protective effects on eczema in children. In a U.K. Birth Cohort Study, higher endotoxin exposure decreased the risk of dust mite sensitivity. The JAX Cohort Study found a bell-shaped dose- response between mouse allergen exposure and incident mouse sensitization that was damped with high endotoxin exposure.

Dr. Elizabeth Matsui suggested that endotoxin might interact with pollutants that affect TLRs such as cigarette smoke, which activates TLR4, and nitrogen dioxide (NO_2), which may indirectly activate TLR2. In the Mouse Allergen and Asthma Cohort Study, Dr. Matsui and her colleagues followed youths from Baltimore City with persistent asthma, conducting quarterly clinical assessments and exposure assessments of indoor air quality for PM, NO_2, nicotine and endotoxin in PM_{10}. They used a recently developed endotoxin assay, the recombinant factor C assay, to measure endotoxin since it is specific to endotoxin, discriminating between endotoxin and fungal glucans. The study population was predominantly male, black and impoverished, with clinical characteristics that included high rates of sensitization to mouse allergen. There was a smoker in approximately one-half of the homes, and indoor PM levels were high. The only correlation of air endotoxin with allergens and pollutants was with mouse allergens. In the setting of high nicotine exposure, higher endotoxin exposure increased the risk of asthma morbidity, whereas in the setting of high NO_2 exposure, higher endotoxin had a protective effect against asthma morbidity. A biological mechanism for the interaction between endotoxin and cigarette smoke is that cigarette smoke exposure enhances TLR4 expression and activity. Dr. Matsui proposed that in contrast, since NO_2 activates TLR2, and activation of TLR2 can dampen TLR4 signaling, that this mechanism could explain NO_2's attenuation of endotoxin's effects on asthma morbidity. She concluded that among urban children with asthma, the effects of endotoxin exposure on asthma are modified by exposure to indoor pollutants, with nicotine having deleterious effects and NO_2 enhancing the protective effects of endotoxin against asthma. These results imply that environment-environment interactions need to be considered in studies of the effects of the environment on asthma, and the effects of interventions might not be as predicted.

Questions and Answers

Dr. Nicholas Newman, University of Cincinnati, asked whether the air monitoring in Dr. Matsui's study was exclusively indoors. She answered that it was all indoor monitoring, and that indoor levels of PM and NO_2 from past studies in Baltimore have shown that they always are much higher than ambient levels.

Early Life Traffic Pollution Exposure and Behavior at School Age

Nicholas Newman, D.O., University of Cincinnati, Cincinnati Children's Hospital

Dr. Newman told participants that ADHD is characterized by inattentiveness and hyperactivity, affecting approximately eight percent of U.S. children in the 4- to 15-year-old age range. It has been associated with environmental exposures to tobacco smoke and blood lead levels. Dr. Newman and his coworkers studied the role of another environmental exposure, traffic-related air pollution (TRAP), in ADHD. TRAP is a complex mixture of fine and ultrafine particles, as well as gases, that is a byproduct of internal combustion. As a surrogate for TRAP, the researchers measured elemental carbon particles attributed to traffic, which are ultrafine, contain toxic compounds on their surfaces and a carbon core, and have been shown to translocate to the brain, liver, spleen and kidneys. They affect the body by causing oxidative stress at the cellular level. Previous studies have associated black carbon, NO_2 exposure, polycyclic aromatic hydrocarbons (PAHs) and mixed particulates in decreased cognition in children; the researchers hypothesized, therefore, that TRAP might affect behavior and in particular hyperactivity, which is a symptom of ADHD.

Participants were recruited from the Cincinnati Childhood Allergy and Air Pollution study (CCAAPS), and followed from birth to 7 years-of-age, with land use regression modeling used to estimate TRAP exposure. Behavior was assessed using the Behavioral Assessment System for Children-Parent Rating Scale, 2nd Edition (BASC-2), for which T score of greater than 60 is interpreted as being at risk for ADHD and greater than 70 indicating clinical ADHD. The researchers discovered that in an unstratified population, hyperactivity was not significantly associated with TRAP exposure when adjusted for confounding factors such as cigarette smoking. When children were divided into groups depending on whether their mothers were educated beyond high school, TRAP was associated with hyperactivity, but only for those with more highly educated mothers. Dr. Newman speculated that more highly educated parents might be more likely to report ADHD, or a stronger signal correlated with maternal education might be obscuring the effects of TRAP. The biological plausibility of TRAP exposure being associated with ADHD is that it is associated with neuroinflammation and mucosal inflammation of the respiratory tract, and the dopaminergic pathways associated with ADHD might be particularly sensitive to oxidative stress. Strengths of the study include that the cohort held together, exposure was well-characterized and BASC-2 is a well-validated instrument; the limitations are reduced generalizability from an atopic cohort, lack of family mental health history and lack of blood lead levels. Ongoing studies with the CCAAPS cohort involve neuroimaging, extensive neurobehavioral assessment, additional biomarkers, collecting information about parents, extending exposure estimates beyond the first year of life and exploring gene-environment interactions.

The Impact of Prenatal and Cumulative Exposure to Air Pollutants on Neurodevelopment

Frederica Perera, Dr.P.H., Ph.D., Columbia University

Dr. Frederica Perera spoke about the impact of prenatal and cumulative exposures to air pollutants on neurodevelopment. The CCCEH is conducting parallel studies of *in utero* exposures and childhood disease in New York City; Krakow, Poland; and two areas in China with high levels of coal burning. Rates of neurodevelopmental disorders have been increasing worldwide, with a 20 percent global prevalence of child and adolescent mental disorders and 15 percent of U.S. children affected by neurodevelopmental disorders. Lower income communities of color experience disproportionate exposure and risk, as well as more material hardship. The fetus and children are more susceptible because of differential exposure and higher biological susceptibility.

Researchers are studying multiple exposures and outcomes in the CCCEH cohort, but Dr. Perera focused her presentation on PAHs and neurodevelopment. Combustion is the main source of ambient PAHs. Indoor sources include smoking, cooking and the burning of incense and candles. PAHs have been linked to multiple health outcomes, being both genotoxic and endocrine disrupting chemicals, effects that are particularly harmful *in utero*. The CCCEH New York City cohort enrolled nonsmoking mothers, primarily black and Dominican, mostly low-income, who were recruited during pregnancy and the children were followed through adolescence. Socioeconomic status (SES) and exposure data (e.g., personal monitoring, questionnaires on maternal hardship), biomarkers (i.e., PAH-DNA adducts, PAH metabolites, other potentially confounding toxins, clinical data), and outcomes (e.g., neurobehavioral development) were measured. PAH exposure was estimated by prenatal questionnaires; area and residential monitoring with geographic information systems modeling; personal exposure monitoring with backpack monitors; urinary metabolite measurement for internal dose; and PAH-DNA adduct measurement for biologically effective dose. The researchers found widespread PAH exposure, with all of the pregnant mothers exposed to airborne PAH and having detectable PAH metabolites, all 3-year-olds having detectable metabolites, and 40 percent of cord blood cells having PAH-DNA adducts. Behavioral and cognitive problems in the children were measured using valid, age-appropriate tests. High PAH prenatal exposure was associated with lower mental development and developmental delay at age 3. At age 5, high prenatal PAH was linked to lower full-scale and verbal IQ. At ages 6 to 8, high prenatal PAH, as well as PAH-DNA adducts in cord and maternal blood, were associated with anxiety and depression in children. Maternal hardship, defined as lack of housing, clothes or food, exacerbated the effects of high cord blood PAH-DNA adducts on IQ. The researchers are assessing potential links between cumulative PAH exposure at age 9 on ADHD risk.

In the mother-and-child cohort study in Poland, a higher SES population that was predominantly Caucasian, there were similar links between high prenatal PAH and decreased intelligence scores. In addition, Dr. Perera stated that there was a steeper increase in maternal demoralization because of child behavioral problems in mothers with high PAH exposure. Currently, she is investigating mechanisms with magnetic resonance imaging (MRI), epigenetic analyses and parallel laboratory studies with animal models. Dr. Perera stated that these results

indicate that prenatal and cumulative PAH exposure has continuing effects on child cognitive and neurological development through adolescence, which has implications for children's future; there are interactions with psychosocial stressors; multifaceted interventions are needed to reduce toxic exposures and address social stressors arising from poverty; environmental risks need to be identified early; and benefits from interventions will continue through childhood over a lifetime and potentially across generations.

Air Cleaner Interventions in Asthma—State of the Evidence

Gregory B. Diette, M.D., M.H.S., *The Johns Hopkins University*

Dr. Greg Diette presented evidence about whether portable air cleaners are effective in reducing asthma morbidity. EPA recommends a multimodal approach to asthma that includes minor, moderate and major interventions. Portable air cleaners are classified as a moderate intervention. The recommendations of the National Heart, Lung, and Blood Institute, in contrast, include an approach that focuses on allergen avoidance and maintain that there is insufficient evidence to support the role of pollutant reduction in asthma. The Institute states that air cleaners remove some allergens, but studies have failed to show that they improve symptoms.

Dr. Diette reviewed evidence on the effectiveness of interventions on asthma. A study that reduced indoor pollution with high-efficiency particulate absorption (HEPA) air cleaners and exterminated cockroaches reduced asthma symptoms, indicating that air cleaners are effective as part of a multimodal intervention. In an investigation of asthma in homes with smokers—with control, HEPA cleaner and behavioral coach groups—the coach was ineffective, but the cleaner reduced PM and asthma symptoms. Another study comparing a sham versus active cleaner intervention showed some evidence of benefit from the active cleaner. Dr. Diette emphasized that not all cleaners are HEPA cleaners, which remove PM greater than 0.3 microns in diameter but do not remove gases. NO_2 and nicotine in air both are important in asthma. In Baltimore, unvented gas-burning stoves, which produce high indoor NO_2 from incomplete combustion, are common. Dr. Diette and his team partnered with Austin Air Systems to produce a HEPA cleaner with activated carbon that could remove particulates and vapors. They tested the effectiveness of this cleaner against replacement of gas-burning stoves with electric stoves or venting gas-burning stoves and found that the air cleaner reduced NO_2, but that the stove replacement was much more effective in reducing NO2; venting stoves had no effect. In regard to adoption, the cleaner is easy to use, costs several hundreds of dollars, needs filter replacement periodically and removes NO_2 whether it is from indoor and outdoor sources. Dr. Diette concluded that multimodal intervention is key in asthma to reduce irritants and allergens; air cleaners could be a part of the intervention but source control is ideal. The American Academy of Allergy, Asthma & Immunology now endorses air cleaner use for asthma to reduce allergens and PM.

Translating the Link between Air Quality and Health through Community Engagement and Partnerships

Lisa Cicutto, Ph.D., R.N., National Jewish Health

Dr. Lisa Cicutto stated that Community Outreach and Translation Cores (COTCs) are included as part of the CEHCs because of the lag between discovery and translation to interventions and policy changes. The goal of the Clean Air Projects program is to translate, disseminate and promote uptake of the best research on lung and environmental health to improve the lives of Coloradoans. The COTC's activities are led by a dynamic Community Advisory Board that identified the priority population as children and youth and advised outreach to that population through schools. The COTC used a five-step method to develop curriculum to link air quality and health: (1) identify existing resources, (2) review existing resources, (3) blueprint resources to the state curriculum, (4) solicit input from teachers, and (5) implement the curriculum.

The environmental scan identified needs, preferences and best practices for environmental education through Internet searches, literature searches, a review of an educational software package, examination of curriculum standards and educator interviews. Resources then were reviewed in a two-step process—an initial review followed by an in-depth review—using *a priori* criteria derived from teacher interviews and *Environmental Education Materials: Guidelines for Excellence*. The review criteria included fairness and accuracy, depth, emphasis on critical thinking, action orientation, use of an inquiry-based framework, instructional soundness, ease of use, and applicability to the topic of linking air quality and health. To be useful, it was essential that resources were blueprinted against Colorado's curriculum standards. Concordance was assessed by constructing a matrix of resources and standards for each grade level and marking which standards were met for each resource. Based on the review, resources were categorized as ready to use, needs enhancement or not useful. Ready-to-use resources were inquiry-based, linked air quality and health and presented a complete lesson plan; those that were not useful had problems such as an incomplete lesson plan and inaccurate information. A majority of resources were judged not useful. Most ready-to-use lesson plans were middle school-level, and surprisingly few were aimed at high school students. Resources were disseminated to Colorado educators by creating a website, sending electronic and postal notices to teachers, and conducting professional development seminars.

The project was promoted by EPA Region 8 and the created website was designed to be easy to use. Lesson plans were searchable by topic, grade and learning objective. The website highlighted activities in the community. There have been approximately 4,000 page views, resources are available through the Partnerships for Environmental Public Health Resource Center, and the website continues to be updated with new lesson plans and professional development opportunities. The program received an EPA Environmental Education Grant, which allowed it to fund activities that have included air quality monitoring, anti-idling campaigns and theatrical presentations. This website can be found at www.capk-12.org.

Panel

Question and Answer

A participant asked Drs. Perera and Newman whether, given the effects of PAHs in early childhood, there would be beneficial health effects if EPA prioritized regulating hydrocarbons from gasoline combustion. Dr. Perera answered that likely there would be health benefits, but EPA already regulates PAHs as hazardous air pollutants, although the Agency has not set National Ambient Air Quality Standards (NAAQS) for PAHs. Dr. Newman added that he had not studied PAHs in particular, but evidence is growing for the need to regulate ultrafine particles separately from other PM because the very high surface-to-volume ratio results in more interactions with biological membranes.

Dr. Susan Buchanan, University of Illinois at Chicago, asked Dr. Cicutto about the input that education specialists had provided in curriculum development. Dr. Cicutto replied that to ensure that the resources were used by educators, the researchers had interviewed science and other curriculum specialists from the school district to develop review criteria and rate the collected resources. These educators received a small gift card in compensation.

A participant observed that for targeted and genome-wide association studies, issues of biological plausibility and sample size need to be considered in designing cohort studies, but in a broader context of exploring interactions, he asked about the existence of guidelines for sample size and study design. Dr. Perera agreed that her sample sizes were small, but the conclusions drawn from them are strengthened by replication in different cohorts, over gradients of exposure and in different ethnic groups; in addition, animal experiments indicate similar interactions. Dr. Matsui added that strategies to maximize statistical power when studying the effects of mixtures include dimension-reducing statistical approaches such as principal components analysis, applied either in an unbiased way or to identify clusters of pollutants that are most relevant to a particular health outcome. Another strategy to reduce dimensionality is to use biomarkers of the effects of mixtures of multiple environmental exposures, which could be developed using cellular assays. She acknowledged that sample size becomes problematic when exploring smaller effects.

Dr. Amy Kyle, UC Berkeley, asked Dr. Perera, based on her results on interactions, whether metrics for psychosocial factors and deprivation should be included in most studies of environmental stressors, and if so, the implications of such inclusion for policy change. Dr. Perera responded that goal of all of the meeting participants is to protect the most vulnerable populations, which among children are those with additional types of stress such as poverty that amplify the toxic effects of pollutants. Achieving this goal will require multifaceted interventions that combine addressing the root causes of poverty with reducing environmental exposures.

KEYNOTE

Sandra Steingraber, Ph.D., Ecologist, Author and Cancer Survivor

Dr. Sandra Steingraber began by thanking the scientists working on pediatric environmental health whose research and findings has made her work, as a researcher and writer, possible.

She explained that her research in pediatric environmental health began with her own pregnancy and she became interested in epigenetics and pediatric toxicology. This led her to write two books*, Having Faith,* which focuses on the period of development between conception and breast feeding and *Raising Elijah* which focuses on the effects of endocrine disruptors on children and the timing and tempo of puberty.

Dr. Steingraber stated that her diagnosis with bladder cancer at the age of 20 led her to pursue a career in environmental health. She explained that as a postdoctoral fellow at Harvard in 1993, she had been studying the health effects of perchloroethylene, a known carcinogen, when she received data documenting the presence of the solvent in the drinking water wells where she grew up. She decided to take a leave of absence from research to write and build support based on existing data with the goal of reducing exposures and creating a healthier environment for all children.

Dr. Steingraber addressed the impact of both toxic chemicals and climate change on children's health. She attributed various diseases including asthma, pediatric cancers, early puberty and learning disabilities to the accumulation of toxic chemical pollutants in our bodies. Regarding climate change, she explained how environmental factors such as drought, floods, dying coral reefs and extinction could result in conditions such as asthma, pediatric cancers, early puberty, and learning disabilities. She also addressed the by-products that result from the combustion of fossil fuels and fugitive emissions in the form of methane, which are potent greenhouse gases that cause global warming. Dr. Steingraber expressed concern regarding the use of fossil fuels for making plastics and pesticides since the by-products are known to cause disease. She was also concerned about unconventional means of fossil fuel extraction until it has been sufficiently investigated and there is a better understanding of the public health impact. She stressed the need for renewable energy to protect children from the toxic by-products of fossil fuel combustion and from the consequences of climate change.

Dr. Steingraber closed by stating that it is impossible to make thoughtful policy decisions without adequate data. She exhorted the meeting participants to join her in turning the future of our Nation toward green engineering and green chemistry to help solve the public health problems for which so many scientists in the audience have worked hard to document and provide an intervention.

CHILDREN'S ENVIRONMENTAL HEALTH—PAST, PRESENT AND THE FUTURE

James H. Johnson, Jr., Ph.D., Director, National Center for Environmental Research, ORD, EPA

Ken Olden, Ph.D., Sc.D., L.H.D., Former NIEHS Director, National Center for Environmental Assessment (NCEA), ORD, EPA

Ramona Trovato, Associate Assistant Administrator, ORD, EPA

Gwen W. Collman, Ph.D., Director, Division of Extramural Research and Training, NIEHS

Dr. James Johnson introduced the speakers for the session celebrating 15 years of the Children's Centers Program, mentioning that the session offers a retrospective look at this Program's origins and how the panel members used their expertise and authority to bring

children's environmental health to the forefront and establish such a distinguished legacy. Dr. Johnson thanked the Children's Centers researchers saying that we could not be more grateful to them for their work.

Ms. Ramona Trovato began by describing how the Office of Children's Health Protection (OCHP) was established in 1997 under the guidance of Administrator Carol Browner. She attributed the establishment of OCHP to the incredible work conducted by a coalition of non-profit stakeholders such as the Healthy Schools Network (HSN) and the Children's Environmental Health Network (CEHN) who brought important issues on children's environmental health to the attention of Administrator Browner and many other policy makers.

Ms. Trovato explained that one of the initial challenges had been to identify how the Federal Agencies could best collaborate on children's environmental health. In 1998, NIEHS and EPA formed a partnership to establish the Children's Centers Program, starting with eight Children's Centers. This program benefitted from NIEHS' experience in funding centers with a strong community component. Ms. Trovato stated that the Children's Centers have been critical to environmental health research and she thanked the researchers for their amazing research and work which has translated into better lives for children. She also mentioned the importance of disseminating findings to parents, schools and communities so that they can make good decisions, which is a key component of the Center program. Ms. Trovato also spoke to the tremendous work conducted by the PEHSU program which was conceived by Dr. Robert Amler at ATSDR as well as the Federal Steering Committee. She acknowledged the work of the practitioners in the PEHSU program in helping to improve the health of children, families, and communities.

Ms. Trovato reiterated the EPA mission of protecting the environment and human health – saying that while children comprise 30 percent of the population, they are 100 percent of the future. She closed by stressing the critical role of research in informing public policy and further emphasizing the importance of research translation to action. She thanked the Children's Centers researchers and the PEHSUs for their contributions and ended by saying that she is proud of the way the agencies came together to make a difference for children in the United States and around the world.

Dr. Ken Olden began by thanking NIEHS staff members who encouraged him to work with the EPA. He also thanked the EPA for collaborating with NIEHS to establish the Children's Centers program. Dr. Olden explained that the Children's Centers program was created to address issues of public concern, and the work of the Centers can inform public policy decisions as it relates to human health and the environment.

Dr. Olden recalled his objectives as the new NIEHS Director in 1991 which included making the Institute responsive to the needs of the American people and to reframe the Institute as a public health agency. He continued by saying that as a person who had spent most of his career at NIH, he had a clear vision of the strengths and weaknesses of the Institute. He felt that NIEHS was an outstanding research organization but also believed that the Institute did not focus on public health - which is more about translating the science into practice. Except for clinical work, the investments at NIH cannot impact areas such as prevention which is what environmental health is about.

At the beginning of his tenure, Dr. Olden arranged regional town meetings to talk with professional organizations and the public about how NIEHS could better serve communities. He asked attendees of these town hall meetings about concerns regarding their health as related to the environment. Following an enlightened conversation with Congressman William Natcher regarding his vision for NIEHS, Dr. Olden recognized that the work of the Institute needed to be rebranded, as the significance of the work was not clear to people.

When Dr. Olden became the Director of NIEHS in 1991, he felt that there was a need to abandon the chemical by chemical approach that was being used in years prior – and ask the big questions. The new goal was to identify the big issues that needed to be addressed as a nation in order to improve environmental health decision making. In addition, improving environmental health decisions should be grounded on differences in exposure based on age and stage of development.

Dr. Olden remarked that at that the start of his tenure they did not have good science on environmental health issues. While meeting with people around the country, Dr. Olden realized the importance of representing children's interests – since they cannot lobby or make investments for their own health. He reiterated that his primary motivation for the work of the Children's Centers was to address scientific issues that made sense in the larger context and identify the big issues.

