

**2007 Children's Environmental Health Workshop:
Discover, Treat, Prevent, Prepare**

**Hamilton Crowne Plaza
1001 14th Street, NW
Washington, DC**

October 11–12, 2007

MEETING SUMMARY

OCTOBER 11, 2007

INTRODUCTION AND OVERVIEW

The U.S. Environmental Protection Agency (EPA) 2007 Children's Environmental Health Workshop: Discover, Treat, Prevent, Prepare was held on October 11–12, 2007, in Washington, DC. The workshop brought together a diverse group of clinicians, researchers, and health advocates from academic, government, and nonprofit organizations. Participants discussed issues in clinical practice, ongoing research in children's environmental health, and opportunities for translating scientific findings. The workshop also served as a stimulus for increased collaborations among the Pediatric Environmental Health Specialty Units (PEHSUs) and the Centers for Children's Environmental Health and Disease Prevention Research. Approximately 133 individuals attended.

Welcome and Review of the Agenda

Nigel Fields, William H. Sanders, III, Dona DeLeon, and Kevin Y. Teichman, U.S. EPA; Paula Davis, Association of Occupational and Environmental Clinics (AOEC)

Mr. Fields thanked attendees for their participation. He noted that the 10th anniversary of Executive Order 13045, Protection of Children from Environmental Health Risks and Safety Risks, was an opportune time to celebrate the progress made in children's environmental health (CEH) and to align perspectives for the future of this field. He invited participants to engage workshop speakers in their discussions about how to further CEH protection.

Ms. Davis, Coordinator of the Pediatric Environmental Health Specialty Units Program (PEHSU) welcomed presenters and workshop participants. She expressed her interest in collaborating with PEHSU colleagues and other scientists involved in CEH to help bridge the gap between research and practice.

Before his recent appointment as Director of the National Center for Environmental Research (NCER), Dr. Sanders previously worked directly with the PEHSUs and indirectly with the Children's Environmental Health Centers (CEHC) in his role as Acting Director of the Office of Children's Health Protection and Environmental Education. He noted the variety of constituents in attendance and remarked that it is a great opportunity for bringing together representatives from the PEHSUs with the CEHC Directors in a central venue. He presented an overview of the workshop agenda, explaining the nature of each session. Dr. Sanders also invited participants to attend the Third Annual Excellence Awards Ceremony at end of the first day.

Ms. DeLeon explained that she is new to the Office of Children's Health Protection and Environmental Education but has spent many years at EPA, including working with and examining the delivery system at

the state and local levels. Implementation of environmental policy is taking place at the local level; how regulation implementation is translated at the local level and communicated to the public is critical to keep environmental progress moving forward. This audience plays an important role in communicating health risks and promoting the science that underlies decision-making to the public working with families and children. She congratulated attendees for the progress that has been made and thanked them for their continuation of these efforts. She welcomed the international visitors and commented that she looks forward to learning more about children's environmental health issues and how EPA can assist researchers in advancing these issues.

Dr. Teichman welcomed participants and remarked that the CEH protection community experienced another tremendous year of growth; he noted that it was appropriate that the workshop was held during Children's Health Month. He also welcomed Dr. William Sanders to EPA's Office of Research and Development (ORD) and expressed his gratitude to the Center for Children's Environmental Health and Disease Prevention Research; the National Institute of Environmental Health Sciences (NIEHS); PEHSUs; the Agency for Toxic Substances and Disease Registry (ATSDR); AOEC; and the new health care provider capacity-building grantees and Children's Environmental Health Champion Award winners.

The mission of EPA is to protect human health and the environment. In attempting to achieve this goal, the Agency is examining one of the most vulnerable populations with increased specificity. There is a wide range of genetic susceptibility among newborns and young children to exposure from household or agricultural pesticides. Where a child lives within the urban environment may significantly influence or impact his or her exposures and health outcomes. With the passing of several federal mandates, EPA has emphasized the identification of child-specific exposures, health risks, and protective actions for more than a decade. Within ORD, these mandates have stimulated a wide array of research activities, with the purposes of studying how chemical exposures change across life stages; gaining a greater understanding about the genetic factors that contribute to children's vulnerability to air pollution, pesticide exposures, and heavy metals; validating novel methods for both aggregate and cumulative exposures to single and multiple chemical, biological, and radiological agents; discovering, translating, and employing biomarkers of exposure effect and susceptibility; and promoting cost-effective sustainable household- and community-level interventions.

EPA scientists and their academic partners have applied their expertise to these efforts because children may be at increased risk from environmental influences as a result of their vulnerable developing systems and enhanced exposures to many agents. These environmental influences include the quality of air, ingested lead, and exposures to chemicals and mold; all of these factors are within society's power to control. ORD researchers have contributed to improving CEH in many ways. The Stochastic Human Exposure and Dose Simulation Multiscale Model is now used as a primary tool for simulating exposures to a variety of chemicals that enter the body to determine how best to advise the public on reducing children's exposures to toxic compounds. During the past 10 years, EPA has improved the ability to monitor chemical exposures and assess the effects based on the development, validation, and implementation of biological markers. EPA scientists and those supported by the Agency are leading efforts to validate noninvasive biomarkers and to apply them in epidemiologic studies and clinical settings. ORD also is contributing to the Agency's next *Report on the Environment* by developing the scientific basis for the use of health outcomes to measure and evaluate environmental policy decisions.

ORD is only one contributor to improving the understanding of CEH; community partners play a critical role in informing, implementing, and translating research findings. Workshop participants have the opportunity to discuss findings and clinical experiences and translate those experiences for advancing more protective medical guidance in environmental policy into the future. Today's sessions, which focus on the translation of research and clinical insights regarding organophosphates (OPs), phthalates, asthma, and exposures to metals, will specifically concentrate on prenatal and early life exposures and the

subsequent health effects associated with these exposures. The next day's sessions will examine what lies ahead for researchers, clinicians, and health advocates as increasingly complex public health challenges that also will impact children's health emerge. These challenges include persistently high rates of low birth weight and preterm births; increasing rates of neurobehavioral disorders in young children, such as autism and attention deficit hyperactivity disorder (ADHD); increasing body burdens of potentially endocrine-disrupting compounds; escalating prevalence rates for obesity and type II diabetes; growing disparities between low-income and minority groups to chemical exposures; the risks of climate change; the emergence and application of nanotechnology; and complex trends in urbanization. EPA will need partners in determining the environmental factors and related health outcomes of these issues.

ORD will continue to work closely with the Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), and international collaborators such as the World Health Organization (WHO) to systematically discover ways to protect children in a rapidly evolving world. The National Children's Study (NCS) holds much promise for gaining a deeper understanding of these complex issues and to make better, more targeted decisions for promoting healthier environments. The NCS represents a truly unprecedented collaboration among government agencies, private industry and foundations, community leaders, and university-based scientists around the nation devoted to improving children's health. EPA conducted and supported much of the science that laid the foundation for this ambitious study. Researchers from the CEHCs participated in workgroups that developed the core hypotheses for the studies, and the Centers also collectively published "Lessons Learned" papers to offer guidance to the NCS for practical approaches to sustaining long-term studies and interpreting complex data.

Last week, EPA joined the National Institute of Child Health and Development (NICHD) in announcing the 22 Health Study Center awards, which joined the previously awarded Vanguard Centers in officially launching the study next year. As the research community moves forward to build on the past decade of success, it is clear that meeting these challenges will require strong, committed partnerships that better link research questions, health care practice, and environmental health.

Children's Environmental Health: Looking Backward, Looking Forward
Howard Frumkin, CDC, and Gwen Collman, NIEHS

In 1993, the National Academy of Sciences published *Pesticides in the Diets of Infants and Children*. This report helped establish the scientific basis for the CEH movement. Executive Order 13045 is a milestone in the movement, but since its enactment, the world has changed in many ways. For instance, 10 years ago, people did not routinely discuss the enhanced vulnerability of children, and preparedness was not a commonly used term in the public health world. Much work has been accomplished in the CEH field during the past 10 years in the areas of research, education, and service. Disease-specific research, community-based participatory research, research on the combination of genetic and environmental factors, and studies on vulnerable populations have expanded. Education has been extended to include fellowship training, and the field has seen an increase in the publication of books, papers, and Web sites related to CEH. The development of community networks, PEHSUs, and technical tools have added to the list of services that the scientific community provides to the public, but it is time to evaluate these accomplishments by asking what they have achieved in terms of improving children's health. Are children healthier now? Do health care providers and parents know how to provide children with safe and wholesome environments more effectively than they did 10 years ago? Has there been a continuing record of policy-making reflecting the importance of CEH?

This month, October 2007, marks the 10th anniversary of the Executive Order, and the CEH community is entering a new decade with the chance to reinvent, reinvigorate, and re-expand efforts and move from an individual clinical approach to a more encompassing legacy approach of caring for future generations. Biomonitoring is a well-established tool for determining known toxicants in the bodies of children. This

tool will be instrumental in focusing future research trends by measuring decreases in current chemicals of concern and identifying possible emerging toxicants. Genetic science will transform the field as research continues and scientists deepen their understanding of gene-environment interactions. In addition, there appears to be a change in the political climate that is more sympathetic to CEH. The child health community must take advantage of these advances to confront current and future challenges. Challenges during the next 10 years include poverty, changing chemical toxicity, dealing with the built environment, climate change, mental health burdens, and communication.

Poverty and lack of insurance are two of the most important threats to children's health, as underscored by the American Cancer Society's 2007 public relations theme, "Access to Health Care." The built environment has impacted children's health by engineering physical activity out of neighborhoods and communities. Children and adults now must drive to most destinations, including grocery stores, pharmacies, shopping malls, and schools. Low physical activity has been linked to childhood obesity and an increase in diabetes, and the increase in vehicle traffic is adding to environmental pollution. The built environment also discourages children from spending time outside. The author of *Last Child in the Woods* advocates "saving our kids from nature-deficit disorder" and maintains that spending time in natural settings is an important part of a healthy childhood. One of the mechanisms of the benefits of nature contact seems to be through attention-restoration theory, which states that attention is focused and distractions are minimized when children have the chance to be outside. This book has given rise to some very interesting efforts. The Children and Nature Network links people working to promote initiatives at the state level, including the "Leave No Child Inside" initiative. A number of federal agencies, such as the U.S. Fish and Wildlife Service, have developed programs about reconnecting children and nature. An initiative called "The National Forum on Children and Nature" seeks to support 20 nationally significant demonstration projects across the country that will restore kids into natural settings, with a focus on underserved and minority children. Research on the health evidence of these initiatives should be part of the CEH portfolio.