A keystone of the Children's Centers program was to have the first set of Centers announced by Vice President Al Gore at the White House, along with support from then-First Lady Hilary Clinton who was very interested in children's health. Dr. Olden expressed appreciation for the Program's growth from eight Centers in 1998 to 14 Centers in 2013. He continues to follow the Centers' work and said that while living in New York, he was aware of the great work at the Children's Center at Columbia University.

Dr. Olden closed by saying that he could have never imagined all the amazing work done by the Children's Centers and the success and impact of the program 15 years later. He continues to

support the program's development because it provides strong science in an area that needs to be addressed from a global perspective.

Dr. Collman has been part of the Children's Centers Program since the start and acknowledged the many colleagues who have been instrumental in numerous roles. She reflected that watching this Program grow during the past 15 years has been similar to being a parent watching a child grow into adolescence. Parents hope their teenagers start to consider the future and wonder when maturity will come; sometimes there are teenagers who are above average. The Children's Centers Program is like one of those super achieving adolescents—so much has been done in a small amount of time. The Program has built a critical mass of experts and scientists, trained many researchers, worked with communities, and added new cohorts. It has not been a static program. Community partners are mature, and the process has been rewarding.

Dr. Collman highlighted CEHC accomplishments. The Program has produced more than 1,000 publications, created new tools and new technologies, incorporated other areas of science (e.g., epidemiology and exposure assessment), helped develop a deeper understanding of environmental causes of children's health outcomes, and provided evidence for regulatory action. In addition, the Centers' science has contributed to many debates at an international level. Important studies have shown the dangers of high levels of lead, BPA, and pesticides (e.g., DDT), and recent work is demonstrating the link between the onset of obesity and the impact of early life exposures on weight control and eating habits. Multidisciplinary and laboratory research have also elucidated the mechanisms of exposures for childhood cancers. The Centers are committed to working with community groups and helping explain the scientific process and translate information to concerned communities and parents.

The NIEHS uses the finding produced by the Centers in many ways. One way is to review the weight of evidence in order to support National Toxicology Program recommendations. The National Toxicology Program has developed new guidelines to weigh evidence from animal and human studies. Assessments underway or completed include: obesity, diabetes and the role of environmental exposures; air pollution and children's respiratory outcomes; and the translational effect of the chemicals that have been studied. In addition, there is heightened awareness for professional organizations' activity such as through discussion of preventive measures or direct action. The American Academy of Pediatrics, American College of Obstetrics and Gynecologists, and American Heart Association have provided guidelines to their respective constituencies that focus on exposures to chemicals and other agents during pregnancy, early childhood and adulthood.. Three advisory reports prepared by the President's Cancer Panel, Institute of Medicine and Interagency Breast Cancer and Environmental Research Coordinating Committee all call for a life-stage approach of environment exposure to wide range of cancers, encourage the translation of research into the community as soon as possible, and advocate the development and adoption of new tools.

With a strong work base of scientists in the United States, opportunities exist to impact global health. NIEHS has recently become a WHO Collaborating Center and will work as one of eight Collaborating Centers. These centers provide assistance to WHO on a variety of health and

environment topics many of which are rooted in poverty and social inequities, such as exposure to rare minerals and metals and air pollution effects. The Institute welcomes the assistance of U.S. scientists especially from the CEHC program interested in working on environmental and public health issues in communities around the world. Dr. Collman invited participants to the January 2014 meeting in Bangkok, Thailand, to discuss these issues. In addition, a new International Society for Children's Health and the Environment has been established to promote and discuss children environmental health needs and encouraged the active involvement of our grantees in this scientific society. Dr. Collman noted the great strength in Children's Centers Program on its 15th anniversary and invited participants to share ideas on how to move the Program forward even further.

Dr. Johnson thanked the panelists for sharing their insights. He acknowledged their contribute ons in helping forge the strong partnership between EPA and NIEHS and encouraged the Centers to continue the race, stating that they make a difference.

SESSION 3: RISKS TO CHILDREN'S HEALTH: CHEMICALS IN CONSUMER PRODUCTS

Moderators: Kim Harley, Ph.D., and Maida Galvez, M.D.

Session 3 focused on chemicals in consumer products and how they affect children's health. A consumer product, defined by the Consumer Product Safety Commission, is "Any article or component part thereof, produced or distributed for sale to a consumer for use or for the personal use, consumption or enjoyment of a consumer in or around a permanent or temporary household or residence, a school, in recreation, or otherwise." In short, a consumer product refers to everyday items that people have in their homes. These items, including processed foods, food packaging and personal care products, contain contaminants such as BPA, phthalates and nanoparticles. Doctors, in general, are not well informed about the contaminants that exist in consumer products.

Certain segments of the population are better educated and have the financial capacity to purchase products marketed as safer alternatives, but many are not, which leads to environmental disparities and in part contributes to health disparities. The general public receives health messages from the media, some of which can be sensationalized, misleading or lack context. This session covered topics including emerging science, chemical exposure, messaging and policy related to health effects in children.

Health Effects of Chemicals in Consumer Products: Flame Retardants

Kim Harley, Ph.D., UC Berkeley

Dr. Harley explained that flame retardants are products added to consumer products (e.g., polyurethane foam furniture, textiles and electronics) to reduce flammability. One of the main routes of exposure occurs when chemicals leach out of the foam and into the environment as part of dust, which is then inhaled or ingested. Young children also are exposed to flame retardants through breastfeeding.

Examples of flame retardants include polybrominated diphenyl ethers (PBDEs), Firemaster 550 and chlorinated tris. At UC Berkeley, most of the research focuses on PBDEs, which have a half-

life of 2 to 12 years. Of the 209 PBDE congeners, 12 are used commercially in penta, octa or deca mixtures. Penta was used in foam, and although it was phased out beginning in 2004, it is still present persists in furniture, and exposures continue.

Elevated PBDE levels are of concern because they have been shown to be endocrine disruptors with a particular effect on thyroid hormone. Additionally, animal studies have demonstrated the neurotoxicity of the chemicals. Notably, 97 percent of the U.S. population has detectable levels of PBDEs, which are higher than in the rest of the world. The highest levels of PBDEs in house dust have been found in Salinas, California, which is home to the CHAMACOS cohort. The higher levels in California can be explained by a law requiring that furniture must be flame retardant for 12 seconds. The people at greatest risk of exposure to PBDEs are young children who crawl on the floor and put objects in their mouth.

The CHAMACOS study has investigated the health effects of PBDEs in a farm-working community. Research has focused on the levels and determinants of exposure as well as association of penta PBDEs with fertility, thyroid function, fetal growth, neurobehavior, obesity and age at puberty. The study also intends to characterize new exposures experienced by children.

Serum levels of penta PBDE are lower in CHAMACOS mothers compared to the national cohort from NHANES. This might be explained by the immigrant status of CHAMACOS mothers. As the length of U.S. residency increases, PBDE levels rise. CHAMACOS children have higher levels of PBDEs than mothers and the national cohort. An analysis of reproductive outcomes indicated that women with higher serum PBDEs experience difficulty becoming pregnant and deliver children with decreased birth weight and lower levels of thyroid stimulating hormone. Maternal PBDE levels were correlated with increased ADHD behavior and lower IQ in their children, indicating effects on neurobehavioral development. Child PBDE levels also were associated with negative changes in IQ. Additional studies have corroborated the demonstrated effects of PBDEs on neurodevelopment.

Preliminary evaluation of the association of PBDEs with obesity or puberty indicated that although child PBDEs are associated with lower BMI at age 7, maternal PBDEs are associated with a trend of larger waist circumference in boys and smaller in girls. Experimental artifacts related to the lipophilic nature of PBDEs (especially congener BDE-153) might explain the surprising findings; future research will explore further the association of PBDEs with weight and puberty.

Importantly, the endpoints in the CHAMACOS study might not be independent, as thyroid hormone changes might explain the effect of PBDEs on fertility, birth weight, BMI and neurobehavioral development. Although PBDE levels are declining across the United States, substitute flame retardant products will need to be evaluated for safety and toxicity. Chlorinated tris, for example, is a carcinogenic chemical that was banned from sleepwear in 1977 but is now appearing in furniture foam and provides a common exposure. Current research is examining the sources of exposure and health effects of chlorinated tris and other organophosphate flame retardants. The UC Berkeley Center also is interested in evaluating

personal care products through the Health and Environmental Research on Make-Up of Salinas Adolescents (HERMOSA) and CHAMACOS studies.

Chemicals in Consumer Products: Trends in Exposure and New Chemicals of Interest

Antonia Calafat, Ph.D., National Center for Environmental Health, Centers for Disease Control and Prevention (CDC)

Dr. Antonia Calafat noted the importance of lifestyle choices in choosing personal care products. Consumer and personal care products contain a mixture of active and inactive chemicals. Although active chemicals (e.g., triclosan, parabens) contribute to the product effects, inactive chemicals
(e.g., phthalates, BPA) do not contribute to the product function and thus are not labeled on the packaging. Increased scrutiny of chemicals in personal care products has stimulated the development of alternative chemicals such as plasticizers and other compounds. BPA, for example, is being replaced by other bisphenols.

The CDC assesses chemical exposures through biomonitoring, which can be a very powerful tool when properly applied. An example of successful biomonitoring revealed a link between SES and triclosan exposures. Triclosan is an antibacterial agent present in products such as soaps. NHANES data showed that although no differences by race/ethnicity or gender were found, triclosan levels (measured in urine) increase with household income, perhaps because people with higher SES are more concerned about microbes. Another example is the gender gap in methyl parabens exposure between men and women; females use more personal care products that contain this preservative. Non-Hispanic blacks also tend to have higher exposures to methyl parabens than non-Hispanic whites or Mexican Americans, reflecting differences in products use across race/ethnicity as well as gender. Diethyl phthalate (DEP) can be used in products with a scent, and non-Hispanic blacks also have higher exposure to DEP. One explanation for these trends is that non-Hispanic blacks tend to use more hair products.

Because of increased public scrutiny and legislative action, phthalates are being replaced with other chemicals in products. NHANES data tracking the concentration of phthalates in 2,500 representative participants showed that the levels of substitute phthalates increase as the levels of original phthalates decrease. Hexamoll® DINCH® is a phthalates replacement plasticizer that also is increasingly being detected in urine samples after the chemical was introduced in 2002. BPA is another plasticizer used in epoxy resins, plastics and food can linings. Increased scrutiny of BPA is shifting use to alternatives such as bisphenol S and bisphenol F.

Data from NHANES show that concentrations of certain flame retardants, specifically PBDEs, might be decreasing. The levels of another flame retardant, chlorinated tris, in dust are several orders of magnitude higher than the levels of its metabolite in urine. This result emphasizes that the ubiquitous nature of chemicals in the environment relative to their trace levels in humans might be of concern if contamination prior to analysis (e.g., through the collection procedure) occurs, and quality control procedures always should be implemented during sample collection. Dr. Calafat emphasized that even if many analytes can be accurately measured, not all analytes are good exposure biomarkers. Future NHANES work and studies on

targeted populations will attempt to track exposures to legacy chemicals and their alternatives, evaluate mixtures, and better interpret biomonitoring data. The trend toward the development and use of nonpersistent chemicals will introduce more variability in concentrations of the chemicals in biological samples that may increase the potential for exposure misclassification. This concern could be addressed by collecting multiple samples from an individual and pooling them prior to analysis.

Chemicals in Consumer Products: An Overview of Clinical Questions to the PEHSU

Maida Galvez, M.D., MPH Icahn School of Medicine at Mount Sinai

Dr. Maida Galvez discussed challenges in health messaging to the general public. People have anxiety about the health effects of chemicals in the environment and how their personal choices might have negatively affected their or their children's health. When starting any health talk, Dr. Galvez recognizes that the general audience is prepared to be scared, and she emphasizes that people should not focus on past exposures but rather how they can reduce future exposures moving forward. Many parenting efforts have a positive impact on children, such as reading to them, giving nutritious food, and providing a loving and supportive environment.

The PEHSUs form a respected national network of expert pediatricians who learn and practice risk communication related to the realm of children's environmental health. They are a resource for filtering what parents need to know, but ultimately it is difficult for them to answer whether a specific product is safe for a child. An analysis of calls to the Region 2 PEHSU (New York, New Jersey, Puerto Rico and the U.S. Virgin Islands) from 2007 to 2012 indicated that 60 percent of inquiries were from the general public and 25 percent were from health care professionals. There was an even split between queries about classic environmental exposures (e.g., lead, mercury, mold, pesticides, asbestos) and current/emerging chemicals of concern (e.g., phthalates, BPA, PBDEs).

The PEHSUs help to communicate what can be done to reduce exposures to environmental chemicals. Dr. Galvez noted that parents do the best they can with the information that they have at the time of a decision. The PEHSUs encourage parents to gather evidence-based information to make the best decisions but in the absence of scientific uncertainty to err on the side of caution and choose what are known to be safer alternatives. Simple messages shared with families to encourage a precautionary approach is to eat fresh fruits and vegetables to reduce exposure to phthalates found in processed foods, avoid the use of #3 and #7 plastics in the microwave and dishwasher, mop and dust regularly, encourage frequent hand washing, minimize handling of receipts to reduce exposure to BPA, and use fewer products less frequently. For example, people who used shampoo, lotion and fragrance three times or less have lower levels of exposure. Existing databases, such as http://www.cosmeticsdatabase.org, can help to identify safer products. Accomplishing all of these actions can be challenging.

The PEHSU organizes its messages according to key topics: What is the exposure? What are the health effects and vulnerabilities in children? What are the action items that parents can pursue to reduce those exposures? Dr. Galvez expressed caution for the need to recognize the role of

health professionals in shifting the burden to consumers when action items are suggested. Parents are stressed, and presenting a list of tasks for parents to accomplish to reduce their children's exposure can be daunting. Legislative policies can be very effective. A National Research Defense Council factsheet, for example, indicates that Congress must ensure that important information about chemical use (e.g., phthalates) is not hidden from people. The Toxic Substances Control Act (TSCA) should be reformed to ensure protection of people and the environment from toxic chemicals.

Educating the public is helpful because grassroots advocacy carries a big impact. It makes a difference when parents complain to legislative bodies that they did not know that BPA was in a product, for example. One grassroots effort led to a ban of BPA in Suffolk County, New York.

Dr. Galvez presented several lessons learned. PEHSUs and the American Academy of Pediatrics should be involved early when developing health messages for the public to ensure consistent messaging. PEHSUs provide an important training foundation for clinicians, who need to be trained to communicate to families. In addition to the fellowship program for physician scientists, a training program is needed for clinicians who want to focus on health policy. The general public is ahead of doctors on environmental issues, so messaging to both audiences often is similar. The evidence base for unintended consequences of action items need to be carefully considered. For example, frequent hand washing using products with triclosan might not be a beneficial practice because exposure to one chemical of concern will be increased even though exposure to other chemicals might be decreased. The national or international context of major concerns (e.g., tobacco smoke, clean water and air) also is important. Exposures related to consumer products are widely prevalent and documented, and it is important to assess the potential for harm prior to releasing new chemicals into the environment.

Chemicals Management Policy: Where Do Consumer Products Fit?

Jerome A. Paulson, M.D., The George Washington University

Many consumers assume that products for sale on store shelves are safe to use and will not cause harm. The reality is that there is not a functional chemical management policy in the United States. The infrastructure does not exist to deal with the 6,200 chemicals actively being used or the 83,000 chemicals that have been on the market in the past 50 years. The primary law in the United States that is supposed to form the foundation of chemical management policy is the Toxic Substances Control Act (TSCA) administrated by EPA. Despite valiant efforts since 1976 when the law was passed, EPA does not control toxic substances in part because of the way the law was written and because of the way it was interpreted by the Supreme Court. Five separate acts of Congress were required to prohibit the few chemicals that have ever been banned under TSCA.

TSCA does not regulate pharmaceuticals, cosmetics or pesticides, which are regulated under separate laws (Federal Food, Drug and Cosmetics Act [FFDCA]; Federal Insecticide, Fungicide and Rodenticide Act [FIFRA]; and Consumer Products Safety Act [CPSA]). The FFDCA, which regulates consumer products, was amended by the Food Quality Protection Act (FQPA) in 1996.

Food and pesticide testing through FFDCA and FIFRA requires premarket testing, postmarket follow-up, and testing specific to pregnant women and children, but cosmetics and other products do not. Labels on pesticides and cosmetics require declaration of active ingredients only, and there is no information about the inactive ingredients (often comprising the vast majority of the product) being applied to the lawn, house or human body. The CPSA has been amended several times and requires that products intended for use by children meet certain standards, including lead content, size of parts, and some phthalates and flame retardants. For the vast majority of consumer products, however, there is no requirement for premarket testing, postmarket follow-up or other monitoring. A statutory or regulatory definition of the term "personal care product" is lacking. The personal care product industry includes a wide range of products dedicated to health and beauty, including perfume, sunscreen, hair and skin care products, cosmetics, and toothpaste, as well as some soaps and cleaning compounds.

In addition to the TSCA, FFDCA, FIFRA and CPSA, chemical management policy is influenced by legislation such as the Clean Air Act (CAA), Clean Water Act, Occupational Safety and Health Act, and others. Pharmaceutical and pesticide management is an active process in which companies are required to perform testing and share the results with regulatory agencies that make a decision about the safety of the product before it is marketed. EPA assesses cumulative and aggregate toxicity for pesticides; this standard should be applied to all chemical management policy. Additionally, a great deal of information about pesticides and pharmaceuticals becomes publically available, but a tremendous barrier related to confidential business information exists for almost all other types of consumer products. It is important that information be made available so that consumers are better informed about what they are buying and using. The current system could be classified as "evidence-avoidance-based" because if companies have information about anything related to TSCA, it must be disclosed, but they can remain in compliance of the law by not gathering the information.

Recommendations based in part on the American Academy of Pediatrics' policy statement suggest that the chemical management system be evidence-based with a foundation of chemical testing (e.g., neurotoxicity, endocrine disruption) as well as aggregate and cumulative risk. Harmonization across different laws will ensure that all products are tested in a similar manner regardless of the end purpose. All regulatory agencies, but particularly EPA under TSCA, need a method of requiring that companies provide additional testing if there is a concern about potential health risks. All chemical products must meet a standard of a reasonable certainty of no harm as for pharmaceutical and pesticide products. Postmarket surveillance is important to monitor the effects of a chemical on the environment and human health over time, and agencies need the ability to remove a chemical if surveillance indicates that it no longer meets safety standards. Finally, corporations who market these products need to fund these efforts as well as develop mechanisms for biomonitoring so that the federal government is relieved from determining how to monitor exposures to all of the complex substances.

Panel

Questions and Answers

In response to a question about the contribution of other agents to the CHAMACOS outcomes, Dr. Harley explained that a benefit of the CHAMACOS study is that the levels of many chemicals were measured and some, like lead, were found to be low. Additional compounds, such as OPs, were analyzed to exclude confounding associations. She acknowledged the importance of performing sensitivity analyses to ascertain whether toxicants that might coexist with PBDEs might be contributing to health issues. BPA and PBDE levels are not correlated. PBDEs and OPs, however, showed similar associations with attention and IQ, so they had to be analyzed carefully to confirm that the effects were independent.

A participant noted that industry is quick to replace toxic chemicals with substitutes as soon as concerns are raised. He asked for recommendations of practical efforts that members of the audience could engage in to encourage comprehensive TSCA reform. Dr. Paulson expressed doubt about the possibility of TSCA reform in near future. Both of the recent EPA Administrators have used the tools available to improve the situation, and it is important for the community to support those efforts. He also suggested that people talk to Congressional representatives to support TSCA reform.

Dr. Paulson described the industry response to the growing body of research surrounding chemical products. He encouraged the audience to read David Michaels' book *Doubt Is Their Product,* which explains how tobacco companies recognized that they only had to create doubt, not refute scientific information. This lack of certainty creates a barrier for legislation related to crafting public health or environmental health policy.

A participant expressed appreciation for the diversity of topics discussed during the meeting, including how the Centers are beginning to consider more than one chemical and disease outcome concurrently. These efforts to better understand the integration of pathways of toxicity might provide more information about the relationships between different human diseases. She encouraged the audience members to consider holistic system approaches. She also expressed surprise that an exposure that increases risk for ADHD might also be associated with a higher BMI. Dr. Harley agreed and explained that the pathways affected by a complex mixture of exposures need further investigation.

HIGHLIGHT—15 YEARS OF THE CEHC PROGRAM

Elizabeth Matsui, M.D., The Johns Hopkins University
Brenda Eskenazi, Ph.D., UC Berkeley
Frederica Perera, Dr.P.H., Ph.D., Columbia University

The Johns Hopkins University

Dr. Matsui presented the three main findings from The Johns Hopkins University Center, which focuses on inner city asthma and the indoor environment. The first major finding of the Center is that mouse allergen exposure is strongly associated with asthma morbidity. Children who were mouse-sensitized had a 50 percent probability of an acute asthma event. Other allergens

do not have such a strong association with pulmonary inflammation specifically associated with mouse allergen exposure, which suggests that public health efforts should focus on mouse allergens. Integrated pest management can reduce mouse allergens by 75 percent. The Center currently is conducting a clinical trial to determine whether integrated pest management reduces the incidence of asthma.

The Center has investigated and established a relationship between indoor PM exposure and asthma symptoms. In a follow-up study, households received an air purifier that decreased the amount of indoor PM and increased children's number of symptom-free days. The study also found an association between indoor NO_2 concentration and asthma symptoms. Air purifiers resulted in a marked reduction in NO_2. The third finding was that greater BMI potentiated the effects of PM exposure.