Climate change is an important and growing environmental health concern. In addition to potential physical effects, children now face potential psychological effects, including some effects that may stem from the fear associated with global warming. Other psychological effects already have been seen in the aftermath of recent hurricanes, which are predicted to become more severe with global warming. This kind of message in the media is becoming more common now, with rather apocalyptic narratives about climate change. Journalistic accounts of schools have described evidence of terror in children about the world and what it has in store for them. This must be considered because climate change is an issue that is going to remain for a long time. The manner in which it is discussed either will scare and immobilize people, or it will spur them to constructive action; the right message must be promoted. The reactions of adults influence children's reactions. Aftereffects of climate-related events must be considered as well; the biggest health burden of Hurricane Katrina, in retrospect, is the mental health burden. The anticipation of bad things happening, the aftermath, and the post-traumatic phase are serious mental health concerns that threaten children, and this needs to be part of CEH thinking.

"The Death of Environmentalism," an essay by Ted Nordhaus and Michael Shellenberger, was considered a "big picture" piece on environmentalism. It challenged some of the basic assumptions of contemporary environmentalism. The book-length expansion of that essay, *Breakthrough*, is provocative reading, and some of its points are very relevant to children's environmental health. Many CEH messages are negative: stopping the bad rather than creating the good. The authors recommend articulating a positive, compelling image of a healthy, wholesome world, rather than focusing so much on the negative. Positive messages are compelling and motivating to the public. Additionally, the challenge of climate change is so massive, global, and complex that it can only be overcome if the issue categories of the past are discarded and an aspirational vision of the future is embraced. According to the authors, environmentalists should think about job creation, economic development, law enforcement, and other important issues traditionally

outside the environmental arena. A similar approach may well be advisable for CEH. In communities where toxic exposures for children are a concern, poor education, joblessness, or squalor in the physical environment often are more important problems than the toxic exposures. The more globally children's problems can be addressed, the better they will be managed; broad thinking and getting outside of traditional categories can be beneficial. Climate change calls for expanded thinking.

One method by which CEH research portfolios can be expanded is to leverage opportunities with other partners, such as the U.S. Fish and Wildlife Service, which is actively involved in getting children back into the outdoors; the U.S. Department of Housing and Urban Development (HUD), which attempts to improve the quality of housing; and the U.S. Department of Education, which is concerned with healthy schools. Leveraging of opportunities and development of new partnerships must be creative, as concerns increase without increasing resources.

Dr. Collman explained that NIEHS has a strong portfolio in research areas that are now classically part of the rubric of CEH, such as basic mechanisms of toxicity during development, early life, and in organ systems related to diseases. The executive orders, reports, and regulations provided an impetus for moving the science forward and moving individual scientific inquiries in individual laboratories to partners across a spectrum of science. These efforts were furthered by the creation of the CEHCs, which bring together scientists of different disciplines to work with local health advocates and community partners. Through multidisciplinary research and outreach projects, the Centers are investigating environmental health challenges facing children and families in their community settings. These partnerships would not be complete without the health care community. Today, this collective network of research, community, and clinical partners can be proud of the training and development programs that are preparing future scientists and health care professionals, including residents, fellows, and academic physicians in becoming tomorrow's experts and leaders in CEH.

SESSION I: EVOLUTION OF BIOMARKERS FOR PESTICIDES: EXAMPLES FROM THE AGRICULTURAL SETTING

Co-Chairs: Catherine Karr and Elaine Faustman, University of Washington

Dr. Karr stated that it was a pleasure to open the first workshop session. The topic of the session is the evolution of biomarkers for pesticides with examples from agricultural settings. The session speakers are accomplished leaders from the public health, research, and clinical sectors who will discuss their experiences with biomarkers with the focus on a specific group of pesticides, the OP insecticides. Despite recent decreases in home and garden use, these insecticides continue to be used heavily in agriculture and are of great interest in the Pacific Northwest because of orchard crop production that relies intensively on OP use. OPs also are of interest because of their legacy of acute toxicity in humans; they are the pesticides most often implicated in symptomatic illness. Another reason to consider OP exposures is the accumulating evidence of neurodevelopmental toxicity related to relatively low chronic exposures in children. This provides a framework for considering the application and use of biomarkers. Biomarkers provide a context for understanding the pathway from release of an organopesticide in a child's environment to the potential for development of clinically significant disease or prognosis. This session will explore biomarkers of exposure in terms of internal dose measures using urinary metabolite monitoring, biomarkers of biologically effective dose or early biological effect, and biomarkers of susceptibility based on genetic polymorphisms in the population.

PEHSUs receive a number of questions from parents, pediatricians, public health officers, federal agency leaders, and policy-makers from "Should I have my child tested?" to "Should we have a national monitoring program for agricultural workers?" Today researchers are at the stage of validating biomarkers and must concentrate their efforts on finding ways for various sectors to utilize these data.