The clinical implication of these findings is that the Center recommends air purifiers for patients with asthma. There is no mechanism for insurers to pay for or subsidize the air purifiers, however. Another recommendation is to assess sources of exposure to NO_2 (e.g., gas appliances) and replace them with alternatives. Dr. Matsui suggested that environmental regulations could be tailored to individual susceptibility.

UC Berkeley

Dr. Eskenazi acknowledged the EPA/NIEHS project officers who have led the CEHC consortium for the last 15 years. She introduced a video about the CHAMACOS study at the Center for Environmental Research and Children's Health at UC Berkeley. The CHAMACOS study is located in the Salinas Valley in Monterey, California, home to thousands of farmworkers, mostly from Mexico. There is a long history of tension between farm owners and agricultural workers in that region. In 1996, the FQPA was passed, which reflected the need to consider the health effects of pesticides and changed the way that pesticides were regulated.

The CHAMACOS study focuses on the effects of pesticides on pregnant women and children in agricultural communities. The effects on children occur via exposure to contaminated food, and also from proximity to agricultural fields and interaction with farmworkers. The Center has since expanded its work to investigate the exposures outside of agriculture. In 1999, the Center built a field office at the county hospital in Salinas, California. More than 600 pregnant women were recruited, and their children have been followed from birth into adolescence. Biological and environmental samples and interviews have been used to assess children's growth and development.

The CHAMACOS study has resulted in more than 100 publications in top journals and has received local, national and international media attention. The study has developed interventions to reduce exposures to farmworkers in the field and in their homes. The ultimate goal is to reduce environmental exposures to all families. CHAMACOS also has trained hundreds of students and staff in the community.

Columbia University

Dr. Perera introduced the focus of the research at the CCCEH, which is to investigate the synergistic effects of multiple exposures. These effects are mediated by epigenetic mechanisms

and changes in neural development. Some of the major findings of the Center are that *in utero* PAH exposure disrupts global DNA methylation, and these patterns persist through age 3. Further, prenatal PAH exposure is associated with hypermethylation of a particular gene, interferon gamma, in cord blood samples. The gene has a critical role in brain development and could mediate the observed effects of PAH exposure on working memory at age 7. *In utero* PAH exposure has been associated with obesity and with cockroach sensitization as well. The Center's research shows that in addition to airway inflammation, phthalates are associated with eczema and childhood behavioral and developmental impairment. Exposure to BPA similarly has effects on asthma and behavioral outcomes.

Parallel experimental studies have demonstrated sex-specific, nonmonotonic effects of BPA exposure on estrogen receptor alpha in the offspring hypothalamus. Those changes in gene expression were associated with changes in methylation and gene expression and could mediate the observed alterations in social and anxiety-like behavior.

A key finding of the Center is that social stressors and toxic pollutants interact. This has led to community outreach efforts to ensure that the local community is informed about how to make their homes and children healthier. The Center's work also has influenced policy, including laws to phase out dirty fuel sources and implement integrated pest management in public housing. The work has brought attention to the need for coordinated social and environmental interventions. It has shown that continuing exposure to environmental pollutants affects children's health and their ability to lead healthy productive lives. The benefits of prevention in childhood will accrue throughout the life course, and there is a need for more research and prevention in children's environmental health.

SESSION 4: NEW FINDINGS AND TOOLS FOR UNDERSTANDING THE EFFECTS OF EARLY EXPOSURES ON BRAIN FUNCTION

Moderator: Elaine Faustman, Ph.D., University of Washington

What Can Brain Imaging Tell Us: The Case of Organophosphate Insecticides

Virginia Rauh, Sc.D., Columbia University

Dr. Virginia Rauh introduced the neuroimaging tools used at the CCCEH. The tools are used for structural imaging, distinct from functional MRI imaging. Traditionally, neuroimaging was used for three purposes, to: (1) understand the relationship between specific areas of the brain and functions they serve, (2) locate areas of the brain that are affected by particular disorders and diseases, and (3) develop strategies to treat various brain disorders and diseases.

In the context of neurotoxicological research, researchers wonder whether clinical symptoms and signature syndromes are associated with chemical exposures. It is not known whether windows of vulnerability exist during which the insult is the greatest or likely to be permanent. Finally, it is necessary to investigate how chemical insults affect the structure and function of the brain in developing and mature organisms. This last question can be addressed using neuroimaging tools.

Nevertheless, there are many challenges because identical environmental exposures can map to many clinical and behavioral symptoms (nonspecific effects); rarely do exposure-related symptoms compose a single behavioral phenotype. Therefore, valid clinical endpoints are difficult to define. Even if there is a clear neural or behavioral signature of exposure, the mapping of brain regions to behavior is quite inexact.

CPF is a chemical that inhibits acetylcholinesterase. It may affect the brain via other mechanisms as well and have long-term neurobehavioral effects for which acetylcholinesterase inhibition is not the appropriate biomarker. The CCCEH has found that *in utero* CPF exposure affects health, behavior and cognition of children at age 7.

Dr. Rauh presented several findings that involve imaging from a pilot study. The first result was that the brains of children who were exposed to CPF had volumetric deformations and differences in specific regions, and a dose-response relationship is observed, with a significant positive relationship between exposure and brain deformation. The implicated brain areas involve attention, language, social cognition, reward, emotion, inhibitory control and executive function. The second major effect was that the brain deformation was associated with lower IQ. Thus, prenatal exposure was associated with structural and functional changes in the developing brain that persist through middle childhood.

The Effects of Environmental Toxicant BDE-49 on Immune Function in Children with Autism

Judy Van de Water, Ph.D.

Dr. Judy Van de Water described the goal of the UC Davis Center, which is to understand the mechanism by which exposures affect cells at a molecular level, and how these changes lead to altered behavioral outcomes. The specific goal is to examine the environmental factors, genes and immune system as they relate to autism susceptibility. Brominated diphenyl ethers (BDEs) are known to affect the nervous system, but their effects on the immune system have been less studied. It is increasingly apparent that the immune system and nervous system co-develop, sharing many signaling molecules, and a perturbation that affects one system may also affect the other.

Autism is a complex disorder for which there are few (if any) biological markers. The heterogeneity of this disorder makes it difficult to study. Researchers hypothesized that exposure to BDEs might cause a disregulated immune profile, which in turn would increase the likelihood of autism. A 2009 study showed that BDE-47 increased inflammatory cytokines and the frequency of autism. In a more recent study, cells exposed to BDE-49 produced more interleukin 4 (IL-4). *In vivo*, children with increased IL-4 levels following ex vivo BDE exposure also exhibited worse cognitive function. BDE affected other immune cells, such as T helper 2 cells, and cytokines, such as IL-13. Future work will focus on the mechanism by which these cytokines lead to behavioral outcomes (autism) and will explore why some children respond differently to the same exposure.

The Impact of Early Environmental Exposures to Lead on Adult Neurodevelopment Status: Neuroradiological and Behavioral Assessments

Kim Dietrich, Ph.D., University of Cincinnati College of Medicine

Dr. Kim Dietrich described a study on the effects of lead exposure in the Cincinnati Lead Study cohort that has been going on for 34 years at the University of Cincinnati College of Medicine. This prospective longitudinal study recruited over 400 women in the first trimester of pregnancy and their children at delivery and continues to follow these subjects into their late 20s and early 30s. The mothers and children lived in areas that historically have had a high incidence of clinical childhood lead poisoning since the 1950s. The exposure levels in this cohort were high by contemporary standards; for example, at least 33 percent of the children had at least one blood lead concentration above 25 ug/dL over the first five years of life, the CDC level of concern in 1985. Although there is an established relationship between lead exposure and IQ, the effects observed in this study were not limited to IQ alone.

When subjects were in their mid-adolescence, researchers found that parental and average postnatal blood lead levels were associated with self-reported delinquent behavior. When followed into early adulthood, childhood blood lead concentrations continued to be associated with officially documented criminal arrests. For example, even when controlling for variables such as other exposures or poor home environment, there remained a significant association between lead exposure and violent offenses (e.g., murder, rape, assault and robbery) such that every 5 micrograms of lead per deciliter of blood averaged over five years resulted in a 30 percent increase in arrests. Upon further follow-up, Cincinnati researchers found that the number of lifetime arrests of participants in this study from ages 18 to 31 years could be predicted by maternal prenatal blood lead concentration and average childhood blood lead concentration. Further work on this cohort used advanced neuroimaging tools to determine how lead exposure affects brain structure, function, physiology and thus behavior. When they were in early adulthood, dose-dependent reductions in brain activation, cortical gray matter in the frontal lobe, injury to myelin and axonal structures were found in subjects exposed to higher levels of lead in childhood. The main lesson for researchers from this study is that the most important effects of early exposures to lead may only be observable after many years. That is, the full spectrum of effects of exposure to central nervous system toxicants, such as lead, may only be observable in the fullness of time in longer term prospective studies.

Translation and Communication of Emerging Methods and Opportunities to Impact Clinical and Research Practice

Discussant: Elaine Faustman, Ph.D.

Panel:

Virginia Rauh, Sc.D.
Judy Van de Water, Ph.D.
Kim Dietrich, Ph.D., M.A.
Kimberley Gray, Ph.D.
Leslie Rubin, M.D.
Elaine Faustman, Ph.D.

Dr. Gray noted that this year is the "year of the brain." The NIH has developed the "neural blueprint" and "neural toolbox" to make quick assessments of the five domains of neural health. These tools exist in multiple languages and could be useful for the Children's Centers.

A participant mentioned that there is a relationship between autoimmune diseases in the mother and autism in her children. The participant described a family in which the first-born son developed autism, whereas the younger sister did not. Autism is a symptom complex, and some individuals might share symptoms, but the causes might be completely different. The autoimmune status of the mother, as well as genetic predisposition and epigenetic markers, all influence the manifestation of autism.

A clinician in the audience noted the importance of windows of susceptibility. Any insult (e.g., pesticides, lead, other chemicals) that occurs soon after conception will affect developmental processes and outcomes. The specific insult may not have a specific outcome; the outcome may be the result of a perturbation during a specific window in development. A participant responded that researchers have not gone far enough in delineating the specific profiles associated with particular exposures. Dr. Eskenazi noted that the timing of exposure often is unknown, especially when no biological samples are available. She also commented that there has not been a discussion of resiliency. Not every child responds the same way to an exposure; for example, not every child becomes autistic if exposed to paradichlorobenzene. Further research is needed to understand the interaction between exposure and other factors that may enhance or ameliorate the effects of exposure. Dr. Rubin noted that the interaction between exposure and other stressors has been examined. The effects are greater when other stressors are involved. A participant noted that the brain is able to repair itself. There are many protective factors, including a healthy diet. All of these must be taken into consideration.

A participant emphasized that it is important not to focus only on what is not known. There is clear evidence that lead exposure produces effects, and this should not be lost underneath the variability of responses to lead. She gave the example that only 11 percent of smokers develop lung cancer, and this led to resistance against policies to regulate tobacco. Similarly, children's responses to exposures can be variable, but it should be emphasized that exposures do have demonstrable effects on health and behavior.

A participant urged caution in how the research findings are communicated to the public. There is a difference between a personalized risk assessment for individuals versus a population-based environmental risk assessment.

KEYNOTE: COULD YOU MAKE YOUR CHILDREN'S HEALTH RESEARCH UNDERSTANDABLE EVEN TO CHILDREN?

Randy Olson, Ph.D., Harvard University

Dr. Randy Olson, a marine biologist, presented a narrative training approach to help scientists better communicate with their audiences. Dr. Olson is a past-professor at the University of New Hampshire and an alumnus of the University of Southern California Film School. He has co-written several books about broad communication and produced the film documentary, *Flock of Dodos*, and he currently gives workshops to science organizations. His first book, *Don't Be Such a Scientist*, described the problem with communicating science to the public, and his second book, *Connection: Hollywood Storytelling and Critical Thinking*, provides communication solutions through narrative training, which is the instilling an instinct of what the narrative is and how information is compiled into a narrative structure. Structure and simplicity are key features that differentiate narrative training from other types of training.

The goal of narrative training is to fully engage one's audience in the message being imparted. A neurocinematics study (Hassan, 2008) used MRI to look at the brain activity of people watching film clips. The researchers saw an index of 70 percent in similar brain activity patterns (i.e., engaged audience) among those watching a video with a tight narrative in contrast to a 10 to 20 percent similarity pattern among those watching a video segment with no storyline.

Dr. Olson shared an example of how narrative principles can help structure information. He worked with scientists planning a convention on sea level rise to modify the online description of the meeting that delineated eight topics of discussion. The original heading "Responding to Sea Level Rise" became "Sea Level Rise: New, Certain and Everywhere," along with changes to font sizes and capitalization. In addition, the original two-paragraph text was recast into three paragraphs that each focused on one of the three words, "new, certain and everywhere." The revisions were based on the WSP model of one Word (theme), one Sentence (ABT), and one Paragraph (logline) and brought the theme down from eight topics to three words.

Dr. Olson focused on the narrative template ABT, which stands for "replacing Ands with Buts and Therefores" and has been used successfully by Trey Parker, co-creator of the television show, *South Park*. ABT is most easily described in terms of a three-act play: Act I provides an exposition ("And"), with a question ("But") segueing into Act II, culminating with an answer and synthesis ("Therefore") in Act III. The ABT template actually has been applied throughout the centuries, by Socrates and the German philosopher Josef Hegel, as well as current neurophysiologists and literature professors.

Dr. Olson applied this technique to study descriptions found on several CEHC university websites: (1) Endocrine disruptors are known to enter the womb *and* can be damaging, *but* whether they have long-term effects is not known; *therefore*, Columbia University researchers are following a group of New York City children since birth to explore this. (2) Exposure to toxin

in utero can lead to diseases later in life, *but* biomarkers can identify these risks; *therefore*, researchers at Brown University are using mouse models to identify biomarkers. He also demonstrated the technique applied to several paintings and as a downloadable app ("Connection Storymaker"). The narrative training workshop allows participants to assess their messages quantitatively (e.g., how many words were used), and the app serves as a tool to help shape one's health research story and develop better narrative instincts.

WEDNESDAY, OCTOBER 30, 2013

SESSION 5: NEXT STEPS FOR COLLABORATION BETWEEN THE CHILDREN'S ENVIRONMENTAL HEALTH CENTERS AND THE PEDIATRIC ENVIRONMENTAL HEALTH SPECIALTY UNITS

Session Overview and Introductory Remarks

Pam Maxson, Ph.D., Duke University

The session began with an overview of the CEHCs and PEHSUs, followed by several presentations about collaboration. Participants then broke into four breakout groups based on geographic regions to discuss opportunities for CEHC and PEHSU collaboration. Topics and specific proposed collaborations from these discussions were provided to the full group.

The mission of the CEHCs is to better understand environmental factors affecting children's health. This is completed by promoting research translation; enhancing communication, innovation and research; and promoting multidisciplinary research. The basic CEHC structure includes three individual research or translational projects and an outreach and translation core.

The PEHSUs aim to improve the environmental health of children by enhancing education and consultative services to clinicians, health professionals and the community and by providing evidence-based information from a network of experts in environmental health. A typical PEHSU staff includes a project director, a coordinator, an occupational environmental medicine physician, a pediatrician and other specialists. PEHSUs are involved in consultation, education/outreach and referral.

Why We Should Collaborate

Patrice Sutton, UC San Francisco

The CEHCs and PEHSUs have a shared goal to translate the environmental health regarding environmental health effects that span the lifetime. Collaboration would be useful for a variety of reasons. (1) Collaboration could advance the uptake of environmental health science in the medical field. Approximately 78 percent of 2,500 American Congress of Obstetricians and Gynecologists (ACOG) obstetricians who replied to UCSF's survey felt that they are interested in promoting prevent harmful environmental exposures, but fewer than 25 percent reported taking their patients' environmental health history. The PEHSUs can serve as an invaluable referral mechanism to support action by obstetricians and gynecologists in the field of environmental health. Recognition of the role of the CEHCs and the PEHSUs in uptake of the science by practicing physicians was recognized in the September 2013 groundbreaking Joint Opinion issued by ACOG and the American Society for Reproductive Medicine which, notably,

was based in part on CEHC research and states that the PEHSUs are a resource for obstetricians and gynecologists.(2) Collaboration can improve public policy, such as working together to advance local, state and national medical societies' positions on environmental health policy. (3) PEHSUs have "an ear to the ground" and are essential to informing the science conducted at the CEHCs. (4) In addition, the PEHSUs serve an important science education and outreach role; for example, they have been effective in getting environmental health science into the local medical societies' news and in conducting outreach to practicing physicians. (5) Collaboration has had proven success. In 2012, the Reproductive and Children's Environmental Health Working Group brought together policymakers, federal agencies (EPA, Agency for Toxic Substances and Disease Registry [ATSDR]), leaders of professional societies and others to begin building an infrastructure for reproductive environmental health.

Overarching Ways to Collaborate

Susan Buchanan, M.D., University of Illinois at Urbana-Champaign

To increase collaboration between the CEHCs and PEHSUs, various activities could be undertaken. The CEHCs could invite the PEHSUs to attend CEHC monthly webinars. Likewise, the PEHSUs could invite CEHCs to attend PEHSU monthly National Conversations. In addition, the PEHSUs/CEHCs could build a long-term infrastructure to bring regional centers together at the institutional, center and individual levels.

There are a number of activities that could be implemented to increase capacity of the CEHCs and PEHSUs. These include co-sponsorship of trainee rotation experience, the PEHSUs helping in the access to clinical populations for research, and the CEHCs consulting with the PEHSUs regarding clinical issues. The CEHCs could inform the PEHSUs of important research findings to enhance clinical translation, risk communication and messaging. The PEHSUs could inform the CEHCs about common exposures resulting in calls/visits to the PEHSUs.

Specific Ideas and Examples for Collaboration

Sheela Sathyanarayana, M.D., University of Washington

There are a number of ways that the PEHSUs and CEHCs can collaborate through a coordinated response and translation of research findings. The importance of timely coordination is seen in the example of arsenic and foods. Seven PEHSUs received 68 concerned calls from parents and/or health care providers and eventually created a factsheet on arsenic as a resource. The factsheet, however, was published about 1 year later. A CEHC with important research results that will be published in the near future could work with the PEHSU network regarding how findings might be shared with the public for more immediate impact, such as through press releases or factsheets for clinicians and families.

The Centers and/or PEHSUs may identify highly exposed children or children with adverse health outcomes with suspected environmental etiologies. These cases represent important opportunities for hypothesis generation to inform CEH research. Developing case reports for publication can move the CEH field forward and highlight research gaps. One example of a sentinel event/case report involves BPA and neurodevelopment, in which the Cincinnati Center identified a pregnant woman with high exposure to BPA and contacted the Region 10 PEHSU to

discuss how to counsel the mother; the infant had abnormal neurobehavioral outcomes. In another case, the UC San Francisco Center found a high level of mercury in a pregnant woman and informed the Region 9 PEHSU and the local department of health about this finding; a discussion led to the finding that the woman used a face cream contaminated with mercury.

Collaboration between the PEHSUs and CEHCs also can occur via combined symposia or conferences. The Symposium on Cumulative Impacts and Children's Environmental Health (January 2013), which included six CEHCs and the Region 9 PEHSU, began a dialogue on cumulative impacts analyses between Centers. A Symposium on Children's Environmental Health Research Matters with the Region 10 PEHSU highlighted community engagement in University of Washington Center's child cohorts, PEHSU factsheets on wildfire/wood-smoke exposures, and regional research on the children's safe products rule. The Region 4 PEHSU and Southeast CEHC combined their expertise in the Break the Cycle of Environmental Health Disparities symposia to focus on environmental impacts in the context of health disparities and both groups and their student trainees made presentations and shared publications.

Collaborative policy efforts include the Program on Reproductive Health and the Environment's Meet the Decision Makers training fellowship; CCCEH's successful efforts in CPF legislation, which has led to further research; and Region 10 PEHSU's testimony on phthalates in children for the Washington State's Children's Health Safe Products Act.

Breakout Group Reports

Attendees were asked to separate into four breakout groups, discuss collaborative activities and share their thoughts to the full group. To facilitate collaboration beyond this meeting, the groups were composed of CEHCs and PEHSUs that were close in geographic area. The breakout groups considered the following questions:

- What collaboration(s) can you commit to or complete in the next 1 to 2 years?
- How can nongovernmental organizations (NGOs), foundations and government partners contribute to or benefit from participation?
- How will you accomplish your collaboration?
- What will you need to make it happen?

Group 1: Dartmouth Center/Region 1 PEHSU and Columbia Center/Region 2 PEHSU

Carmen Marsit, Geisel School of Medicine at Dartmouth University, said that despite the geographic distance among some of these CEHCs and PEHSUs, collaborative opportunities include joint meetings and attendance at each organization's presentations or events as well as work with local clinicians to increase their awareness of PEHSU resources. The CEHCs will include the PEHSUs on their news lists and press releases to keep the PEHSUs informed about forthcoming study findings and publications. Another area for collaboration is to involve NGOs; it would be helpful to compile and share information about potential NGO stakeholders with the CEHCs and PEHSUs.