Efforts to use biomarkers in population-based monitoring in the States of Washington and California for occupational surveillance may inform the following questions: Should we have a national medical monitoring program for agriculturally exposed workers? What would such a program constitute? Lastly, from a risk assessment perspective, policy-makers may ask researchers: Can we use biomonitoring to evaluate whether regulation of diazaron and chlorpyrifos (CPF) has reduced exposure in at-risk populations such as children? Policy-makers may follow the unfolding story of the paraoxonase gene (*PONI*) as an effect modifier and ask: Should regulatory decision-making incorporate evaluation and protection of the most genetically vulnerable subset of the population? These are questions to consider during the presentations. The presenters will provide insight into progress toward validation of biomarkers and their utility as well as various limitations and knowledge gaps that need to be overcome, so that researchers can move forward to increase the clinical public health and risk assessment relevancy of biomarkers.

Biomarkers of Pesticide Exposure: Lessons for Children in Agricultural Communities

Elaine Faustman, University of Washington

Dr. Faustman stated that her presentation would focus on some of the biomarkers of pesticide exposure and some of the lessons for children in agricultural communities, including exposure to internal dose, biologically effective dose, early biological effect, altered structure and function, clinical disease, and the relationship with biomarkers of exposure and biomarkers of effect. In Washington State, OPs are used on apple and potato crops. OPs have various structures that differ by ethyl and methyl moieties, and up to 40 different OPs are in common use. The differences in patterns of the methyl and ethyl group metabolites can allow for the tracking of sources and attributable uses of these pesticides. Linking this information within the exposure response biomarker paradigm is important. Agricultural pesticides and contributions of occupational factors to home, adult, and child contamination will be discussed.

The complex series of metabolites that are formed following OP exposure presents a challenge to examining and interpreting what a biomarker of exposure might mean from the environment versus an internal dose of biomarker (e.g., urinary metabolites). Genetic polymorphism in the enzymes involved in the metabolism of these compounds present significant challenges, but modeling approaches that measure specific and nonspecific metabolites from OPs allow researchers to compare exposure markers. National Health and Nutrition Examination Survey (NHANES) data show U.S. population averages and show that children's exposures are higher than average adult exposures, and this becomes important if the exposures remain elevated over multiple years. In terms of assessing children's exposure based on the take-home pathway, this is the hypothesis that was put forth: Adult workplace exposure increases pesticides in dust in vehicles and homes and, therefore, to children through direct physical contact with the adults and indirectly through contaminated homes and cars. For example, a study of homes and vehicles of farmworkers in the Pacific Northwest found that the workers had higher levels of pesticides in the dust of their vehicles and homes and OP markers one to two orders of magnitude higher than U.S. averages. Their children's levels also were skewed to higher values compared with NHANES data. Modeling across specific metabolites allows researchers to detect high-risk exposure subgroups. Another study examined various crops and the distributions of specific metabolites in nonfarmworkers and farmworkers adults and children. Results showed a higher association of OP metabolites among those working with pome fruit, and this was identified as a potential place for intervention. All of the correlations were positive, illustrating a strong workplace take-home pathway. Using these models, sources of where the metabolite was attributable to child exposure were identified. These data have informed decisions about intervention procedures and allows targeting of populations that have been neglected in terms of public health intervention.

Two longitudinal studies measuring OP metabolites revealed another issue involved in biomarker analyses: variability. The variability was less between children than the variability within an individual

child; metabolites will vary considerably following repeated sampling of children. Within-person distributions are wider than distributions among a whole population. This has important ramifications in understanding the potential environmental effects of certain agents. Because there are a variety of factors (e.g., half-life, dynamics of exposure, and continued exposure), sampling approaches must be considered that increase understanding of how individuals versus populations are being exposed.

Biomarkers of exposure cannot be used for all types of studies, but they are very useful for understanding the patterns of exposures and source attribution. Other studies may be necessary to identify highly exposed groups and plan interventions. EPA studies will allow researchers to link multiple sampling of exposure and internal dose with potential early markers of response, such as enzyme changes and gene expression markers. Physiologically based toxicokinetic models are being built for OPs, with polymorphic information being added at multiple stages for the myriad of enzymes that are involved in OP metabolism. This is important so that genotypes can be used to help identify at-risk populations and to determine what these differences may mean for exposure and responses. Once these tools are further developed, they can be used for research and clinical applications. Dr. Faustman's group will be testing the hypotheses of how much knowledge about the genotype-phenotype makes a difference in understanding differences in between-person variability and how much knowledge about gene expression contributes to understanding responses within the same person over time. Future work includes identifying the genotype and phenotype for key genes that metabolize OPs to improve prediction of exposure response and at-risk individuals in agricultural communities. Learning more about polymorphisms of oxidant responsive pathways will allow researchers to better evaluate the potential for genomic biomarkers of early response to be linked with OP metabolites of exposure, better predict relationship of biomarkers of effect (e.g., acetylcholine) to respond in a dose-response manner to OP exposures in adults and children, and better predict whether "omic" biomarkers of disease are correlated with OP exposure.