Group 2: University of Washington Center/Region 10 PEHSU and University of Illinois at Urbana-Champaign Centers/Region 5 PEHSU

Nick Newman, Region 5 PEHSU, reported that Group 2 focused its discussion on pesticides. Information could be deployed by creating a Web-based module or update an existing online database. An alternate approach is to connect with clinician resources (e.g., UpToDate®, MedScape, Epocrates®, WebMD) to disseminate a more in-depth knowledge about pesticides and other environmental health topics to the public. The PEHSUs could contribute to the CEHCs' endocrine disruption research and outreach activities by providing contacts with local networks.

Group 3: The Johns Hopkins University Center/Region 3 PEHSU, Duke Center/Region 4 PEHSU and Region 6

Ed Levin, Duke University, summarized Group 3's discussion on enhancing communication, particularly through electronic media such as via joint webinars and videos. In addition, to accommodate busy schedules, asynchronous types of communication are useful. Blogs, chat rooms and online drop boxes could be used to post recent articles. Other collaborative opportunities include facilitating the dissemination of focused CEHC research and interactions between the organizations.

Group 4: UC Berkeley and Davis/Region 9 PEHSU, Region 7 PEHSU and National Jewish Health Center/Region 8 PEHSU

Robert Gould, UC San Francisco, stated that Group 4 encompassed a diverse background of participants and covered a wide geographic range. Collaborative ideas include developing ways to work across these distances. For those without a Center nearby, can one be identified to work with, even if it is outside the region? Challenges include the lack of funding for the PEHSUs as well as funding for sustainable, collaborative work among the organizations. In addition, a long-term method to track the various resources (e.g., programs, presentations, community partners) and expedite collaborations with the PEHSUs and CEHCs is needed; an EPA staff member from Region 9 has volunteered to facilitate the compilation of this information. Researchers in these CEHCs and PEHSUs have many other partners (e.g., contacts within professional, medical and public health associations) who might assist with the development of policy as well as greater collaboration with hospital-based institutions to incorporate the PEHSU/CEHC expertise.

Questions and Answers

Dr. Sheela Sathyanarayana thanked participants and organizers for their discussion. She invited funders (e.g., EPA, NIEHS, CDC) to share their thoughts on how to incentivize the collaborations. Are there opportunities for short- and long-term collaborations?

One participant noted that the ATSDR built collaboration into its funding announcements, particularly with schools of nursing and medical schools, for the translation and uptake in the medical school curriculum, and he encouraged incorporating collaboration early in the training of medical professionals.

Another participant responded that this is included in the Children's Centers Program. Each Center is required to have a health specialist; the description of the health specialist could be made clearer. Each Center receives $1 million for three projects and two cores. Rather than be prescriptive, the Program is structured to allow the Centers to self-assemble, meaning that CEHC Directors determine their partners (e.g., PEHSUs). For peer-review purposes, however, clinical partners must be local.

Mr. Rich Callan, EPA, said that further discussions will continue, and he encouraged collaboration among the Centers and PEHSUs. He suggested that attendees might follow-up with each other immediately after this meeting (e.g., complete sign-up sheets to exchange emails, plan monthly calls). EPA would like to see this discussion grow and looks forward to hearing about future partners.

One area to work on now concerns opportunities for PEHSUs and CEHCs to work together to respond to time-sensitive environmental issues. NIH has an R21 grants program that accepts applications on an ongoing basis for time-sensitive issues, and NIEHS staff are available to answer questions about this.

Ms. Khesha Reed, EPA Office of Children's Health Protection, commented that EPA's Children Health Coordinators in the regions are available as a resource. Many coordinators currently work with PEHSUs, and they also would welcome the opportunity to work with the Centers.

Dr. Sathyanarayana encouraged participants to report on their collaborations at next year's meeting.

SESSION 6: SOCIAL CONTEXT OF ENVIRONMENTAL EXPOSURES

Moderator: Marie Lynn Miranda, Ph.D., University of Michigan

Exposure to environmental toxicants is modulated by social and environmental stress; air pollution has a different effect on child development in the context of a community in which there is a great deal of social stress and no housing stability, employment stability, crime or places for children to play. The interaction between chemical and psychosocial stress has synergistic and nonlinear effects on growth, neural development and immune function.

Prenatal Stress and Neurotoxic Metals: If One Is Bad, Then Two Must Be…?

Deborah Cory-Slechta, Ph.D., University of Rochester Medical School

The reason to study risk factors in combination is that most diseases and disorders are complex; they arise from the interaction of multiple risk factors. In many places, neurotoxic exposures and social or environmental stress co-occur. Most importantly, chemical, social and environmental stressors share biological substrates and produce common adverse effects. The effects of psychosocial stress and toxic metals are mediated by the hypothalamic-pituitary-adrenal (HPA) axis. These stressors also share common adverse outcomes, particularly deficits in cognitive ability, memory and attention.

In an experiment in which rats were exposed continuously to lead, a subset of those also was exposed to prenatal stress. Mice exposed to the combination of stressors were less able to

learn prototypical responding to a fixed interval schedule of food reinforcement, a behavioral paradigm considered a surrogate for impulsivity. The stressors affected male and female rats differently. The stressors had molecular as well as behavioral effects; the researchers found increased hippocampal nuclear glucocorticoid receptors in male rats and effects on frontal cortex serotonin in females. A similar study on the combined effects of methylmercury and stress found that this combination produces synergistic effects, impairing learning and memory in female offspring. The combined stressors led to changes in brain chemistry. The neurochemical effects of methylmercury were sexually dimorphic and nonmonotonic, sometimes peaking at intermediate methylmercury concentrations.

In a subsequent experiment, mice were exposed to lead and prenatal stress and then given a history of positive reward or subjected to forced swimming (negative experience). The consequences of lead and prenatal stress were influenced by behavioral experience in the consequent trajectory of lead and stress-related neurochemical changes. Dr. Cory-Slechta noted that although this finding is not surprising, it often is ignored in neurodevelopmental toxicology studies.

Many studies have led to the conclusion that the study of chemical risk factors in isolation from other predisposing risk factors underestimates human health risks. They are studied in the absence of context. There is a need to move beyond experimental models focused on single risk factors because they are not consistent with the reality of human diseases and disorders, most of which are complex and multifactorial. The attributable risks of chemicals will differ depending on the psychosocial context.

Maternal Stress and Pollution: Rewiring Brain in Offspring

Richard L. Auten, M.D., Duke University Medical Center

Dr. Richard Auten described his work on the interaction of genetic, environmental and social factors influencing the health of a developing human. Stressors affecting the human HPA axis modify its susceptibility to pollutants, and this susceptibility can be transduced from mother to fetus, thus affecting the child's response to later adverse life events, including exposure to poor diet. The challenge in research is to balance the precision of single-agent toxicological approaches with the reality of multifactorial "real world" exposures. Multiple complex exposures are difficult to analyze. Animal models allow a greater complexity of experimental design while allowing the control to understand precisely how interactions affect outcomes.

This study's focus on diesel and stress was motivated by earlier work examining maternal diesel inhalation during pregnancy before birth and effects on offspring susceptibility to high-fat diet and obesity. In the experiment, the combined maternal exposure to diesel and offspring exposure to a high-fat diet led to offspring obesity as well as to effects on behavior and on immune function. The combined exposure increased anxiety and decreased learning in offspring. Male offspring were affected more adversely than females.

It has been challenging to simulate stressors similar to those experienced by humans in the animal models. Mothers exposed to social isolation and bright lights produce offspring with increased cortisol levels, impaired learning, and increased anxiety and depression. In this study,

researchers used a milder form of stress by reducing the bedding of the mice. The mothers increased their activity to search for bedding and did not attend to the pups. The pups in turn had higher cortisol responses and decreased learning. If the nest restriction happened only during pregnancy and was then restored after the pups were born, the pups still exhibited adverse health effects, indicating that maternal stress is transmitted prenatally to the developing fetus. The combination of diesel exposure and nest deprivation affected neural and immune function in the offspring, and the pups' response was sexually dimorphic, with stronger effects seen in the males. The combined stressors had effects on microglia, which are critical for fate specification in neurons. This could be a mechanism by which stress affects brain chemistry and development.

An Ecological Approach to Human Health Studies and Health Promotion

Mark Miller, M.D., UC San Francisco PEHSU

Dr. Mark Miller emphasized the importance of feedback between animal models and human studies in increasing the understanding of the impacts of exposure on children's health. Although science traditionally has been reductionistic and effective at isolating factors, this forum has demonstrated how important it is to examine the synergistic effects brought by the interactions of different exposures. In the world of alternative or complementary medicine, people are reconnecting mind and body; science also is beginning to demonstrate the importance of the interactions between genetic, environmental and psychosocial exposures. Exposures and effects occur at a variety of scales, from the molecular level to individual relationships and even the larger-scale social structures. To move toward evidence-based, science-based policy, it is necessary to think in an integrated manner about the environmental and social factors that affect health.

Rodents placed in an enriched environment have improved health outcomes; some of the molecular basis for this effect already is known. This presents an opportunity to consider the role of the environment in mitigating the effects of exposures to toxicants. Interventional studies examining the effects of lead exposure in an enriched environment are needed to determine whether there are methods to design the environment so as to ameliorate the effects of environmental toxicants.

Panel

Questions and Answers

Dr. Eskenazi noted that, as an epidemiologist, she struggles with how to unite animal models with human studies. Animal studies typically have limited sample sizes and also do not take into account the innate variation in reactivity that is observed in humans. Dr. Marie Lynn Miranda suggested that animal and epidemiological studies must meet in the middle; there is a constant feedback loop in which epidemiological and clinical observations inform the design of animal model experiments, and experiments might point to new social and environmental factors that should be examined in epidemiological studies. This feedback is what makes the work at the CEHC Centers so important.
Dr. Cory-Slechta acknowledged that there always will be a sample size issue in animal studies.

Better methods to analyze interactions are needed. In addition, animals should be separated based on their innate reactivity and personality; each child has a unique profile of predisposing factors. This will require the development of new statistical methods for analysis. Dr. Miranda noted that there has been a great deal of investment in technologies to generate data but little investment in the development of methods to analyze the data. Methods development will be critical for further progress.

Dr. Miller grappled with how to incentivize collaborations between the PEHSUs and CEHC. How to incentivize collaborations is an issue that should be addressed at the federal level.

Dr. Devon Payne-Sturges, EPA, indicated that Dr. Madeleine Scammel, an EPA Science To Achieve Results (STAR) grantee who works on cumulative risk assessment at Boston University, is borrowing methods in mathematics (Gaulois lattice method) to examine the effects of combined factors, and other STAR grantees are developing statistical methods. Every grantee is required to produce annual reports. It would be useful to complete a review of cumulative risk assessments with EPA and combine these issues with Children's Centers.

Dr. Sally Darney, EPA, and Dr. Miranda noted that there is interest in investigating how enriched environments can enhance or mitigate stresses.

A participant asked whether anybody has investigated the combined effects of lead and mercury. Dr. Cory-Slechta indicated that these would be next steps. She is more interested in the synergistic effects of exposures affecting the same biological substrate. The case must be made that lead, mercury and stress share the same biological substrates.

Dr. Auten indicated that the difficulty is to investigate unknown biological pathways that deal with resiliency. For example, adaptive immunity can influence how things play out with subsequent exposures later in life. Dr. Neumann noted that human exposure typically occurs with a long half-life so it is essentially a lifetime exposure at some level, whereas animal models usually are exposed for a well-defined period. What is the best way to interpret the results from animal models in terms of observational epidemiology? Dr. Cory-Slechta explained that the merit of exposing animals for a specific window is to determine the maternal contribution to the effects on offspring. Nevertheless, it is important to study the effects of both short windows and chronic exposures to separate the cause and effects. Dr. Miranda noted that some exposures tend to be chronically episodic exposures. In both animal studies presented today, there is long-term chronic exposure during the prenatal or postnatal period. Dr. Auten explained that the nature of the exposure (e.g., chronic, episodic) has implications for resiliency. Homeostatic mechanisms resist these insults but may be able to resist them only to a point. If periodicity or magnitude is excessive, homeostatic mechanisms may not be able to mitigate the negative effects of exposures. Dr. Cory-Slechta commented that the focus on the maternal exposure is with an eye toward intervention. If maternal exposure leads to lifetime changes, and most screening programs occur in children, then the screening and intervention are happening too late in life. It is critical to understand the maternal contribution, because early intervention is an important window of opportunity.

HIGHLIGHT—15 YEARS OF THE CEHC PROGRAM

Elaine Faustman, Ph.D., University of Washington

The University of Washington Center focuses on translating results of the study to participants who reside primarily in the agricultural community, in which there is tension surrounding the issues of pesticide use and best practices. The Center takes a multipronged approach, in the field and in the laboratory, investigating the interactions between genes and environment across time. Methodologies include animal studies, cell culture studies and extrapolations to observations in the field.

The Center has been using community-based participatory research for 15 years to investigate mechanisms of environmental exposure. The Community Advisory Board was founded in 1999. A hallmark of the CEHC program is the investigation of episodic, practice-driven exposures: chronic and repeated high dose exposures. Repeated environmental and biospecimen sampling occurs over time. Studies investigate the effects of chemical and nonchemical stressors on respiratory health by pairing migrant farmworkers with non-farmworkers for comparison. Questionnaires and biomarkers are used to assess stress.

At heart of this Center is community intervention, activities of which have touched more than 15,000 people. The identification of critical pathways of exposure has been very important for understanding how pesticides affect farmworkers and their families and for determining appropriate interventions. In spite of the time and inconvenience, participants have cooperated with the researchers to find solutions together. The Center has organized bimonthly journal clubs, toolkits, webinars and other outreach activities to ensure that the community receives the benefits of this research.

SESSION 7: THE CLINICAL AND TRANSLATIONAL IMPLICATIONS OF EPIGENETICS IN CHILDREN'S ENVIRONMENTAL HEALTH

Moderator: Joe Wiemels, Ph.D., UC Berkeley

The Role of Epigenetics in the Spectrum of Human Health: From Basic Development Processes to Population Research and Therapeutics

Joe Wiemels, Ph.D., UC Berkeley

Dr. Wiemels introduced the discussion about epigenetics with the statement, "Your DNA is not your destiny." DNA is the same in all body cells but is packaged and marked differently based on cell types, which allows them to have distinct cell functions. The science of epigenetics focuses on how DNA is packaged, the differences in packaging between different cell types, and how this packaging affects gene function. DNA is wrapped on histones and commonly acetylated or methylated; these modifications alter gene expression. Although epigenetic marks are heritable from one cell to its daughter cells, epigenetic features are modifiable as cells differentiate into different functions. For example, as stem cells develop into functional blood cells, their DNA is demethylated at genes important for blood cell function.

Most epigenetic variation is established early in development. After fertilization, somatic cells are first demethylated, and then heavily methylated. Early fetal development is a time in life

during which methylation patterns rapidly change. By birth, most of these patterns are fixed for life, and certain features of epigenetic patterns can affect childhood and lifetime disease risk. Some epigenetic changes are adaptations to our growth environment: adaptation to nutrition, behavior and chemical environments affects the epigenetic markers in cells. Many diseases (cancer and others) are linked to epigenetic modifications. Many drugs have epigenetic mechanisms of action.

How Early BPA, Lead and Phthalates Exposures Alter the Epigenome and Health Outcomes Later in Life

Dana Dolinoy, Ph.D., University of Michigan

Dr. Dana Dolinoy introduced her work about how exposures to BPA, lead and phthalates can affect the risk for metabolic syndrome later in life. There are many mechanisms by which these toxicants affect disease risk, one of which is epigenetics. The epigenome is modifiable using nutrition and pharmaceuticals to counteract the effects of environmental exposures and thus represents an opportunity for intervention.

To investigate environmental effects on the epigenome and the potential for intervention, Dr. Dolinoy described the viable yellow agouti mouse model. Yellow mice are not methylated at the agouti locus and have an increased risk of metabolic syndrome and obesity, whereas brown mice are methylated at this locus, so the agouti gene is not expressed, and the mice remain lean. Maternal nutrition as well as exposures to chemicals such as BPA affects the distribution of coat colors in the offspring, indicating that environmental exposures affect DNA methylation at the agouti locus and perhaps elsewhere. Nutritional supplementation with methyl donors such as folate can reverse the BPA-induced shift in coat colors and DNA methylation.

The explosion of technology surrounding epigenetics will allow researchers to move from single candidate gene studies to investigating the full epigenome; collaborations with bioinformaticians will be necessary to analyze the resulting data. In studying the epigenome, it will be important to link epigenetic changes to phenotypes. Some epigenetic effects could be bystander effects and might not have an effect on gene expression or affect health.

The University of Michigan Center focuses on how chemicals alter the epigenome, particularly early in life, because the epigenome is programmed early in development. In this study, mice were exposed to different diets before being mated, and the pups were followed through lactation. Diet affected the coat color distribution of the pups in a nonmonotonic fashion, with high maternal exposure shifting the coat color distribution toward the yellow range but lower exposure levels resulting in the opposite. Other genes also respond nonmonotonically upon exposure. Pathway analysis of differentially methylated genes showed that methylation changes disproportionately affected metabolic pathways and immune response pathways.

Dr. Dolinoy described another experiment in which body weight, body composition and activity were measured in response to maternal BPA exposure. The animals were fed a normal-fat diet. Although BPA is typically believed to be an obesogen, in this mouse model, BPA causes hyperactivity, lower body mass, lower food intake and a better hormone profile in female offspring. Researchers plan to further investigate by challenging these mice with a high-fat diet

and also by analyzing how BPA might mediate its effects on hyperactivity by affecting gene expression in the brain.

In another exposure study, mice were exposed to lead perinatally. Lead is a well-characterized neurotoxin, but its effects as an obesogen are less known. Pregnant mice were exposed to lead via their water at three doses, and there was a detectable shift in the distribution of coat colors of the offspring. Higher doses of lead caused an increase in the number of yellow offspring. There was a sexually dimorphic effect; male offspring had increased body weight, but the female offspring did not. Lead was shown to cause locus- and sex-specific methylation effects at weaning, persistent increased food intake and body fat in males. Future studies will investigate how methylation patterns shift over time, whether these patterns are gene or tissue specific, and how they are affected by lead exposure.

Mechanistic Pathways between Environmental Exposures and Epigenetic Changes

Frederica Perera, Ph.D., Dr.P.H., Columbia University

Dr. Perera introduced the mission of the CCCEH, which is to prevent childhood neurodevelopmental impairment, asthma, obesity and cancer through early identification of environmental risk factors and translation to intervention. Prenatal exposures to PAH and BPA can have consequences throughout life and even transgenerational effects. The mechanisms by which *in utero* exposures affect fetal development include genotoxicity (DNA damage and mutations), oxidative stress, epigenetic alterations and interference with normal hormonal pathways. The Center focuses on exposures during the prenatal window because epigenetic programming occurs during this time.

The goal of the study was to determine whether exposure to PAH and BPA is associated with changes in DNA methylation, especially at loci that are critical in fetal brain development. In the Center's cohort study that enrolled 720 mother-child pairs, prenatal or postnatal exposure to PAH and BPA was associated with adverse reproductive and neurobehavioral outcomes. Prenatal PAH exposure was associated with changes in brain morphology as assessed by MRI at ages 7 through 9 and lower levels of global DNA methylation. Patterns of methylation in cord blood (at birth) were correlated with methylation patterns at 3 years of age, indicating that modifications *in utero* can persist in childhood.

The study has also focused on specific candidate genes, chosen because of their known importance in early brain development and roles in endocrine function, immune function and inflammatory pathways. The first example, interferon gamma, is a pro-inflammatory cytokine involved in neurogenesis. It is known to mediate the effects of maternal inflammation on the fetus. In cord blood samples from the Center's cohort, prenatal PAH was associated with increased promoter methylation of interferon gamma in regions 1 and 2 of the gene.

Brain-derived neurotrophic factor (BDNF), another candidate gene, is involved in the survival and differentiation of neuronal cells. It is expressed in the hippocampus and other regions of the brain. In the Center's studies conducted in New York City as well as in China, exposure to PAH was associated with lower BDNF protein in cord blood.

ERα (Estrogen receptor alpha) is another candidate, involved in fetal neurodevelopment, and previously associated with BPA exposure.

In collaboration with the University of Cincinnati. Center researchers analyzed cord bloods from the cohort using the Illumina 450k microarray. More than 2,000 of these sites showed differential methylation patterns in response to prenatal exposure to PAH. The researchers currently are conducting a pathway analysis using gene ontology to determine which cellular functions are affected by the changes in DNA methylation. Thus far, they have identified a number of pathways relevant to neurodevelopment.

In parallel laboratory experiments, gestational exposure to BPA resulted in sex-specific changes in ERαexpression in the offspring hypothalamus that were associated with changes in DNA methylation also in the offspring hypothalamus, and with alteration in social and anxiety-like behavior in the offspring.

Center investigators are able to utilize these datasets to explore the role of epigenetic mechanisms in mediating other exposure-outcome associations observed in the cohort, for example with exposure to phthalates and pyrethroids.

The focus on environmental epigenetics is important because it provides a mechanism that can theoretically be targeted for intervention and prevention.

Translation of research is key to prevention, and the Center's research already has had impact on policy, including laws to reduce emissions from diesel busses and trucks and other combustion sources in New York City as well as other measures to reduce exposures. Preventive policies are needed to protect children at this vulnerable lifestage.

Questions and Answers

Dr. Jennifer Lowry, Children's Mercy Hospital, expressed concern that, although translation and prevention are necessary directions, clinical practitioners often misinterpret the information they receive from researchers. There is a need to conduct translation and outreach so that research findings are interpreted accurately. Dr. Newman agreed, commenting that findings should not be disseminated prematurely to prevent misinterpretation by clinicians and community members.