Discussion

A participant requested clarification on the comment regarding how exposure measurement techniques may need to be modified for assessment of chemicals with short chemical half-lives. Dr. Faustman replied that the NCS holds a lot of promise to look at longitudinal exposures, but there are unique questions for some agents, for which the exposure and compounds are dynamic enough that additional assessments could be used in the NCS to answer some of these more specific questions. Her presentation illustrated the kind of information that can be gained from longitudinal studies versus specific studies and how this information can be integrated to build a cohesive picture.

A participant asked if the study examined children under age 6. Dr. Faustman replied that the study included younger children but did not examine crawling behavior.

A participant asked Dr. Faustman to discuss intervention and evaluation studies regarding the take-home pathway conducted at the University of Washington Center. Dr. Faustman indicated that a paired study was conducted where interventions were performed at the community- and household-level. The data are being analyzed, but early results show positive associations with intervention actions taken in the homes.

OP Pesticide Exposures and Neurodevelopment in Children From Farmworker Families **Kim Harley, University of California at Berkeley**

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study is a longitudinal birth cohort study of Mexican farmworker children and their mothers in the agricultural Salinas Valley region of California. The goals of this study were to: (1) estimate source and pathways of

OP pesticide exposure and levels of *in utero* and postnatal pesticide exposures in children living in agricultural communities; and (2) determine the relationship of this exposure with neurodevelopment, growth, and respiratory disease. The Berkeley team measured biomarkers of OP exposure using dialkylphosphate (DAP) metabolites measured in maternal and child urine. Increasing age, proximity to agricultural fields, and increased consumption of fresh fruits and vegetables were associated with higher DAP levels in young children in this cohort. Prenatal and child DAP levels were compared with early childhood neurodevelopmental and neurobehavioral outcomes using the Brazelton Neonatal Behavioral Assessment Scale, Bayley Scales of Infant Development, the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III), and the Child Behavior Checklist (CBCL). Reflexes in neonates were more likely to be abnormal in association with high maternal DAPs, but no associations were established between prenatal DAPs and six of the other seven Brazelton clusters. In addition, as the mothers' prenatal levels increased, Bayley Mental Development Index scores decreased in children at 24 months of age. Higher prenatal DAPs were also associated with increased likelihood of Pervasive Developmental Disorder, as assessed by the CBCL at 24 and 42 months of age. Findings were driven primarily by the dimethylphosphate, as opposed to diethylphosphate metabolites. These results were compared with similar studies at Mt. Sinai Hospital and Columbia University in New York City (NYC). Although these studies looked at different populations, the results mirrored results found in California. The NYC cohorts were made up of Mexican, Puerto Rican, and Dominican Hispanics; African Americans; and non-Hispanic Whites in an urban environment. The majority of the Berkeley cohort was comprised of Mexican Hispanics from an agricultural environment. Despite these differences, some patterns have emerged across these three cohort studies. Prenatal OP exposures in two cohorts were associated with increased odds of abnormal reflexes in neonates, and in all three cohorts with poorer mental development in 2- and 3-year-olds and poorer verbal IQ in 3.5–5-year-olds. Increased odds of pervasive developmental disorder was found in the two cohorts that examined this outcome.

Discussion

A participant asked if fruit and vegetable consumption could explain better performance in children. Dr. Harley responded that fruit and vegetable consumption was factored into the model and did not account for any differences.

A participant asked about potential confounders in the study. Dr. Harley answered that the study adjusted for factors that could have a bearing on development and intellect (e.g., parental IQ, socioeconomics, etc.).

A participant commented about the findings of a rat study that showed higher performance levels associated with CPF exposure and suggested that the researchers examine the higher performing children in the study to determine if they had higher prenatal exposures.

Cholinesterase Monitoring in Washington State

John Furman, Washington State Department of Labor and Industries

In 2003, the Washington State Department of Labor and Industries began an occupational medical surveillance program of agricultural pesticide handlers that measured cholinesterase (ChE) levels throughout the pesticide application season to detect overexposure to pesticides and prevent illness, increase hazard awareness, identify unsafe environments, and fix problems. Symptoms of ChE illness range from mild to severe and include dizziness, blurred vision, nausea, headache, stomach cramps, diarrhea, hypotension, and seizures; often, many of these symptoms are misdiagnosed.

Acetylcholinesterase is an enzyme that removes the chemical neurotransmitter acetylcholine from the neuronal synapse. Humans, insects, and other species have this basic acetylcholine system.

Cholinesterase-inhibiting pesticides have been developed to kill insects, but overexposure in humans results in sustained levels of acetylcholine and overstimulation of neuronal pathways and eventual exhaustion of neuronal pathways. Pesticide handlers of Toxicity Class I and II pesticides are monitored for ChE levels in red blood cells (RBCs) and serum. Exposure-free baselines are established annually during periods when handlers have not handled pesticides for at least 30 days. Analyses are conducted within the same laboratory to control for interlaboratory variations. Employees who handle these pesticides for more than 30 hours in any 30-day span are tested every 30 days. Employees may decline participation but must undergo an informed consent process with a medical provider if they opt out. ChE depression of 20 percent or more from baseline requires the employer to perform a work practice evaluation and intervene to reduce any chances of further exposure. Depression of 30 percent or more in RBC ChE or 40 percent or more in serum ChE requires the employee to be removed from handling until their levels return to within 20 percent of baseline. In addition to monitoring and enforcement, the program also provides follow-up services for those with significant ChE depression and consultation services to employers to help them reduce further exposures, reduce possible risk of long-term adverse health effects, and decrease take-home exposures. These follow-up efforts are offered to employees and employers even if they no longer participate in the program. The program has led to increased knowledge on the use of these pesticides, increased hazard awareness, changes in pest management practices, greater access to medical services, and more informed diagnoses and treatment of pesticide-related illness. Additionally, the findings of this program are being integrated into a state-wide pesticide handler training program.