Dr. Kari Nadeau, Stanford University, mentioned that he has observed "connectivity," or a ripple effect, in methylation at specific alleles. In other words, methylation at one site may increase the likelihood of methylation at nearby sites (and vice versa for demethylation). Thus, there is potential for amplification of environmental exposures, as the methylation patterns spread spatially through the genome. Dr. Dolinoy agreed that methylation is correlated spatially in the genome and noted that it is important to use the right statistical methods to analyze and report methylation patterns.

Another participant noted that some of the clinical trials at The Johns Hopkins University Center might accelerate the tests of multifactorial interventions and noted that the research community should consider how to build community-based efficacy trials. Dr. Dean Baker, UC Irvine, elaborated that Centers have normal avenues for community outreach and translation,

but a formal mechanism (e.g., talks and focus groups) is needed to obtain feedback from the community. In addition, Centers should share lessons learned about methods for translating research findings to the community in their region.

EPA/NIEHS CHILDREN'S CENTERS PROGRAM OFFICE REMARKS

Nica Louie, M.S., EPA

Ms. Louie thanked meeting participants on behalf of the EPA and NIEHS Children's Centers program staff and expressed gratitude for the ability to host the annual Children's Centers meeting - despite the Federal government shutdown. She said that in order to leave the meeting with the words and wisdom of Dr. Christopher, she would offer brief closing remarks and then end the meeting with the keynote address.

She began by stating that a meeting on children's environmental health transcends every individual, every affiliation, organization and personal goal. Stressing that such a meeting is about moving a really vital field forward. She expressed appreciation to the exceptional presenters, keynote speakers and expert panelists that made the conference a success and acknowledged the tremendous efforts of the Steering Committee members (listed alphabetically):

Martha Berger (EPA/OCHP), Pat Buffler (UC Berkeley), Rich Callan (EPA/NCER), Jenny Collins (NIEHS), Sally Darney (EPA/ORD), Ken Elstein (EPA), Elaine Faustman (University of Washington), Kim Gray (NIEHS), Jennifer Lowry (Region 7 PEHSU), Jennifer Mall (EPA/NCER), Marie Lynn Miranda (University of Michigan), Devon Payne Sturges (EPA/NCER), Sheela Sathyanarayana (Region 10 PEHSU), and Virginia Rauh (Columbia University).

Ms. Louie expressed gratitude that the PEHSUs were able to join the annual Children's Centers meeting and thanked her fellow program staff Rich Callan, Kim Gray and Cindy Lawler, as well as EPA Communications Director, Kelly Widener and The Scientific Consulting Group, Inc. (contractor) whose personal sacrifices made the meeting possible.

She closed by thanking EPA and NIEHS senior management, Jim Johnson, Linda Birnbaum and Gwen Collman for their support and expressed hope that the participants leave the meeting empowered, with new collaborative opportunities and experience tremendous success. She recalled EPA Administrator McCarthy's urging to renew the commitment to children's health and encouragement to sprint through the marathon.

KEYNOTE: PROTECTING ALL CHILDREN'S HEALTH: RECOGNIZING AND MITIGATING THE EFFECTS OF CHRONIC EXPOSURE TO ADVERSITY

Gail Christopher, D.N., Kellogg Foundation

Dr. Gail Christopher, who serves as Vice President for Program Strategy at her foundation, expressed her deep respect for the pioneering and cutting-edge work of the Children's Centers. In establishing the Kellogg Foundation, W.K. Kellogg stipulated only one condition: that it be used to help children. The foundation's mission statement is, "We envision a Nation that marshals its resources to ensure that all children thrive." Most children born today in the

United States are of color, and they bear a disproportionate burden of adversity, including adversity from exposure to environmental toxins.

Dr. Christopher discussed the interface between social determinants of health and environmental justice. Social determinants of health are defined broadly as the circumstances in which people are born, grow up, play, live and work. If society addressed the social determinants of health, which are shaped by the distribution of power, there would be no need to address environmental justice. In the United States, the distribution of power arises from a historical legacy of determining a person's value based on their physical characteristics. Uprooting this belief often is ignored in addressing disparities and inequities. The Kellogg Foundation recognizes the need for leaders to deal with the unfinished business of structural inequalities. Dr. Christopher enjoined the participants as leaders to understand that uprooting structural inequalities is central to translating their work to policies and actions.

Children experience double jeopardy when they live in both poor families and poor neighborhoods. A disproportionate number of black and Hispanic children live in poor families and poor neighborhoods compared with white children. Schools today are more segregated than when the U.S. Supreme Court decided the case of Brown v. Board of Education. Past inequalities persist at great cost to society. The gap in earning between people of color and non-Hispanic whites continues and is worse in times of recession. If current inequities are not addressed, they will produce more harm to the Nation's children in the future, a population that is projected to be "majority minority" by 2018. There are continued disparities in birth outcomes for African-American and white women that also depend on the mother's employment opportunities and educational levels. In addition to blacks, disparities affect all groups perceived as different, including Alaska Native peoples, Native Americans, Hispanics and Appalachian whites. The term "racial equity" describes actions to address existing race-based disparities, which include economics, housing, education, exposure to disease, burden of disease and access to quality health care. To achieve racial equity, everyone must participate; it cannot be a "we-they" conversation. Dr. Christopher shared a personal story that is part of her motivation to work toward achieving racial equity. Her 6-week-old baby had a congenital heart defect, but her doctor failed to inform her of an operation that could have saved her child's life. Dr. Christopher's baby died 1 month after being diagnosed. Dr. Christopher stated that her personal loss pales in comparison to the widespread denial of opportunities to people based on racism.

The effects of inequities and disparities are particularly evident in the cumulative impacts of stress. As the Children's Centers have shown, stress dramatically accelerates health risks. The CDC has developed 59 data-based indicators to determine the factors that need to be changed and the way to change them to address disparities in stress. Exposure to environmental toxins is missing, however, from these indicators. Of the 59, 13 were selected as actionable, including adverse childhood experiences, experience of racial discrimination by pregnant women and children, segregation in communities, smoking in the home, child or adult obesity, food insecurity, depression in youth, and incarceration rates. Dr. Christopher provided an example of a community response to a stressor: the strong local food movement that has formed in Detroit, Michigan, in response to food insecurity.

Dr. Christopher outlined personal actions that can be taken to address the legacy of determining a person's value based on his or her physical characteristics. These actions address unconscious biases and microaggression. She urged everyone to take the test developed by Harvard University to assess implicit social biases. Although progress has been made in some social institutions, implicit biases have not been addressed sufficiently in the health care system. Microaggression result from the ways in which actions are interpreted and misinterpreted on a daily basis, leading to a stress response. Organizations can make concrete changes to change the work environment and reduce this source of stress. There is a need to create dynamics in communities to minimize individuals' exposure to unconscious bias and microaggression. The Kellogg Foundation has invested $100 million in communities and seen amazing transformations. She urged scientists to bring the lens of the legacy of disparities to their work and commit to finding holistic and context-based answers. There is a need to provide the social supports that will protect children from harm from disparities. Dr. Christopher thanked the participants for inviting her and expressed her pleasure from learning about a community that is willing to work together to transcend the legacy of disparities.

ADJOURNMENT

The meeting organizers thanked the speakers and participants and adjourned the meeting at 1:15 p.m.

Speaker Biosketches

Gina McCarthy
U.S. Environmental Protection Agency (EPA)

Gina McCarthy is the Administrator of the U.S. Environmental Protection Agency.

Appointed by President Obama in 2009 as Assistant Administrator for EPA's Office of Air and Radiation, Gina McCarthy has been a leading advocate for common-sense strategies to protect public health and the environment.

Previously, Ms. McCarthy served as the Commissioner of the Connecticut Department of Environmental Protection. During her career, which spans more than 30 years, she has worked at both the state and local levels on critical environmental issues and helped coordinate policies on economic growth, energy, transportation and the environment.

Ms. McCarthy received a B.A. in Social Anthropology from the University of Massachusetts at Boston and a joint M.S. in Environmental Health Engineering and Planning and Policy from Tufts University.

When she is not in Washington, DC, Ms. McCarthy lives in the Greater Boston area with her husband and two dogs, just a short bike ride away from their three children, Daniel, Maggie and Julie.

Linda S. Birnbaum, Ph.D.
National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH)

Dr. Birnbaum is the Director of the NIEHS of the NIH and the National Toxicology Program (NTP). As NIEHS and NTP Director, Dr. Birnbaum oversees a budget of $730 million that funds biomedical research to discover how the environment influences human health and disease. The Institute also supports training, education, technology transfer and community outreach. NIEHS currently funds more than 1,000 research grants.

A board certified toxicologist, Dr. Birnbaum has served as a federal scientist for nearly 34 years. Prior to her appointment as NIEHS and NTP Director in 2009, she spent 19 years at the U.S. Environmental Protection Agency (EPA), where she directed the largest division focusing on environmental health research. Dr. Birnbaum started her federal career with 10 years at the NIEHS, first as a senior staff fellow in the NTP, then as a principal investigator and research microbiologist, and finally as a group leader for the Institute's Chemical Disposition Group.

Dr. Birnbaum has received many awards and recognitions. In October 2010, she was elected to the Institute of Medicine of the National Academies, one of the highest honors in the fields of medicine and health. She was elected to the Collegium Ramazzini, and received an honorary Doctor of Science from the University of Rochester and a Distinguished Alumna Award from the University of Illinois. Other awards include the 2011 NIH Director's Award, Women in Toxicology Elsevier Mentoring Award, Society of Toxicology Public Communications Award, EPA's Health Science Achievement Award and Diversity Leadership Award, National Center for Women's 2012 Health Policy Hero Award, Breast Cancer Fund Heroes Award, 2013 American Public Health Association Homer N. Calver Award, 2013 Children's Environmental Health Network Child Health Advocate Award, and 14 Scientific and Technological Achievement Awards, which reflect the recommendations of EPA's external Science Advisory Board, for specific publications.

She is the author of more than 600 peer-reviewed publications, book chapters and reports. Dr. Birnbaum's own research focuses on the pharmacokinetic behavior of environmental chemicals; mechanisms of action of toxicants, including endocrine disruption; and linking of real-world exposures to health effects. She is also an adjunct professor in the Gillings School of Global Public Health, the Curriculum in Toxicology, and the Department of Environmental Sciences and Engineering at the University of North Carolina at Chapel Hill, as well as in the Integrated Toxicology and Environmental Health Program at Duke University.

Lek Kadeli, M.A.
U.S. Environmental Protection Agency (EPA), Office of Research and Development (ORD)

Mr. Kadeli is the Acting Assistant Administrator in EPA's ORD. He has more than 29 years of management experience in both government and the private sector, with broad experience in leading organizational change and improvement, policy development, resource management, information management, and technology.

Mr. Kadeli began his EPA career in 1990 as an analyst in the Office of the Comptroller, and also served as the Senior Budget Officer in EPA's Office of International Activities. He moved to ORD in 1993 to serve as Chief of Resource Planning and Program Coordination, and in 1998 served as the Acting Deputy Director of ORD's National Exposure Research Laboratory in Research Triangle Park, North Carolina. He was the director of ORD's Office of Resources Management and Administration from 2001 to 2005 before becoming the Deputy Assistant Administrator for Management. He previously served as the Acting Assistant Administrator for ORD from January through December of 2009.

Mr. Kadeli received two of the Agency's highest awards for exemplary service: a Gold Medal for Distinguished Service and the Lee Thomas Award for Excellence in Management.

Mr. Kadeli graduated from George Mason University in 1983 with a B.A. in International Relations. In 1986, he earned an M.A. in National Security Studies from Georgetown University.

Gail C. Christopher, D.N.
W.K. Kellogg Foundation

Dr. Christopher is Vice President for Program Strategy at the W.K. Kellogg Foundation. In this role, she leads the Food, Health and Well-Being, Racial Equity, Community and Civic Engagement and Leadership programming.

Dr. Christopher is a nationally recognized leader in health policy, with particular expertise and experience in the issues related to social determinants of health, health disparities and public policy issues of concern to our Nation's future. She has more than 20 years of experience in designing and managing national initiatives and nonprofit organizations. She brings extensive knowledge and experience in creating a comprehensive approach to well-being and is nationally recognized for her pioneering work to infuse holistic health and diversity concepts into public sector programs and policy discourse. Her distinguished career and contributions to public service were honored in 1996 when she was elected as a Fellow of the National Academy of Public Administration. A prolific writer and presenter, Dr. Christopher is the author or co-author of three books, a monthly column in the *Federal Times*, and more than 250 articles, presentations and publications.

Dr. Christopher holds a Doctorate of Naprapathy degree from the Chicago National College of Naprapathy in Illinois and completed advanced study in the interdisciplinary Ph.D. program in holistic health and clinical nutrition at the Union for Experimenting Colleges and Universities at Union Graduate School of Cincinnati, Ohio. She is President of the Board of Directors of the Trust for America's Health.

Sandra Steingraber, Ph.D.

Ecologist, author and cancer survivor, Sandra Steingraber, Ph.D., is an internationally recognized authority on the environmental links to cancer and human health. Dr. Steingraber's highly acclaimed book, *Living Downstream: An Ecologist's Personal Investigation of Cancer and the Environment*, presents cancer as a human rights issue. Originally published in 1997, it was the first study to bring together data on toxic releases with data from U.S. cancer registries and won praise from international media.

Dr. Steingraber's second book, *Having Faith: An Ecologist's Journey to Motherhood,* explores the intimate ecology of motherhood. Both a memoir of her own pregnancy and an investigation of fetal toxicology, *Having Faith* reveals the extent to which environmental hazards now threaten each stage of infant development and was featured in a PBS documentary by Bill Moyers. Called "a poet with a knife" by *Sojourner* magazine, Dr. Steingraber is the recipient of many prestigious awards, and the Sierra Club has heralded her as "the new Rachel Carson." An enthusiastic and sought-after public speaker, Dr. Steingraber also has keynoted at conferences on human health and the environment throughout the United States and Canada, including at Harvard, Yale, Cornell, Columbia and the Woods Hole Research Center. Interviews with Dr. Steingraber have appeared in *The Chicago Tribune, USA Today, The Cleveland Plain Dealer,* and on National Public Radio, "The Today Show" and "Good Morning America."

Randy Olson, Ph.D.
Wrigley Institute for Environmental Studies at the University of Southern California (USC)

Dr. Olson is the writer/director of the feature films *Flock of Dodos: The Evolution-Intelligent Design Circus*, (Tribeca '06, Showtime '07), *Sizzle: A Global Warming Comedy* (Outfest '08), and author of *Don't Be Such a Scientist: Talking Substance in an Age of Style* (Island Press '09).

Dr. Olson's work focuses on the challenges involved in communicating science to the general public and on the current attacks on mainstream science in fields such as evolution and climate science. He is a former marine biologist (Ph.D., Harvard University) who achieved tenure at the University of New Hampshire before changing careers to filmmaking by obtaining an M.F.A. in Cinema from the University of Southern California (USC). He is an adjunct faculty member with the Wrigley Institute for Environmental Studies at USC. His production company, Prairie Starfish Productions, is based at Raleigh Studios in Los Angeles.

Ramona Trovato
U.S. Environmental Protection Agency (EPA)

Ms. Trovato is the Associate Assistant Administrator for the U.S. Environmental Protection Agency's Office of Research and Development. During her career at the EPA, Ms. Trovato has had the opportunity to work in 7 major organizations in headquarters: Office of Research and Development, Office of the Administrator, Office of Water, Office of Enforcement and Compliance Assurance, Office of Air and Radiation, Office of Environmental Information and Office of Solid Waste and Emergency Response. She also worked in Region 3.

Ms. Trovato has received several awards that are particularly noteworthy. During her government service she was recognized with the Distinguished Career Award in recognition of extraordinary leadership and exceptional dedication in serving the American people; the President's Meritorious Executive Rank Award for leadership, for achieving results in environmental and public health protection, and for building strong coalitions and partnerships to achieve environmental and public health goals; the EPA's Silver Medal for developing the National Environmental Laboratory Accreditation Conference; and the President's Award of the Association of Public Health Laboratories for meritorious service to public health laboratories. In 2005, she received EPA's Children's Environmental Health Champion Award. During this time, Ms. Trovato worked on many complex environmental issues with many thoughtful, professional, and hard-working people to find solutions that were protective of the environment and public health, and cost effective. She is most proud of her work in protecting and promoting children's health; finding a safe solution for disposal of low-level, transuranic waste; consolidating 8 different Clean Water Act penalty policies; developing and implementing the comprehensive State ground water protection program; working with the private sector and states to make the best and highest use of properties cleaned up under the Superfund program; enhancing the IT department's commitment to service through improved understanding of program needs; nurturing, developing and implementing the National Environmental Laboratory Accreditation Program; and working to assure that the country has the environmental laboratory capability and capacity to respond to emergencies related to homeland security.

Ms. Trovato received a B.S. Degree in Zoology from the University of Maryland at College Park in 1974. She undertook additional studies in chemistry, facilitation, negotiation, information technology management, management and leadership throughout her career.

James H. Johnson, Jr., Ph.D.
U.S. Environmental Protection Agency (EPA), Office of Research and Development (ORD)

Dr. Johnson is the Director of the National Center for Environmental Research (NCER) at EPA's ORD. In this role, Dr. Johnson continues a life-long career dedicated to sustaining and advancing scientific research and education initiatives supporting environmental protection, quality of life programs and policies, and environmental workforce development. Dr. Johnson has served on numerous committees and boards for the National Academies, EPA and academic institutions. He is a member of the Anne Arundel Community College (MD) Board of Trustees, and is Professor Emeritus of Civil Engineering and Dean Emeritus of the College of Engineering, Architecture and Computer Sciences at Howard University.

Dr. Johnson earned his B.S. in Civil Engineering from Howard University, M.S. from the University of Illinois, and Ph.D. in Applied Sciences from the University of Delaware. He is the 2005 recipient of the National Society of Black Engineers' Lifetime Achievement Award in Academia and the 2008 Water Environment Federation Gordon Maskew Fair Award. His research interests include the treatment and disposal of hazardous substances, the use of nanomaterials for environmental restoration, the evaluation of environmental policy issues in relation to minorities, and the development of environmental curricula and strategies to increase the pool of underrepresented groups in the science, technology, engineering and math (STEM) disciplines.

Kenneth Olden, Sc.D., L.H.D.
U.S. Environmental Protection Agency (EPA), National Center for Environmental Assessment (NCEA)

Dr. Olden joined NCEA in July 2012 with a strong legacy of promoting scientific excellence in environmental health. From 1991 to 2005, he served as the Director of the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP) in the U.S. Department of Health and Human Services. He made history in this role as the first African-American to direct one of the National Institutes of Health. In 2005, he returned to his research position as chief of the Metastasis Group in the Laboratory of Molecular Carcinogenesis at the NIEHS, and for academic year 2006–2007, held the position of Yerby Visiting Professor at the Harvard School of Public Health.

Most recently, Dr. Olden served as the Founding Dean of the School of Public Health at Hunter College, City University of New York. He has published extensively in peer-reviewed literature, chaired or co-chaired numerous national and international meetings, and has been an invited speaker, often as keynote, at more than 200 symposia. He has won a long list of honors and awards, including the Presidential Distinguished Executive Rank Award, the Presidential Meritorious Executive Rank Award for sustained extraordinary accomplishments, the Toxicology Forum's Distinguished Fellow Award, the HHS Secretary's Distinguished Service Award, the American College of Toxicology's First Distinguished Service Award and the National Minority Health Leadership Award.

Alone among Institute directors, he was awarded three of the most prestigious awards in public health: the Calver Award (2002), the Sedgwick Medal (2004) and the Julius B. Richmond Award (2005). Most recently, he received the Cato T. Laurencin M.D., Ph.D. Lifetime Research Award from the National Medical Association Institute, the largest and oldest national organization representing African-American physicians and their patients in the United States. He was elected to membership in the Institute of Medicine at the National Academy of Sciences in 1994 and appointed member of the Visiting Committee for the Harvard University Board of Overseers from 2007 to 2010.

Dr. Olden holds the following degrees:

- Temple University, Philadelphia, Ph.D., Cell Biology and Biochemistry, 1970.
- University of Michigan, Ann Arbor, M.S., Genetics.
- Knoxville College, B.S., Biology.

Additionally, Dr. Olden has numerous honorary degrees from several prestigious colleges and universities.

Richard Auten, M.D.
Duke University Medical Center

Dr. Auten received his Bachelor of Arts and medical degrees at the University of North Carolina at Chapel Hill. After training in pediatrics at the University of Rochester, he practiced as a pediatrician for 3 years and returned to the University of Rochester for a neonatal medicine fellowship. He joined the faculty of the Department of Pediatrics in 1990 and is now a Professor of Pediatrics. His research interests have focused on the mechanisms of neonatal lung injury, as well as the interaction between fetal inflammatory exposures and abnormal postnatal development. His research has been supported by the American Lung Association, the Children's Miracle Network, the U.S. Environmental Protection Agency, the National Institutes of Health and the March of Dimes, as well as industry contracts. He is the author of more than 60 peer-reviewed scientific publications and serves on the editorial boards of the *American Journal of Physiology* and the *American Journal of Perinatology*.