Discussion

A participant requested clarification on the percentage of employees declining participation with the program. Dr. Furman replied that the program is averaging a 12 percent declination rate, and there has been a sustained participation during the past 3 years.

A participant asked about the change in minimum hours of handling for workers to be tested. Dr. Furman responded that the initial recommendation by the researchers was 30 hours, but political intervention arrived at the 50-hour minimum. No significant correlations were found between handling hours and ChE depression after 3 years of testing; however, a legal suit forced the issue, and the hours have been changed to the initial recommended minimum of 30.

A participant asked if OP pesticides are being replaced by other pesticides. Dr. Furman answered that part of the program follow-up procedures capture this information, and a significant number of employers who were previously engaged in the program have switched to safer products.

A participant asked about published findings that demonstrate that these types of interventions lead to health outcomes and behavior change. Dr. Furman replied that research reports for each of the 3 years are posted at <http://www.lni.wa.gov/Safety/Topics/AtoZ/Cholinesterase/default.asp>.

Biomarkers of Pesticide Exposure: Lessons for Children in Agricultural Communities **Catherine Karr, University of Washington**

Dr. Karr discussed the utility of ChE testing in clinical practice as a diagnostic tool for identifying pesticide poisoning in children. Although significant exposure occurs in agricultural workplaces, playgrounds, and orchards in agricultural Pacific Northwest, poisoning is not always considered by pediatricians. When it is suspected, it is difficult to interpret cholinesterase tests because there often is no baseline with which to compare it. Additionally, while cholinesterase tests are useful for diagnosing or confirming OP poisoning, there is no test for detecting chronic exposure, which may have health implications. In addition, while the symptoms in classic adult occupational poisoning have been

identified, in children they are not so clear, making diagnoses in children more difficult. Overexposed children are much more likely to manifest central nervous system (CNS) symptoms, and very young children cannot verbalize these symptoms and often present with subtle signs. Children are more likely to develop seizures as a result of OP poisoning. The classic hypersecretion (e.g., tearing, diarrhea, urinary incontinence, sweating) seen in adults often is not seen in children, and the poisoning is misdiagnosed as a more common infectious illness, such as flu or gastroenteritis.

Although there is great variability in the normal population, ChE testing still can play a role in the context of post-exposure followup testing, which can discern if there were significant changes in an individual. ChE testing is useful for acute OP poisoning via the cholinergic pathway, but there is evidence that neurodevelopmental toxicity can occur by alternate mechanisms. *In vivo* embryonic and neonatal rat models and neuronal rat cell line studies show effects seen throughout brain regions, including those with very little cholinergic innervation. Cell loss and apoptosis occurs immediately after exposure, neural deficits appear later in adolescent and adult animals, brain cell numbers are reduced, and neurite projections and synaptic communications are disrupted. This translates into a disruption of signaling pathways that are very important for normal neurological development in children and immature animals, and it is thought that these may underlie some of these observations in the epidemiological studies, such as effects on performance, attention, and behavior in humans.

A targeted survey in Washington State was conducted of healthcare providers and *promotoras* (lay health providers) who serve farm families and farmworkers in agricultural regions. Results showed that 49 percent of respondents had received any training on pesticides and health, and 22 percent had received child-specific information on pesticides and health. Based on these findings, the Washington PEHSU, in collaboration with the Pacific Northwest Agricultural Safety and Health Center, developed a Web-based CME product, "OP Pesticides and Child Health: A Primer for Healthcare Providers," which includes translation of findings from the NIEHS/EPA CEHCs regarding chronic toxicity. Additionally, in-person training has been conducted for *promotoras* who did not show an interest in the Web product.

Dr. Karr ended her presentation by raising some questions to motivate moving beyond ChE testing and focusing further on noncholinergic endpoints. She indicated the need for more rapid tests that can be used in clinical practice to confirm acute exposure to OPs and help provide indication for preventive guidance to parents. Finally, she urged participants to begin thinking about OP exposures in children with neurodevelopmental disabilities (e.g., ADHD or autism). In addition to potential etiologic relationships, these subgroups may be particularly vulnerable to the toxicity of OP exposure.

Integrated Pest Management in New York City Public Housing **Frederica Perera, Columbia University**

Dr. Perera outlined some of the studies being conducted at the Columbia Center for Children's Environmental Health. Based on high levels of CPF exposure, as measured by plasma concentrations in mothers and newborns in the Columbia cohort, the researchers instituted: (1) an educational intervention with newsletters to members of the cohort and community; (2) an integrated pest management (IPM) project; and (3) an effort to develop an early life reference dose (RfD) of OPs. Levels of use of CPF are down, following the EPA phaseout for residential use, and the Columbia study recorded a significant drop in plasma levels of chlorpyrifos in umbilical cord blood. High prenatal exposure, as measured by elevated umbilical cord levels, was associated with a decrease in developmental scores at 3 years using the Bayley Scales at age 3, and at 5 years using the WPPSI. The adverse effect was observed with the highest concentrations of CPF occurring before the EPA ban.