Susan Buchanan, M.D., M.P.H.
University of Illinois Department of Environmental and Occupational Health Sciences

Dr. Buchanan is the Director of the Great Lakes Center for Children's Environmental Health, which is the federally funded Pediatric Environmental Health Specialty Unit for the U.S. Environmental Protection Agency's Region 5. She also is a Clinical Assistant Professor at the University of Illinois Department of Environmental and Occupational Health Sciences.

Dr. Buchanan graduated from the Ohio State University College of Medicine and completed a Family Medicine residency at the Medical Center Hospital of Vermont. After 9 years of clinical Family Medicine practice, she sought additional training and board certification in Occupational and Environmental Medicine. She is Associate Professor of Environmental and Occupational Health Sciences at the University of Illinois at Chicago (UIC) School of Public Health, where she teaches and conducts research on prenatal exposure to environmental pollutants. She is Director of the UIC residency program in Occupational and Environmental Medicine.

Antonia Calafat, Ph.D.
U.S. Centers for Disease Control and Prevention (CDC)

Dr. Calafat is the Chief of the Organic Analytical Toxicology Branch at the Division of Laboratory Sciences, National Center for Environmental Health of the CDC. She earned her Bachelor's, Master's and Doctoral degrees in Chemistry from the University of the Balearic Islands (Spain). Prior to her career at CDC, she was a Fulbright Scholar and a Research Associate at Emory University. She currently leads CDC's biomonitoring programs for assessing human exposure to pesticides, polycyclic aromatic hydrocarbons and persistent organic pollutants such as polyfluoroalkyl compounds. She also leads CDC's biomonitoring programs for polybrominated diphenyl ethers, polychlorinated dibenzo-p-dioxins, furans, biphenyls and chemicals added to consumer and personal care products, such as phthalates and phenols (e.g., bisphenol A, triclosan and parabens). She has developed and maintained extensive collaborative research with leading scientists in the fields of exposure science, epidemiology, toxicology and health assessment. Her research has made relevant contributions to CDC's biomonitoring program, including the CDC's National Reports on Human Exposure to Environmental Chemicals.

Lisa Cicutto, Ph.D., R.N.
National Jewish Health and University of Colorado Denver Children's Environmental Health Center

Dr. Cicutto directs the Clinical Science Program at the University of Colorado Denver and is currently the Director of Community Outreach and Research at National Jewish Health and Co-Director of the Community Outreach and Translation Core of the Denver Children's Environmental Health Center funded by the National Institute of Environmental Health Sciences and the U.S. Environmental Protection Agency. In her role, she is dedicated to reducing the lung health burden of communities through the translation and uptake of the best available research and evidence. She has more than 20 years of experience working in community settings—primarily schools, child-care settings and homes—to develop, implement and evaluate programs that are responsive to community needs while being evidence-based and supportive of the partnerships that often are needed with health care providers. One of the school-based asthma education programs of which she led the development, implementation and evaluation is now a mandated program in Ontario Public Health.

Gwen W. Collman, Ph.D.
Division of Extramural Research and Training, National Institute of Environmental Health Sciences (NIEHS)

Dr. Collman is Director of the NIEHS Division of Extramural Research and Training where she leads approximately 60 professional staff in areas of scientific program administration, peer review, and the management and administration of about 1,500 active grants each year. She directs scientific activities across the field of environmental health sciences, including basic sciences (i.e., DNA repair, epigenetics, environmental genomics), organ-specific toxicology (i.e., reproductive, neurotoxicology, respiratory), public health-related programs (i.e., environmental epidemiology, environmental public health), and training and career development. She also oversees the implementation of the Superfund Research Program and the Worker Education and Training Program. Dr. Collman served in program development and management, beginning in 1992 as a member, then as Chief, of the Susceptibility and Population Health Branch. She directed research on the role of genetic and environmental factors on the development of human disease, from animal models of genetic susceptibility to population studies focusing on etiology and intervention. She was responsible for building the NIEHS grant portfolio in environmental and molecular epidemiology, and developed several complex multidisciplinary research programs. These include the NIEHS Breast Cancer and the Environment Research Centers Program; the NIEHS/U.S. EPA Centers for Children's Environmental Health and Disease Prevention; and the Genes, Environment and Health Initiative. Also under her guidance, a team created a vision for the Partnerships for Environmental Public Health programs for the next decade.

Deborah A. Cory-Slechta, Ph.D.
University of Rochester School of Medicine and Dentistry

Dr. Cory-Slechta is currently a Professor of Environmental Medicine and Pediatrics; former Dean for Research, Chair of the Department of Environmental Medicine and Director of the National Institute of Environmental Health Sciences (NIEHS) Environmental Health Sciences Center at the University of Rochester Medical School; and former Director of the Environmental and Occupational Health Sciences Institute (EOHSI) of Rutgers/Robert Wood Johnson Medical School. Dr. Cory-Slechta has served on the editorial boards of *Neurotoxicology*, *Toxicology*, *Toxicological Sciences*, *Fundamental and Applied Toxicology*, *Neurotoxicology and Teratology*, and the *American Journal of Mental Retardation.* She also has served in elected positions as President of the Neurotoxicology Specialty Section of the Society of Toxicology, and President of the Behavioral Toxicology Society, and been named a Fellow of the American Psychological Association. Her research on the role of environmental

neurotoxicants in developmental disabilities and neurodegenerative diseases has resulted in more than 150 papers and book chapters to date.

Kathryn Cottingham, Ph.D.
Dartmouth College

Dr. Cottingham is an ecologist and biostatistician who began working on children's exposure to arsenic as part of Dartmouth's formative Center for Children's Environmental Health and Disease Prevention Research. She led the 3-year pilot project investigating how infants born to the women in the prospective New Hampshire Birth Cohort (NHBC) are exposed to arsenic via both food and water and currently co-leads an ongoing exposure assessment that will be used to quantify effects of arsenic on growth and neurodevelopment through age 5. Dr. Cottingham and colleagues have conducted market-basket surveys of arsenic concentrations in infant formulas and weaning foods, evaluated associations between rice consumption and short- and long-term biomarkers of arsenic exposure, and quantified the relative exposure of infants in the NHBC to arsenic via breast milk versus formula. Their ongoing work includes assessing infant exposure to arsenic via rice cereal and other high-arsenic foods during weaning.

Michael Crupain, M.D., M.P.H.
Consumer Reports Foods Safety and Sustainability Center

Dr. Crupain is an Associate Director of the Consumer Reports Safety and Sustainability group and directs food safety testing for the Consumer Reports Foods Safety and Sustainability Center. He is interested in the intersection of food, agriculture and health policy, and is board-certified in Preventive Medicine. He completed his medical training at New York Medical College and residency at The Johns Hopkins Bloomberg School of Public Health, where he also teaches.

Kim Dietrich, Ph.D., M.A.
University of Cincinnati College of Medicine, Department of Environmental Health

Dr. Dietrich is a lifespan developmental neuropsychologist and Professor of Environmental Health, Director of the Division of Epidemiology and Biostatistics, and Associate Director of the Molecular Epidemiology in Children's Environmental Health training program at the University of Cincinnati College of Medicine. Dr. Dietrich has served as a consultant to numerous national and international organizations concerned with the impact of environmental chemical exposures on the health and development of young children. He is the author of the Cincinnati Lead Study, the longest running longitudinal prospective investigation of lead and child neuropsychological and behavioral development. Over the course of his nearly 40-year-long career in pediatric neuroepidemiology, he has examined the impact of a wide variety of early environmental chemical and social influences on infant, child, adolescent and adult development.

Gregory Diette, M.D., M.H.S.
The Johns Hopkins University

Dr. Diette is Professor of Medicine, Epidemiology and Environmental Health Sciences. He is a pulmonologist with a practice devoted to the care of patients with obstructive lung diseases, including asthma and chronic obstructive pulmonary disease (COPD). He has an extensive portfolio of patient-based research in asthma and COPD, supported by the National Institutes of Health and other sponsors. Dr. Diette's current research focuses on identifying factors that cause or provoke asthma with special interest in air pollutants (particulate matter, NO_2, secondhand smoke) and allergens (including mouse) that are especially problematic in inner-city homes. His research includes the effects of these pollutants and allergens on inflammation and oxidative stress. More recently, his research has been examining how dietary patterns, especially a Western-style diet, may increase susceptibility to inhalable pollutants and allergens.

Dana Dolinoy, Ph.D.
University of Michigan School of Public Health

Dr. Dolinoy serves as the John G. Searle Assistant Professor of Environmental Health Sciences at the University of Michigan (UM) School of Public Health and leads the Environmental Epigenetics and Nutrition Laboratory, which investigates how nutritional and environmental factors interact with epigenetic gene regulation to shape health and disease. Dr. Dolinoy is as an investigator in the U.S. Environmental Protection Agency/National Institute of Environmental Health Sciences-funded UM Children's Environmental Health and Disease Prevention Research Center, investigating early exposure to bisphenol A (BPA), lead and phthalates; epigenetics; and later-in-life body weight and hormone outcomes. In 2011, Dr. Dolinoy received the Norman Kretchmer Memorial Award from the American Society for Nutrition and the Classic Paper of the Year Award from *Environmental Health Perspectives*.

Brenda Eskenazi, Ph.D., M.A.
University of California, Berkeley

Dr. Eskenazi is the Jennifer and Brian Maxwell Professor of Maternal and Child Health and Epidemiology at the University of California, Berkeley. She is a neuropsychologist and epidemiologist whose long-standing research interest has been the effects of toxicants, including lead, solvents, environmental tobacco smoke, dioxin and pesticides, on human reproduction (both male and female) and child development. She is the Principal Investigator (PI) and Director of an National Institutes of Health/U.S. Environmental Protection Agency Center for Excellence in Children's Environmental Health Research and its keystone project, CHAMACOS, which investigates the exposure pathways and health effects of pesticide exposure in farmworkers and their children and develops interventions to prevent future exposure. She is currently investigating associations between pubertal development and endocrine-disrupting chemicals, including flame retardants and pesticides, in children of the CHAMACOS cohort. Dr. Eskenazi was also the PI on a grant aimed at understanding the effects of U.S.-Mexico migration on childhood obesity; she conducted research on food insecurity, obesity and maternal perception of child weight. She also is the PI on other National Institute of Environmental Health Sciences-funded projects on endocrine disruption: one based in Seveso, Italy, investigating the reproductive health of a cohort of women exposed to high levels of dioxin by studying the age of onset of menarche among other endpoints; and another examining the effects of persistent and nonpersistent endocrine disruptors on neurodevelopment. Dr. Eskenazi recently has been awarded the LiKaShing Award and the John R. Goldsmith Award for lifetime achievement in environmental epidemiology.

Maida Galvez, M.D., M.P.H.
Icahn School of Medicine at Mount Sinai

Dr. Galvez is an Associate Professor of Preventive Medicine and Pediatrics at the Icahn School of Medicine at Mount Sinai in New York City. She directs the Region 2 Pediatric Environmental Health Specialty Unit at Mount Sinai. She was Co-Principal Investigator and designated New Investigator of the National Institute of Environmental Health Sciences/U.S. Environmental Protection Agency (EPA)-funded Children's Environmental Health and Disease Prevention Research Center community-based project, Growing Up Healthy in East Harlem. She is a co-investigator, responsible for pubertal staging methodology, in the national consortium of Breast Cancer Environment Research Centers and lead pediatrician in the Centers for Disease Control and Prevention-funded IMPACT Diabetes project. Dr. Galvez currently serves on the EPA federal advisory board for the Office of Children's Health Protection, on the EPA Scientific Advisory Board Human Health Committee and as President of District 2 Chapter 3 of the American Academy of Pediatrics.

Kim Harley, Ph.D.
Center for Environmental Research and Children's Health (CERCH), University of California, Berkeley (UCB)

Dr. Harley is an Associate Adjunct Professor of Public Health at UCB. She is a reproductive and perinatal epidemiologist whose research focuses on the association between endocrine-disrupting chemicals and child development, including neurodevelopment, obesity and the onset of puberty. Dr. Harley also is Associate Director for Health Effects of UCB's Center for Environmental Research and Children's Health (CERCH) and coordinates the CHAMACOS Study of immigrant farmworker women and their children living in the Salinas Valley. Her research focuses on the effects of environmental chemical exposures to mothers and children living in a migrant farm worker community. Her work has focused on the reproductive and developmental effects of bisphenol A (BPA), PBDEs, DDT and organophosphate pesticides.

Elizabeth Matsui, M.D., M.H.S.
Children's Environmental Health Center (CEHC), The Johns Hopkins University

Dr. Matsui's research program focuses on the clinical investigation of allergen and pollutant exposure and allergic airways disease. She also is a practicing pediatric allergist/immunologist. She holds a Master's Degree in Epidemiology and has directed The Johns Hopkins Children's Center's Data Management and Analysis Core for the past 7 years. She serves as the Project Leader for the Hopkins Children's Center, directing studies focused on the effect of dietary interventions on asthma. In addition to her roles in the Hopkins Children's Center, she is a Co-Investigator in the Inner-City Asthma Consortium, a Co-Investigator on an R01-funded prospective cohort study of mouse workers at The Jackson Laboratory and the Principal Investigator of a U01-funded, multicenter clinical trial of home mouse allergen abatement in mouse-allergic children with asthma.

Pam Maxson, Ph.D.
Southern Center on Environmentally Driven Disparities in Birth Outcomes, Duke University

Dr. Maxson is the Research Director of the Children's Environmental Health Initiative at the School of Natural Resources and Environment at the University of Michigan. She is the Project Manager for the Southern Center on Environmentally Driven Disparities in Birth Outcomes (SCEDDBO), as well as the Director of its Community Outreach and Translational Core. Dr. Maxson's research interests lie in the influence of chemical and nonchemical stressors on pregnancy and childhood outcomes. She has extensive experience collaborating with physicians, research scientists and the community on the interface of research and practice in health and the environment.

Dr. Mark Miller, M.D., M.P.H.
University of California, San Francisco (UCSF)

Dr. Miller is an Assistant Clinical Professor in the Department of Pediatrics at the UCSF and the Director of the UCSF Pediatric Environmental Health Specialty Unit (PEHSU). He is a Public Health Medical Officer and the Director of the Children's Environmental Health Program for the California Environmental Protection Agency Office of Environmental Health Hazard Assessment. He also works with the Center for Integrative Research on Childhood Leukemia and the Environment at the University of California, Berkeley (UCB). He completed his M.D. degree and pediatric residency from Michigan State University College of Human Medicine, an M.P.H. in Environmental Health Sciences from UCB, and a residency in Preventive Medicine with the California Department of Health Services. Dr. Miller spent 13 years as a pediatrician in private practice in Chico, California. He is a founding member and on the Board of Councilors of the International Society for Children's Health and the Environment. His articles on pediatric environmental health issues have appeared in such publications as *Pediatrics*, *Environmental Health Perspectives* and the *Handbook of Pediatric Environmental Health* (American Academy of Pediatrics).

Nicholas Newman, D.O., M.S.
Cincinnati Children's Hospital/University of Cincinnati Pediatric Environmental Health Specialty Unit (PEHSU)

Dr. Newman is a board-certified pediatrician and occupational/ environmental medicine physician and the Site Director of the Region 5 PEHSU Satellite at Cincinnati Children's Hospital Medical Center. Dr. Newman is interested in understanding the effects of common environmental toxicants on children and in translating this information into actions that will improve children's health.

Jerome A. Paulson, M.D.
The George Washington University School of Medicine and Health Sciences

Dr. Paulson is a Professor of Pediatrics at The George Washington University School of Medicine and Health Sciences and Professor of Environmental and Occupational Health at The George Washington School of Public Health and Health Services.

Dr. Paulson is the Medical Director for National and Global Affairs of the Child Health Advocacy Institute at the Children's National Medical Center. He is the Director of the Mid-Atlantic Center for Children's Health and the Environment and of the Environmental Health Track at The George Washington University School of Medicine and Health Sciences.

Dr. Paulson is the chairperson of the executive committee of the Council on Environmental Health of the American Academy of Pediatrics. He also serves on the Children's Health Protection Advisory Committee for the U.S. Environmental Protection Agency. He was a recipient of a Soros Advocacy Fellowship for Physicians from the Open Society Institute; worked with the Children's Environmental Health Network; and has served as a Special Assistant to the Director of the National Center on Environmental Health of the Centers for Disease Control and Prevention, working on children's environmental health issues. He has developed several new courses for The George Washington School of Public Health about children's health and the environment. He is the editor of the October 2001 and the February and April 2007 editions of *Pediatric Clinics of North America* on children's environmental health.

Frederica Perera, Dr.P.H., Ph.D.
Columbia University Children's Environmental Health Center (CEHC)

Dr. Perera is a Professor at Columbia University's Mailman School of Public Health, where she serves as Director of the Columbia Center for Children's Environmental Health. Dr. Perera is internationally recognized for pioneering the field of molecular epidemiology, utilizing biomarkers to understand links between environmental exposures and disease. Currently, she and her colleagues are applying advanced molecular and imaging techniques within longitudinal cohort studies of pregnant women and their children, with the goal of identifying preventable risk factors for developmental disorders, asthma, obesity and cancer in childhood. Her areas of specialization include prevention of environmental risks to children, molecular epidemiology, disease prevention, environment-susceptibility interactions, and risk assessment. She is the author of more than 300 publications, including 260 peer reviewed articles, and has received numerous honors, including First Irving J. Selikoff Cancer Research Award, The Ramazzini Institute (1995); The Century Club Award *Newsweek* (1997); First Children's Environmental Health Award, The Pew Center for Children's Health and the Environment (1999); Distinguished Lecturer, Occupational and Environmental Cancer, National Cancer Institute (2002); Doctoris Honoris Causa, Jagiellonian University, Krakow, Poland (2004); Children's Environmental Health Excellence Award, U.S. Environmental Protection Agency (2005); and the Children's Environmental Health Network (CEHN) Award (2008).

Lesliam Quirós-Alcalá, Ph.D.
University of California, Berkeley

Dr. Quirós-Alcalá is a Postdoctoral Fellow at the Center for Environmental Research and Children's Health at the University of California, Berkeley. Her research explores the effects of environmental contaminants on women's and children's health and evaluates factors related to exposures in susceptible populations. Her current research focuses on bisphenol A exposure in Latino mothers and children, and studying the effects of current-use pesticides on brain and nervous system development in children.

Urvashi Rangan, Ph.D.
Consumer Reports' Consumer Safety and Sustainability Group

Dr. Rangan is an environmental health scientist and toxicologist. She leads Consumer Reports' Consumer Safety and Sustainability Group and serves as the Executive Director of its Food Safety and Sustainability Center. Dr. Rangan oversees all of Consumer Reports' safety testing projects and risk assessments. She serves as the lead spokesperson on these issues, translating complex scientific concepts into actionable consumer advice and policy recommendations. She has expertise in food safety issues, food labeling, risk assessment and sustainable production practices. In addition to appearing frequently in major news outlets, she testifies to government bodies, has given lectures at various universities and conferences, and has directly challenged critics of a sustainable food system.

Virginia Rauh, Sc.D.
Columbia Center for Children's Environmental Health, Columbia University Mailman School of Public Health

Dr. Rauh is Professor of Population and Family Health at the Mailman School of Public Health, Columbia University, and Deputy Director of the Columbia Center for Children's Environmental Health. She is a perinatal epidemiologist with a focus on the adverse impact of exposure to air pollutants, including secondhand smoke and pesticides, on pregnancy and child health. She has been the Principal Investigator on numerous major research projects, including the impact of organophosphorus insecticides and secondhand smoke on child neurodevelopment and structural brain abnormalities (MRI); a randomized intervention trial for low-birth weight infants; a multisite study of lifestyles in pregnancy; a study of developmental outcomes of children born to inner-city adolescent mothers; a multilevel analysis of the impact of Head Start on New York City school children; and a study of links between race, stressors and preterm birth. She serves on numerous national committees, including advisory groups at the National Institute of Environmental Health Sciences, The Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Scientific Advisory Board for the U.S. Environmental Protection Agency.

Sheela Sathyanarayana, M.D., M.P.H.
Department of Pediatrics, University of Washington

Dr. Sathyanarayana is an Assistant Professor of Pediatrics and Adjunct Assistant Professor in the Department of Environmental and Occupational Health Sciences at the University of Washington. Dr. Sathyanarayana serves as the Co-Director of the Pediatric Environmental Health Specialty Unit (PEHSU) in Region 10, where she performs environmental health consults for health care professionals, government entities and individual families related to environmental exposures and children's health. Her research interests focus on exposures to endocrine-disrupting chemicals, including phthalates and bisphenol A, and their impact on reproductive development. Currently, Dr. Sathyanarayana is the Center Director and Clinical Director for The Infant Development and Environment Study, which is a multicenter cohort study of phthalate exposures in pregnancy and health outcomes in children. She recently was named Outstanding New Investigator within the University of Washington Center for Ecogenetics and Environmental Health (CEEH). She currently serves as the Co-Chair for the U.S. Environmental Protection Agency's Children's Health Protection Advisory Committee.

Patrice Sutton, M.P.H.
Children's Environmental Health Research Center, University of California, San Francisco

Ms. Sutton is a Research Scientist at the University of California, San Francisco, Program on Reproductive Health and the Environment (PRHE). She is the Director of PRHE's Community Outreach and Translation Core, spearheading collaborative efforts to advance reproductive environmental health in clinical and policy arenas. Ms. Sutton has more than 25 years of experience in occupational and environmental health research, industrial hygiene, public health practice, policy development, and community-based advocacy. As a contractor to California's State Health Department from 1987 to 2006, she was responsible for conducting all aspects of research investigations that spanned a disparate range of issues, including lead poisoning, tuberculosis, asthma and pesticide-related illness. She has extensive experience in collaborating with directly impacted workplace and community-based populations, labor, and governmental and nongovernmental organizations in the development of research strategies and policy recommendations to protect public health.

Judy Van de Water, Ph.D.
National Institute of Environmental Health Sciences (NIEHS) Center for Children's Environmental Health, University of California, Davis (UC Davis)

Dr. Van de Water joined the faculty in the Department of Internal Medicine at the University of California, Davis, in 1999. In 2000, she also joined the faculty of the newly formed UC Davis M.I.N.D. Institute when she began her research on the immunobiology of autism.

Dr. Van de Water's laboratory pursues research programs pertaining to autoimmune and clinical immune-based disorders, including the biological aspects of autism spectrum disorders. The application of Dr. Van de Water's immunopathology background has been instrumental in the dissection of the immune anomalies noted in some individuals with autism, and in the differentiation of various autism behavioral phenotypes at a biological level. Dr. Van de Water is currently the Director of the NIEHS-funded Center for Children's Environmental Health at UC Davis, investigating potential environmental risk factors contributing to the incidence and severity of childhood autism.

Joseph L. Wiemels, Ph.D.
University of California, Berkeley (UCB)/University of California, San Francisco (UCSF)

Dr. Wiemels is a Professor of Epidemiology at University of California, San Francisco. He did a postdoctoral fellowship studying the etiology of childhood leukemia in the United Kingdom. Returning to California in 2000, Dr. Wiemels has been a faculty member at UCSF and working with UCB colleagues on the California Childhood Leukemia Study, as well as spearheading other efforts at UCSF aimed at understanding the causes of brain cancer, meningioma, and skin and pancreatic cancers. He works to build connections between epidemiology and molecular genetics, and define the stepwise progression of cancer and the body's own attempts to react against tumors.

Poster Abstracts

Utilizing GIS and Mapping for More Equitable Distributions of Environmental Health Services to Spanish-Speaking Populations

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Background: The Region II PEHSU, which covers New York, New Jersey, Puerto Rico and the U.S. Virgin Islands, was created to ensure that communities have access to specialized medical knowledge for children faced with environmental hazards. According to the Natural Resource Defense Council, a disproportionate amount of the Region II Spanish-speaking population live in poor housing with existing patterns of environmental injustice.

Aim: Knowledge of the geographic distributions of potential toxic environmental exposures, as well as key demographic indicators, is essential to target outreach to vulnerable populations and to address environmental health disparities.

Methods: We used Geographic Information System (GIS) data on childhood disease, environmental exposures and demographic indicators for Region II Spanish-speaking communities at the county level. Environmental justice organizations, as well as PEHSU historical calls and outreach events from the database, were integrated into the GIS to assess future outreach steps and high-priority sites.

Results: To address our objective of improving PEHSU programs by focusing on vulnerable communities, a series of maps were constructed. These maps determine the density of children under 18 years old; families with children living in poverty; Spanish-speaking families with children; core chemical releases; and prevalence of childhood asthma, lead poisoning, low birth weight and obesity in federal Region II.

Conclusion: The study analysis will provide information to advance the development of new tools, such as a map atlas to assist communities with environmental risk assessments and hazardous prioritization, and to create a model of service expansion for other PEHSU sites, both nationally and internationally.

Formaldehyde Exposure Levels During Pregnancy

Azita Amiri [1, 2], Clinical Assistant Professor; Azin Nowrouzi [3]; Gordon McGregor [4]; Michelle Fanucchi[5]; Erica Pryor[2]; Lisa Schwiebert [6]; Charles A. Downs [8]; Marti Rice [6]; and Anne Turner-Henson [7]
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[6]School of Medicine, University of Alabama at Birmingham, Birmingham, AL
[7]Nell Hodgson Woodruff School of Nursing, Emory University; City, ST

Introduction: Chronic exposure to formaldehyde during pregnancy has been linked to adverse pregnancy outcomes such as abortion, congenital malformation, fetal growth restriction, and premature birth, although few studies have examined formaldehyde exposure during pregnancy.

Purpose: To determine personal exposure to formaldehyde during pregnancy and to identify residential sources of formaldehyde.

Method: Formaldehyde exposure (vapor badge, urine formic acid) was examined in 140 women in their second trimester of pregnancy during the winter and spring of 2013. One time urine samples were collected during a routine prenatal visit, and women wore the vapor badges for 24 hours. Urine cotinine and self-reporting of potential residential sources of formaldehyde were measured.

Results: The mean level of formaldehyde exposure using the vapor monitor badges was 0.04 parts per million (ppm) (SD = 0.06); 36.4 percent of participants exceeded Minimum Risk Levels (MRLs) of 0.03 ppm, the Agency for Toxic Substances and Disease Registry (ATSDR) standard for personal exposure for 14-364 days. Formaldehyde levels by vapor monitor badge (< 0.03 and > 0.03 ppm) were correlated with season of data collection ($p < 0.008$), indoor temperature of dwellings ($p < 0.014$), and house remodeling ($p < 0.037$). No significant relationship was found between formaldehyde detected by vapor monitor badge, formic acid and cotinine.

Conclusion: Home and lifestyle behaviors can lead to air pollutant risks due to formaldehyde. More than one third of participants in this study had formaldehyde exposure levels for a 24-hour period exceeding ATSDR recommended levels for 14-364 days. Promoting home and lifestyle behaviors to reduce formaldehyde exposures as well as other indoor air pollutants should be included as part of prenatal care.

Assessment of the Proinflammatory Potential of Indoor Air Particulate Matter Based on the Cytokine Release in a Cryopreserved Human Whole Blood System

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There is a growing recognition that indoor particulate matter (PM) can impact respiratory health. The composition of indoor air PM differs from outdoor, with indoor PM generally containing more biologically derived components. Assessment of human health based on biologically derived components (e.g., endotoxin from Gram-negative bacteria) limits our understanding of the human health effects to indoor PM. In this study, we evaluated an innovative human *in vitro* assay, the human whole-blood pyrogen assay, to study the pro-inflammatory potential of indoor PM collected in urban homes in Baltimore, MD. PM mass and endotoxin concentrations were determined by gravimetric analysis and testing filter extracts with the Limulus Amoebocyte Lysate assay, respectively. The pro-inflammatory potency of the whole extracts and endotoxin-depleted extracts, based on the release of cytokines by blood immune cells, was evaluated with the whole-blood pyrogen assay. PM mass and endotoxin concentration did not explain the inflammatory potency of the PM. Depletion of endotoxin in the extracts abolished the TNF-α response but only reduced IL-1β and IL-6 by 40 percent and 50 percent, respectively. Taken together, our results suggest that the pro-inflammatory potential of indoor PM from homes of an urban setting is not limited to endotoxin, and that gravimetric and endotoxin measurements of PM do not fully reflect its pro-inflammatory potency. This study demonstrates the limitation of using endotoxin alone to assess pro-inflammatory potential of PM and that the human whole-blood pyrogen assay provides a more comprehensive assessment of the pro-inflammatory potency of indoor air PM in an urban environment.

Fast Food Intake Predicts Several Indices of Asthma Morbidity in an Urban, Pediatric Population

Emily Brigham[1], Pulmonary Postdoctoral Fellow; Sonali Bose[1]; Jean Curtin-Brosnan[2]; Elizabeth Matsui[3]; Nadia Hansel[1]; Charles Aloe[3]; Greg Diette[1]; and Meredith McCormack[1]
[1]Department of Pulmonary Medicine, [2]Department of Pediatrics, [3]Department of Pediatric Allergy and Immunology, The Johns Hopkins University School of Medicine, Baltimore, MD

Rationale: Asthma is a common pulmonary diagnosis in the pediatric population and continues to increase in prevalence. Asthma disproportionately affects inner-city minority children. Identifying modifiable risk factors for poor asthma control is a research priority. In adult populations, one well-recognized risk factor for asthma is obesity, although studies aiming to identify a link in children have yielded mixed results. A potential mediating factor is diet, which has been linked to both the development of childhood obesity and asthma. We investigated the association between fast food intake (representing a high-fat, high-salt, high-calorie diet) and asthma morbidity in an urban, minority pediatric population.

Methods: DISCOVER is an ongoing, NIH-funded project studying indoor air pollution and asthma, longitudinally evaluating 180 children (ages 5–12) in Baltimore City. Each child enrolled has an initial clinic visit during which they complete a detailed questionnaire with their primary caregiver and completed pulmonary function tests (PFTs). We compared responses to a fast food intake frequency question in cross-section to PFTs, body mass index (BMI), reported medication and urgent care use, and selected questions regarding asthma symptoms in the last 12 months. Asthma symptom responses were compared in each category of fast food intake (low: < 1 time per week, moderate: 2–3 times per week, and high: 4–6 times per week). Responses were compared by chi-squared analysis, nonparametric test of trend and logistic regression.

Results: Preliminary results on 150 children demonstrated 102 (68%) with low, 36 (24%) with moderate and 12 (8%) with high intake. BMI was evaluated as a discrete, categorical variable (normal weight, overweight, and obese) and was not significantly associated with fast food intake. Fast food was associated with symptoms of nighttime wheeze and cough, and this relationship was not significantly modified by BMI. Symptoms remained associated after logistic regression with control for age, race and sex. Fast food intake was not associated with urgent care use, medication use or other evaluated symptoms.

Conclusion: In a cohort of urban, predominantly African-American children, high fast food intake is associated with at least two symptoms of asthma morbidity: dry cough and nighttime wheeze. Diet may be an important, modifiable risk factor to improve asthma outcomes for inner-city children, a highly affected group.

Comparison of Children's Personal Exposure to and Environmental Measurements of Airborne Pollutants With Biomarkers of Exposure

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A sub-study of the Children's Health After the Storm (CHATS), an environmental health study of children in Louisiana and Mississippi, has the purpose of assessing ways to minimize exposure misclassification bias and identifying an exposure metric with a strong association to biomarkers of exposure.

For each child, we conducted 1-week measurements of personal exposure, and indoor and outdoor concentrations of particulate matter (PM^{10}), second-hand smoke (SHS), and gaseous pollutants; and assessments of corresponding urinary biomarkers of exposure.

Data show that personal exposures to PM^{10} and SHS (mean 38 $\mu g/m^3$ and 20 $\mu g/m^3$) exceed the indoor and outdoor concentrations. The personal exposure and indoor levels are highly correlated, but neither are correlated with outdoor measurements. The level of personal PM exposure is significantly influenced by the personal SHS and indoor PM concentrations, and the compliance to protocol for wearing the personal monitor at a lesser degree. The ranked personal and indoor SHS concentrations are moderately but significantly correlated to the urinary marker.

Strong personal indoor correlations indicate that a significant portion of personal exposure occurs inside the residence. A similar level of associations of personal and indoor SHS measures with urinary marker indicates that SHS exposures mainly occur in the home. However, the deviation of personal exposure measurements from the corresponding indoor concentrations can be up to 50 percent for the group with higher personal monitor-wearing compliance. This demonstrates the need for personal exposure monitoring with the adherence to the sampling protocol to capture the level that children are exposed to accurately.

Early Life Exposure to Arsenic Via Food and Water

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Background: Although childhood exposure to high concentrations of arsenic (As) in drinking water has been associated with adverse health effects, less is known about the effects of lower levels of exposure from water or food, the likely exposure route for most infants.

Aims: We estimated the potential exposure to arsenic via water and food in a population of U.S. infants who are potentially exposed to arsenic via well water, and compared these estimates to measured urinary arsenic.

Methods: We used telephone surveys of infant feeding patterns at 4, 8, and 12 months and measurements of arsenic in water, formula powder, breast milk, and rice cereal to estimate an infant's arsenic ingestion (n ~ 300). We further collected a 3-day food diary and tested infant urine samples at 6 weeks of age to determine the correlation between estimated arsenic ingestion and biomarker concentrations (n = 71).

Results and Conclusions: Exclusively breast-fed infants had lower estimated arsenic exposure and urinary arsenic concentrations at 6 weeks of age than exclusively formula-fed infants ($P < 0.0001$). More than 10 percent of infants were estimated to be consuming formula made with water that was above the current World Health Organization maximum contaminant level (10 µg/L). During weaning, 90 percent of families fed their infants rice cereal, most starting between 4 and 6 months of age. Estimated arsenic exposure due to rice cereal was 1.5-7.4 µg As per day, higher than for breast milk or formula except when the formula was made with high-arsenic water. Both water and food appear to be exposure routes for arsenic for infants in our population.

Infant Toenails as a Biomarker of *In Utero* Arsenic Exposure

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Background: A growing body of evidence suggests that *in utero* and early life exposure to arsenic may have detrimental effects on children, even at low-to-moderate levels, which are common in the United States and elsewhere. However, studies to date have used a wide variety of different biomarkers, such as urine, blood, hair and nails to estimate gestational exposure that have not been extensively tested for their reliability. We evaluated infant toenails as a biomarker of arsenic exposure in birth cohorts from New Hampshire and Rhode Island.

Methods: We tested 170 mother-infant toenail samples from the New Hampshire Birth Cohort Study using inductively coupled plasma mass spectrometry. We further compared infant toenail arsenic concentration to maternal urinary arsenic at 24-28 weeks of gestation (excluding arsenobetaine and arsenocholine), as well as maternal arsenic consumption from water and rice. We used multiple linear regression models to examine relationships between arsenic biomarkers and used structural equation modeling to combine maternal arsenic biomarker measures into a latent class variable of maternal arsenic exposure. For validation, we examined the correlation between maternal-infant toenail concentrations in an independent birth cohort of 130 mother-infant pairs from Rhode Island.

Results: In both the New Hampshire and Rhode Island mother-infant cohorts, infant toenail arsenic concentration correlated most strongly with maternal postpartum toenail concentrations (Spearman correlation coefficient 0.34 and 0.29, respectively). In adjusted linear regression models of the New Hampshire cohort, a doubling of maternal toenail arsenic concentration was associated with a 53.8 percent (95% CI: 33.9, 76.7) increase in infant toenail arsenic concentration. An increase of one standard deviation of a latent variable of maternal arsenic exposure in a structural equation model was associated with nearly a 50 percent increase in infant toenail arsenic concentration [1.45 (95% CI: 1.23, 1.72)].

Conclusion: In this study population of U.S. women exposed to low levels of arsenic, infant toenails appear to be a reliable biomarker for estimating arsenic exposure during gestation that is relatively easy to collect.

Partnerships for Environmental Public Health (PEPH) Evaluation Tools

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This poster provides an overview of the PEPH Evaluation Metrics manual. The poster addresses why the manual was developed and for whom. It provides information on the five core PEPH activities that are addressed in the manual: partnering, leveraging, products and dissemination, capacity building, and education and training. It showcases examples of the components included in each chapter, including example metrics and Metrics in Action. Finally, the poster highlights the Web-based training that accompanies the manual. The manual and training are available at http://www.niehs.nih.gov/pephmetrics.

A Prospective Birth Cohort Study Involving Environmental Uranium Exposure on Navajo Nation

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Background: In October, 2007, the U.S. House Committee on Oversight and Government Reform held hearings and subsequently appropriated funds to study the environmental effects of uranium mining on the Navajo Nation. The Navajo Nation was heavily mined for uranium to support development of the atomic bomb and subsequent cold-war weapons production from 1942 through the late 1960s. The last mines closed in the mid-1980s, leaving 1,100 mine waste sites associated with 520 discrete mines, most of which have never been fully remediated. No comprehensive health studies have been conducted to assess the impact to the Navajo people from exposures to these wastes. The Agency for Toxic Substances and Disease Registry (ATSDR) staff held meetings with community members and stakeholders and determined that investigating the effects of environmental exposures to uranium wastes on Navajo pregnancies and birth outcomes would appropriately respond to both the community concerns and to the congressional mandate.

Objective: In August 2010, the Centers for Disease Control and Prevention (CDC) awarded a cooperative agreement to the University of New Mexico (UNM) Community Environmental Health Program (CEHP) to work with CDC/Agency for Toxic Substances and Disease Registry (ATSDR), Navajo Area Indian Health Service (NAIHS) and the Navajo Nation to design and conduct a prospective study to determine whether uranium exposures affect pregnancy, birth outcomes and child development on the Navajo Nation. The project also should provide broad public health benefits for Navajo communities through education on environmental prenatal risks, early assessment, and referral for identified developmental delays.

Implementation: A research plan was developed by the UNM Team, in consultation with Navajo Nation agencies, community members and NAIHS staff, and has been approved by UNM and Navajo Nation human research review boards and the federal OMB. This research involves recruiting and following 1,500 pregnant women living on the Navajo Nation during their pregnancy, at delivery and following the infants through their first year. Environmental monitoring, biological sample analysis, surveys and developmental screenings will be performed. Information gathered and analyzed will be provided to the Navajo Nation and NAIHS to improve future pregnancy and birth outcomes and services and to inform policy on the cleanup of environmental hazards.

"I did it for us, and I would do it again."
Rural Latino Experiences Providing Biospecimens for Research

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Racial and ethnical minorities historically have been underrepresented in biomedical research. Latinos exhibit lower rates of participation and higher rates of attrition in biomedical research than non-Hispanic whites and other ethnic groups, and rural Latinos are even less likely to participate in biomedical research. Participation of such groups in biomedical research is critical to advancing global knowledge and reducing health disparities. Several studies have explored the barriers and facilitators of participation for these vulnerable populations. However, few, if any, have described the experiences of a minority population that has provided biospecimens for research.

Method Development and Field Application for Multiday Polycyclic Aromatic Hydrocarbon Sampler

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A 96-hour integrated filter-based sampler for collection of airborne polycyclic aromatic hydrocarbons (PAHs) with 4, 5 and 6 rings was developed for use in environmental monitoring and applied in Bakersfield, California. We developed and evaluated a filter-based, 96-hour PAH sampler against 24-hour, filter-based samplers in a bus garage with PAH concentrations comparable to outdoor environmental conditions. The method was found to be precise (average coefficient of variation was 6%). For the 10 PAHs analyzed, the mean of the 96-hour integrated samples collected in triplicate was within 30 percent of the mean sum of the four sequential 24-hour samples. The field experiment was conducted in Bakersfield, California, at 14 locations, mostly public schools. We collected 96-hour integrated samples for four time intervals from November 2010 to January 2011. At one site, we also collected continuous particle-bound PAHs of 3-rings or greater using the PAS2000 monitor (EcoChem Analytics, League City, TX). Duplicates were collected at two sites. There were 54 96-hour $PM_{2.5}$ samples collected over four intervals at a total of 14 locations, including duplicate samples collected at 2 locations. Concentrations of PAHs during the sampling periods were low, with only 13 percent of individual PAH concentrations measured greater than 1 ng/m^3. For ∑10PAH, the Pearson correlation coefficient between all pairs of duplicates is 0.93, and the CV for the set of duplicates is 3 percent. The Pearson correlation coefficient between the ∑10PAH concentrations and the PAS2000 mean 96-hour concentrations was 0.95. The mean concentration of the filter-based ∑10PAH concentrations were consistently lower than the PAS2000. Because of the low concentrations in the field experiment and the relatively low number of sites, we did not perform formal tests of spatial autocorrelation. However, we observed that higher PAH concentrations were closer to railyards and locations of high traffic intensity. In conclusion, we have presented the development and application of a precise and sensitive field method for collecting 96-hour PAH concentrations at environmental levels.

Malaysian Diaper Powder as a Source of Elevated Blood Lead

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Introduction: Although the majority of childhood lead exposure in the United States results from ingestion of lead-based paint dust, nonpaint sources are increasingly implicated. We present a case of elevated blood lead (EBL) in a 9-month-old infant due to a Malaysian folk remedy.

Case Report: An infant girl born in the United States to a Malaysian father and Taiwanese mother had an elevated screening capillary blood lead level (BLL) of 18 mcg/dL (CDC reference < 5 mcg/dL) at her 9-month health supervision visit. A venous specimen drawn 4 days later was 13 mcg/dL. Her zinc protoporphyrin levels, complete blood count (CBC) and iron studies were normal. She was asymptomatic with normal past medical and developmental histories; she was not yet independently mobile. Environmental history was negative for residential lead hazards as the family's home was built in the year 2000. Further history revealed that parents were applying an imported diaper powder solely to her vaginal area once or twice weekly. The powder was sold at a Malaysian corner store/pharmacy and sent by a relative. Quantitative analysis indicated the pale yellow powder contained 62 percent lead. Mineralogical analysis confirmed that the powder was predominately lead monoxide (litharge), and also contained magnesium carbonate and the magnesium silicate mineral talc. Scanning electron microscopy showed all particles measured less than 250 μm, the maximum value for hand-mouth transfer, and many were of respirable sizes (< 2 – 5 μm). Four weeks after discontinuing its use, the infant's venous BLL fell to 8 mcg/dL.

Discussion: Although inorganic lead can be absorbed transdermally and via mucosal tissues, our patient was likely exposed through additional routes, including hand-mouth transfer, inhalation of airborne powder, swallowing of lead particles cleared from the respiratory tract, contamination of foodstuffs and contact with contaminated surfaces. To our knowledge, this is the first case of EBL due to infant diaper powder reported in the United States.

Conclusion: Folk remedies, including skin care products, are a potential explanation for EBL in childhood, particularly in children for whom no residential source of lead is discovered. Health care providers should query families of young children regarding their cultural practices and maintain a low threshold for lead screening.