The IPM intervention was formed through a partnership with the NYC Department of Health and Mental Hygiene and the NYC Housing Authority. It involved professional cleaning to remove food sources and

cockroach frass (fecal matter) in kitchens and bathrooms of 194 intervention and 129 control apartments. Following intervention, cockroach populations were decreased, allergens were significantly decreased, and nearly a 50 percent decrease was seen in the use of bombs and sprays by the IPM group. Effects on asthma symptoms are being evaluated. Based on these results, the housing authority is expanding the IPM to other building sites in NYC.

Use of Biomarkers and Physiologically Based Pharmacokinetic (PBPK) Modeling in Risk Analysis for Developmental Effects of Chlorpyrifos
Robin Whyatt, Columbia University

The newly received EPA Science To Achieve Results grant is designed to use the exposure response relationship seen in the Columbia study and, using PBPK modeling, derive an RfD dose for CPF based on the developmental effects of the maternal dose during pregnancy. The study approach is enhancing an already-developed CPF PBPK model to estimate dosimetry during pregnancy. It will incorporate human interindividual variability in key metabolic parameters, based in part on newer metabolism measurements in human livers and exposure time pattern data to convert observed CPF levels in cord and maternal blood to both intake doses and internal concentrations of active metabolite for benchmark modeling. The specific measurements to be used from the Columbia study include cord blood levels of CPF at delivery, maternal blood levels 1–2 days following delivery, indoor and personal air levels of CPF, and urinary levels of a CPF metabolite (TCPY). These data will be used with NHANES data to estimate what percentage of the population in the United States has detectable levels of CPF in their urine. More information on this study can be found at <http://www.mailman.hs.columbia.edu/ccceh/about.html>.

Discussion

A representative from the New England Asthma Regional Council offered information about research on the effectiveness of IPM, particularly for homes in low-income populations, that was translated into policies and procedures. In conjunction with HUD, the New England Council will be releasing a DVD for tenants and housing managers on how to use IPM. In addition, over the next few months, the Council will be releasing a toolkit for policy-makers on how to promote IPM from a policy level on federal, state, and local levels and a toolkit for housing managers on how to work with their tenants to put IPM into place using the Boston Housing Authority's successful model. More information can be found at the New England Asthma Regional Council Web Site (<http://www.asthmaregionalcouncil.org>).

SESSION II: PHTHALATES EXPOSURE IN CHILDHOOD: IS THERE EVIDENCE OF HARM?
Chair: Maida P. Galvez, Mount Sinai School of Medicine

The goals of this presentation were to describe phthalate exposure levels in pregnant women, toddlers, and school age children; identify important sources of exposure in these populations; and understand the known and potential health outcomes. Based on exposure studies in animals, there is evidence for adverse birth outcomes, from fetal demise to modulation of gestational age to adverse impacts on the male reproductive system, including decreased anogenital distance in male infants and decreased testicular function and fertility. Phthalates are found in a wide range of products, and there is potential for inhalation, ingestion, and dermal absorption, the major pathways of exposure. The premature baby population, which is exposed through medical IV tubing in intensive care units (ICUs), is considered highly sensitive to exposures. The potential of phthalates to act as endocrine disruptors is a concern, based on animal studies and a small but growing body of evidence in human studies.

Legislation banning phthalate use in children's toys was first implemented in the European Union, and subsequent media reports raised parental anxiety about a number of items in their homes that may potentially expose their children. Primary pediatric physicians are in a difficult position, faced with

clinical questions that are difficult to answer. Pediatricians receive limited training in CEH in medical school, have limited knowledge of emerging exposures of concern such as phthalates, and are exposed to conflicting messages in the media. Dr. Galvez concluded her presentation by introducing the speakers for this session.

Phthalate Exposures During Pregnancy

Robin Whyatt, Columbia University

The Columbia Center for Children's Environmental Health is conducting research on phthalate exposure during pregnancy from inner city communities in NYC because it is a universal issue in the United States. A number of phthalates are endocrine disruptors, including those acting as anti-androgens. Experimental and epidemiological evidence indicates that a number of phthalates are reproductive toxicants and are associated with malformation in the developing male reproductive tract and other reproductive outcomes. Recent epidemiologic data indicate that prenatal exposure may modulate the timing of labor.

The specific aims of the research are to: (1) characterize phthalate exposures during pregnancy among NYC African American and Dominican women (n = 350); (2) examine effects of prenatal phthalate exposures on modulation of gene expression in placental tissue; and (3) examine the effects of prenatal phthalate exposure on gestational age and fetal growth. This cohort is comprised of 300 mother-newborn pairs from a larger 725-person cohort and has the same inclusion/exclusion residential criteria as the full cohort. Phthalates were measured in personal air samples during pregnancy, and biological samples and gene expression were examined. The conclusions of this study are that phthalate exposures are widespread among NYC African Americans and Dominicans during pregnancy; phthalates are detected in 85–100 percent of indoor air, personal air and maternal urine samples; indoor air levels appear stable over time and are significantly correlated with personal air levels in most cases; there is a significant correlation between air and urine levels in two phthalates; and di(2-ethylhexyl)phthalate (DEHP) exposures may be modulating gestational age.