Maternal Iron Metabolism Gene Variants Modify Umbilical Cord Blood Lead Levels by Gene-Environment Interaction

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Background: Given the relationship between iron metabolism and lead toxicokinetics, we hypothesized that polymorphisms in iron metabolism genes might modify maternal-fetal lead transfer.

Objective: To determine whether maternal and/or infant transferrin (TF) and hemochromatosis (HFE) gene missense variants modify the association between maternal blood lead (MBL) and umbilical cord blood lead (UCBL).

Methods: We studied 476 mother-infant pairs whose archived blood specimens were genotyped for TF P570S, HFE H63D and HFE C282Y. MBL and UCBL were collected within 12 hours of delivery. Linear regression models were used to examine the association between log-transformed MBL and UCBL, and to explore gene-environment interactions.

Results: The geometric mean MBL was 0.61 µg/dL (range 0.03, 3.2) and UCBL 0.42 (< 0.02, 3.9). Gene variants were common, with carrier frequencies ranging from 12 to 31 percent; all were in Hardy-Weinberg equilibrium. In the full regression model, log MBL was associated with log UCBL (β = 0.92, 95% CI: 0.82, 1.03) such that a 1 percent increase in MBL was associated with a 0.92 percent increase in UCBL. Maternal hematocrit at 28 weeks (β Interaction = -0.02, 95% CI: -0.05, 0.003) and at delivery (β Interaction = -0.02, 95% CI: -0.04, 0.001) were inversely associated with UCBL. Infants born to C282Y variants had 38 percent lower UCBL ($p < 0.05$) than those born to wild-type mothers (β Interaction = -0.27, 95% CI: -0.52, -0.01).

Conclusion: Maternal HFE C282Y gene variant status is associated with reduced placental transfer of lead. If incorporated into preventive strategies, maternal genotype information has the potential to reduce *in utero* lead exposure.

Finding the Environmental Causes of Leukemia in Children: Center for Integrative Research on Childhood Leukemia and the Environment at the University of California, Berkeley

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Introduction: Leukemia is the most common cancer in children. Genetic factors and environmental factors are both thought to contribute to childhood leukemia, and prenatal and early-life exposures appear to be important. Fortunately, mortality from childhood leukemia has decreased greatly with better treatments. However, the causes are mostly not yet known.

Our Goal: Our fundamental goal is to develop and implement methods that can determine preventable or modifiable environmental factors that contribute to leukemia in children and the mechanisms by which the disease develops.

Approaches: We draw on the long-standing California Childhood Leukemia Study to conduct epidemiological studies of factors that may contribute to the development of leukemia.

We build collaborations with investigators and studies around the world to pool data and knowledge to increase the power of studies, leading the development of a Childhood Leukemia International Consortium, training new investigators and initiating new projects.

We improve methods to measure environmental factors, with a focus on homes, including measurements using house dust, to better assess prenatal and early-life exposures.

We create ways to detect markers of exposure in small quantities of biospecimens (such as blood).

We look at how environmental factors cause both genetic and epigenetic changes that may contribute to leukemia and develop new methods to measure this. We connect with organizations and individuals interested in improving children's environmental health and explain our results using traditional and new media, including video.

Results: Our poster provides links to key results through abstracts, links to Web resources, including video, and readable bar codes for mobile devices.

Arsenic and Rice: Translating Research to Address Healthcare Providers' Needs

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Background: Recent publications show elevated inorganic arsenic in rice grain and rice products. Minimal information has been provided to health care providers, yet clinicians are faced with providing guidance on rice consumption regularly.

Aim: Identify key information for clinicians faced with providing guidance on rice consumption for the pediatric population.

Methods: Review and analyze peer-reviewed articles and government populations.

Key Information for Health Care Providers: Arsenic, a known human carcinogen, is associated with neuro-developmental and other adverse health effects. Cancer risk has been demonstrated to be greater with early life exposure to arsenic. The U.S. Environmental Protection Agency standard of 10 µg As/L of water is associated with estimated lifetime excess cancer risk of 1 in 300 (NRC). There is no standard for food. More than 85 percent of rice grain and rice products contain inorganic arsenic, with 23 percent containing concentrations that pose a potential cancer risk > 1 in 300. Eating 0.56 cups of cooked rice/day is comparable to drinking 1L/d of 10 µg As/L drinking water. The top 1 percent of rice-eating children consumes at least 1.75 cups of cooked rice/day, associated with an excess cancer risk far above 1 in 300. The top 1 percent of childhood rice consumers has a median urinary arsenic level double that of non-rice consuming children. Arsenic in rice poses increased health risk in children and heavy rice-eating populations, including Asian Americans, individuals with celiac disease or severe food allergies, and others.

Conclusion: Researchers should keep clinicians updated via publications they read with more detailed information translating current findings of relevance. Clinicians can identify and counsel heavy-rice consuming patients and consider providing practical rice intake reduction measures in a culturally sensitive way.

Being Overweight Confers Susceptibility to Indoor Pollutants Among Urban Children and Adolescents With Persistent Asthma

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Background: Both obesity and exposure to indoor pollutants, which have been associated with asthma morbidity, are common in urban minority populations. Whether obesity is a risk factor for the effects of indoor pollutant exposure on asthma is unknown.

Aims: To examine the effect of weight on the relationship between indoor pollutants and asthma in urban minority children.

Methods: One hundred and forty-eight 5- to 17-year-old children with asthma were followed for 1 year. Asthma symptoms, acute care visits, lung function, pulmonary inflammation and indoor pollutants were assessed every 3 months. Weight category was based on body mass index percentile.

Results: Participants were predominantly black (91%) and had public health insurance (85%). Four percent were underweight, 53 percent were normal weight, 15 percent were overweight, and 28 percent were obese. Overweight and obese participants had more symptoms associated with fine particulate matter ($PM_{2.5}$) exposure than normal weight participants across a range of asthma symptoms. Overweight and obese participants also had more asthma symptoms associated with NO_2 exposure than normal weight participants, although this was not observed across all asthma symptom outcomes. Weight did not affect the relationship between coarse particulate matter ($PM_{2.5–10}$) and asthma. Relationships between indoor pollutant exposure and acute care visits, lung function, and pulmonary inflammation did not differ by weight.

Conclusions: Being overweight may increase susceptibility to indoor $PM_{2.5}$ and NO_2 in urban children with asthma. Interventions aimed at weight loss may reduce $PM_{2.5}$- and NO_2-associated asthma morbidity; interventions aimed at reducing indoor pollutant levels may be particularly beneficial in overweight children.

Translating Research in Environmental Health to Pediatric Practice: A Survey of Pediatric Hematologists and Oncologists

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Background: Clinical practice plays an important role in advancing children's environmental health and preventing harmful exposures. Although scientific studies have highlighted evidence of environmental contributions to childhood cancer incidence, we hypothesize that there have not been corresponding advances to incorporate this evidence into routine clinical practice.

Aims: To assess environmental history-taking behavior and perceptions of environmental health among pediatric hematologists and oncologists.

Methods: A Web-based survey was conducted among 427 members of professional clinical networks across the country. Abstracts from the 2011-2012 American Society of Pediatric Hematology/Oncology (ASPHO) meetings also were reviewed to identify current clinical studies that investigate environmental risk factors.

Results: There were 191 respondents who completed the survey (45 percent). Environmental exposures are of concern to clinicians, but a lack of familiarity or comfort in discussing these issues with patient's families presents a significant barrier. Although 76 percent of practitioners suspected some cases to have environmental etiologies, few asked about environmental exposures. Greater than 90 percent of clinicians responding stated they would find it helpful to have more information regarding the association between childhood cancers and environmental exposures. Of the ASPHO abstracts reviewed, less than 1 percent investigated environmental factors.

Conclusions: This research implies a need for increased training and awareness of environmental health among pediatric practitioners, as well as a need for interventions related to history-taking such as identifying behavior change strategies or incorporating self-administered intake questionnaires into patient care. By publishing research findings in journals that clinicians read, environmental epidemiologists can help bridge this knowledge gap and increase physician comfort in communicating research findings to patients.

Kids + Chemical Safety: A Tool for Educating the Public About Chemicals

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With an increasingly "plugged-in", connected, and informed public, there is an evolving need for rapid availability and global dissemination of accurate information. Important decisions about personal health, and public health and safety are made daily by the scientific and medical community, legislators, the public and the media often based on inaccurate, incomplete or biased information on the Internet. The exposure of children to chemicals in their environment and the possible effects on childhood growth and development is a paramount social concern. Many websites dedicated to children and chemical exposures are available. However, these websites can be generally characterized as either government sites that are technically dense, not interactive with users, and primarily targeted to the scientific community; or sites developed by special interest groups that lack technical depth, may or may not accurately represent the toxicology of the subject chemicals, or may or may not be interactive with users, but that are nevertheless written at a level understandable to a broad public audience. A challenge for protection of children's health to chemical exposures is to develop a website that can rapidly communicate independent, scientifically accurate information needed to make important decisions in a way that a broad user audience can understand and apply. Kids + Chemical Safety is a scientifically accurate website, staffed by experts in toxicology, public health protection and scientific communication that evenly represents perspectives, provides current information, and is interactive and understandable to serve a broad audience, inclusive of scientists, parents and the media.

Ambient Air Pollution and Traffic Exposures and Congenital Heart Defects in the San Joaquin Valley of California

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Congenital anomalies are a leading cause of infant mortality and an important contributor to childhood and adult morbidity. Major structural congenital anomalies are diagnosed in 2–4 percent of births, and the heart is the most common organ affected. Environmental contaminants have been suggested as risk factors for some anomaly groups, including heart defects. We used maternal interview data from the California Center of the National Birth Defects Prevention Study (n = 813 cases and n = 828 controls).

Air pollutant and traffic exposure data were calculated at the geocoded maternal residence during the first 2 months of pregnancy. We estimated the odds of congenital heart defects using logistic regression, comparing the highest to lowest quartile of each exposure and adjusting for maternal race/ethnicity, education and vitamin use. The majority of mothers were Hispanic and had at least a high school education. A quarter of the population was exposed to active or passive smoke. Mothers of cases were less likely to take multivitamins in early pregnancy and more likely to be multiparous. The correlations of CO with NO (r = 0.81), NO_2 (r = 0.73) and $PM_{2.5}$ (r = 0.84) were high, which reflects the common source of motor vehicles. Ozone was negatively correlated with the traffic-related pollutants.

Overall, there was no clear association between traffic-related air pollution and congenital heart defects. Exposure to PM_{10} and traffic density during early pregnancy may contribute to the occurrence of ventricular septal defects in this population. Results were mixed for other pollutants and showed little consistency with previous studies

Ambient Polycyclic Aromatic Hydrocarbons and Pulmonary Function in Children

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Background: Polycyclic aromatic hydrocarbons (PAHs) are formed by incomplete combustion of carbon-containing fuels, and exposure to PAHs has been associated with increased risk of wheezing and impaired T regulatory cell function in a cohort of asthmatic children living in Fresno, CA.

Objective: To assess whether exposure to PAHs is associated with lower lung function in children, with and without asthma.

Methods: Children ages 9 to 18 living in Fresno were recruited (n = 297; 135 with asthma, 162 without asthma) for respiratory health evaluation, including medical history, current symptoms, and pre- and post-bronchodilator spirometry. Exposure to PAHs based on a previously published land-use regression model was estimated for each child. Linear regression was used to evaluate the association between annual mean PAH exposure in the year prior to testing and maximum post-bronchodilator FEV1.

Results: Mean PAH exposure was 2.99 ng/m^3. In a model adjusted for age, sex, race, height and socioeconomic status, a 1 ng/m^3 increase in PAH was associated with a 0.11 L (-0.21, -0.02) decrease in FEV1 among non-asthmatic children and a 0.01 L (-0.12, 0.09) decrease among asthmatic children.

Conclusion: This is the first study to assess the effect of individual PAH exposure estimates on lung function in children or adults. Surprisingly, we found a significant effect in non-asthmatic children but not in asthmatic children. The primary source of PAH exposures in these children is likely traffic emissions. If the results of this preliminary analysis are confirmed, greater efforts to control PAH exposure from traffic and other sources would be warranted.

Home Interventions Are Effective at Decreasing Indoor Nitrogen Dioxide Concentrations

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Rationale: Nitrogen dioxide (NO_2) is a byproduct of combustion that is produced by indoor gas appliances, including cooking stoves. Exposure to indoor NO_2 is associated with worse respiratory symptoms in those with obstructive airways disease. We conducted a randomized trial in Baltimore City homes to evaluate the effectiveness of home-based interventions aimed at reducing indoor NO_2 concentrations in homes with unvented gas stoves.

Methods: Homes were recruited in partnership with the Baltimore City Health Department's Healthy Homes Inspections and Health Services Program between June 2009 and March 2011. Homes in Baltimore City with unvented gas stoves were eligible for randomization into one of three groups: (1) replacement of existing gas stove with an electric stove; (2) installation of ventilation hood over an existing gas stove; and (3) placement of portable air cleaners with High-Efficiency Particulate Air (HEPA) and carbon filters in the home. All participants had home inspections and 7 days of continuous air quality assessment, including NO_2 monitoring using passive badges at baseline, 1 week, and 3 months postintervention.

Results: One hundred homes were randomized to receive either replacement with electric stove (n = 24), ventilation hood installation (n = 24) or air cleaner placement (n = 52). When compared to baseline (19.7 ppb), replacement of gas stoves with electric stoves resulted in a decrease of indoor NO_2 concentrations at 1 week (10.9 ppb) and at 3 months (9.7 ppb, a decrease of 51%, p-value = 0.01); 88 percent of homes had decreased NO_2 concentrations at 3 months. Compared to baseline NO_2 concentrations (19.2 ppb), homes receiving air cleaners had a decrease in median indoor NO_2 concentrations at 1 week (14.1 ppb) and 3 months (15.5 ppb, a decrease of 19%, p-value = 0.05); 66 percent of homes had decreased concentrations at 3 months. Ventilation hood installation did not result in a significant change in median NO_2 concentrations at 1 week or 3 months when compared to baseline.

Conclusions: Our results show that replacing gas stoves with electric stoves or placement of air cleaners with HEPA and carbon filters can decrease indoor NO_2 concentrations in urban homes with unvented gas stoves. Additional studies now are needed to assess the health impact of NO_2 reduction on people with obstructive lung disease.

Optimizing the Built and Natural Environments in a Community for Children's Health and Well-Being

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An emerging concept in the field of children's environmental health is the need for a systems approach to characterize and optimize the built and natural environments where children live, learn and play. A holistic, systems model should enable decision makers in community sectors, such as land use planning, buildings and infrastructure, and transportation, to adequately consider children's lifestage-specific needs in community design and remediation efforts. Research to understand the linkages between cumulative environmental exposures (chemical and non-chemical) that occur in community settings and childhood health outcomes is central to this systems approach and informs decisions that prevent or diminish potentially harmful exposures and associated health risks. Equally important is research about how characteristics of the built and natural environments, such as natural lighting in schools and affordable access to green space and nature, can interact to actively promote children's health and well-being. This poster highlights research under way in EPA's Office of Research and Development's Sustainable and Healthy Communities Research Program to provide state and local governments and community planners with the knowledge and tools they need to support decisions and health impact assessments specific to children's environments. Examples include an eco-health browser used to document the benefits of natural environments for children's health; community assessment tools to help identify problems; geospatial tools that integrate ecosystem goods and services with demographics and features of the built environment at national to local scales; and an Environmental Quality Index that incorporates public health data pertinent to birth outcomes and childhood diseases at the county scale.

Determining the Effects of Arsenic on Developmental Signaling Pathways *In Utero*

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Emerging evidence now suggests that *in utero* arsenic exposure poses health risks to the developing fetus. This evidence consists of both epidemiological studies and data from a number of animal models, and shows an association between prenatal arsenic exposure and adverse developmental outcomes. However, the majority of these studies utilized levels of arsenic exposure not commonly found in the United States. Thus, the relevance of these findings to the lower levels of arsenic commonly found in the United States remain unknown, as do the mechanisms underlying such effects on early child development. Using a cohort of pregnant women exposed to arsenic at low levels, we have begun to increase our understanding of the impact of low-dose arsenic exposure on fetal health by: (1) identifying arsenic-associated fetal tissue biomarkers, (2) examining biomarkers of pivotal developmental signaling pathways, (3) elucidating the mechanism by which arsenic modulates these developmental signaling pathways, and (4) determining the association between expression of these biomarkers and specific developmental endpoints. Here, we will present our rationale, methodology and results to date, focusing on recent work identifying the expression of the arsenic transporter AQP9 as a robust fetal biomarker for arsenic exposure. Further, we have identified a positive association between the placental expression of phospholipase ENPP2 and infant birth weight. These findings suggest one path by which arsenic may affect birth outcome.

Retrospective Study of Medical Radiation Exposure in a Cohort of Children Diagnosed With Leukemia, 2000 to 2010: A Single Institution Study

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Background: Prenatal or early childhood exposure to medical radiation used in diagnosis or treatment is an identified risk for childhood cancers but can be difficult to document. The author developed a family questionnaire/interview form to identify possible exposures at the Children's Hospital of Pittsburgh (CHP).

Aims: This retrospective study examines prenatal and early childhood medical radiation exposure in a cohort of children diagnosed with either acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) from 2000 to 2010. The hospital is a tristate regional referral center that treats 150 to 180 new cases of cancer in children per year. About 30 percent of these diagnosed children have AML or ALL.

Methods: Each consented family so far (approximately 50% of the cohort) has been interviewed in person or by phone call. Medical staff and psycho-social staff referred patient families for an interview with the author.

Results: To date, the author has been able to interview for exposures in about 50 percent of the cohort over the last 10 years. Among the interviewed families, about 70 percent had a documented medical radiation exposure among the following: preconception sinus or chest X-ray or CT of either parent, sinus X-ray in mother, or diagnostic radiation in child.

Local Trends in Particulate Matter Air Pollution and Heavy Metals at an Elementary School in Manhattan's Chinatown With Documented High Asthma Rates

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Supported by the New York State Department of Environmental Conservation and the New York City Department of Education, Office of Mayor Michael Bloomberg; and Three Village Allergy & Asthma, PLLC, South Setauket, NY

Objective: To explore recent trends in the air pollution exposures of children attending school in Manhattan's Chinatown in the context of high asthma prevalence.

Methods: We reviewed ambient air monitoring data reported by the New York Department of Environmental Conservation for the Division Street Monitoring Site in New York City. We evaluated the trends over time in particulate matter pollution, as well as the direction and magnitude of changes in chemical composition of this pollution. We compared this data with guidelines established by the U.S. Environmental Protection Agency, the World Health Organization and the Texas Commission on Environmental Quality.

Results: Overall levels of daily and annual particulate matter air pollution averages ($PM_{2.5}$ and PM_{10}) have decreased at this site between 2007 and 2011. Opposing this trend was a rapid rise in certain $PM_{2.5}$ chemical constituent concentrations, including cerium and arsenic.

Conclusions: Relative increases in the concentration of certain chemical components of particulate matter air pollution may explain the high rates of asthma in a setting of declining overall particulate matter pollution. Efforts to decrease the level of particulate matter air pollution are necessary but not sufficient to protect pediatric respiratory health. We must conduct further research into the effects of chronic metal exposure, continue the observed reductions in overall particulate matter levels and initiate reductions in specific metal concentrations.

Key Words: Particulate Matter, Air Pollution, Manhattan, Chinatown, Asthma, Asian-American, Arsenic, Cerium, Diesel Exhaust, $PM_{2.5}$ and PM_{10}.

Reproductive Environmental Health Education for OB/GYN Specialists

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Background: Because environmental health affects reproduction, and current OB/GYN residency curricula do not address the subject, we aimed to design an elective rotation in Reproductive Environmental Health & Justice (REHJ), in conjunction with UCSF PEHSU.

Objective: The purpose of this elective is to provide OB/GYN Residents/Fellows with experience in all aspects of reproductive environmental health. During the rotation at the UCSF PEHSU, the Fellow will learn to bring scientific analysis and medical knowledge to reproductive environmental health issues, and to communicate about these issues in a culturally appropriate way to a broader audience, including the general public, the media, and the broader health care community. An additional objective is to develop competencies for the specialty of Reproductive Environmental Health and appropriate measures (performance indicators) for the achievement of these competencies.

Methods: The proposed rotation was modeled on the extant pediatric Resident/Fellow rotation at the UCSF Pediatric Environmental Health Specialty Unit, using the current PEHSU faculty and clinic resources, in collaboration with UCSF OB/GYN faculty, for proposed REHJ rotation. Proposed competencies for Fellows in Reproductive Environmental Health were drafted with input from competencies proposed by the Institution of Medicine, Ambulatory Pediatric Association and the American College of Occupational and Environmental Health.

Results: An elective rotation, devised as a month-long block in the context of a 3-year fellowship in Maternal Fetal Medicine or a 4-year residency in Obstetrics and Gynecology, is proposed. Twenty-seven Reproductive Environmental Health competencies are proposed. The competencies are presented from three separate perspectives: academic, individual patient care and community advocacy.

Conclusion: The proposed REHJ elective for OBGYN residents and MFM Fellows is intended to promote the dissemination of important concepts in the OB/GYN community. These competencies are intended to assist in structuring the training experience, achieving consensus with respect to expectations of Fellows and faculty, providing opportunities for Fellows to assess their own needs or gaps in training, and identifying the expertise of fellowship graduates to potential employers.

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