Discussion

A participant asked about data on the time of urine collection in relation to when the mothers may have been using cosmetics. Dr. Whyatt responded that these data have not been analyzed for diurnal variability.

A participant asked about air fresheners, because many of them contain phthalates, including those labeled as “all natural.” Dr. Whyatt indicated that they collected extensive questionnaire data related to product use, but the data have not been analyzed in relation to outcome measures. There is such variability between products and within brands of products that the questionnaires may not be capturing the intended information.

A participant asked if the study will be expanded beyond minority populations. Dr. Whyatt explained that there are no plans to extend the study beyond the Center's cohort, but phthalate studies are being planned for the Krakow cohort.

Infant Phthalate Exposures and Potential Developmental Impacts

Sheela Sathyanarayana, University of Washington

The University of Washington and Northwest PEHSU, in concert with the University of Rochester, examined data from the Study for Future Families, a mother-baby cohort study in Missouri, California, and Minnesota, to determine whether infant personal care product use was associated with urine phthalate concentrations and whether maternal phthalate exposure was associated with developmental outcomes in infants. The demographic characteristics of the cohort study included 163 infants ages 2–24 months, with

an even distribution between genders; a racial profile of 80 percent white and 11 percent Hispanic and Latino; high socioeconomic status; 50 percent of participants from Minnesota and 25 percent each from Missouri and California; and 91 percent of families reporting health insurance. Infant urine samples were tested for detectable concentrations of nine known phthalate metabolites, and all infants samples contained at least one detectable phthalate metabolite. More than 80 percent had detectable concentrations for seven of the metabolites, and over 50 percent showed detectable concentrations for all nine. These concentrations are similar to or lower than children 6–11 years of age in NHANES data. This may be because younger children are not as involved in their environments unless they are walking or crawling; therefore, most of their exposures come from their parents and diet. Metabolites were measured to test for an association with reported use of a variety of baby products, including baby powder, baby lotion, baby shampoo, diaper cream, and baby wipes. Infants whose mothers reported using baby lotion, shampoo, and powder showed increases in urine phthalate metabolites compared to infants who were not exposed. Results of this study suggest that phthalate exposure in infants is widespread, distribution is varied in infants, and dermally applied baby care products may significantly contribute to infant phthalate body burden. Reported exposure to baby lotion, baby powder, and baby shampoo was significantly associated with increased urinary concentrations of monoethyl (MEP), monobutyl (MMP), and monoisobutyl, and the associations were stronger in younger infants.

To determine whether maternal phthalate exposure was associated with developmental outcomes in infants, the researchers examined anogenital distance as a marker in infants because of animal model evidence that abnormal anogenital distance is associated with phthalate exposure and genital tract abnormalities. Exposure in rodents is related to shorter anogenital distance, impaired testicular descent, hypospadias, low sperm count, and sometimes testicular tumors. Because short anogenital distance is the most important marker, the researchers first created a model estimating the standard for distance associated with age and weight. The phthalates associated with the shorter distance included MBP, MEP, and DEHP phthalate metabolites. Increasing phthalate metabolite concentrations were associated with decreasing anogenital distance in a dose-response manner. The clinical implications of these findings associated exposure with a shorter anogenital distance and suggest that phthalates may act through an endocrine disrupting mechanism to affect hormonal development of genital structures. Researchers also found an association between increased phthalate metabolite concentrations, decreased testicular descent, and smaller penile volume, but these were not significant. Further research is needed to determine if distance is a marker of abnormal male reproductive development in humans.

Discussion

A participant asked why an earlier study did not find a metabolite effect. Dr. Sathyanarayana indicated that the sample size was not large enough for that study, and that they had used the anogenital index, which was not an appropriate statistical model for predicting the expected distance. Based on feedback to the earlier study regarding these issues, the research team for this study constructed a new age- and weight-based model for conducting analyses, but the results of this study have not yet been published.

A participant requested clarification on the hormone involved in these studies and asked if phthalates could be tested for with amniocentesis. Dr. Sathyanarayana explained that the theory is that androgen decreases overall *in utero* as a result of exposure, but it is difficult to determine whether it is testosterone or some other hormone. One problem with using amniocentesis for phthalate detection is that the procedure is not a standard test, and it is usually carried out on high-risk pregnancies, decreasing its feasibility as an accurate marker for the general population.

A participant asked about the specific components of the baby products that are associated with phthalate exposures. Dr. Sathyanarayana replied that there is no method to determine the components because there are no labeling requirements for chemicals, which is why studies that identify phthalate-associated

products are important. California is beginning to mandate disclosure of phthalates and other reproductive and carcinogenic compounds for products sold in that state. In addition, phthalates are plasticizers that help bind other compounds together, so it is possible that the manufacturing process may be responsible, not necessarily the product components.

A participant asked whether synthetic hormone use during pregnancy was controlled for and whether any of the male infants had hypospadias or cryptorchidism. Dr. Sathyanarayana responded that the mothers were asked about hormone use during pregnancy, and all reported no use. None of the boys had frank phenotypic abnormalities.

A participant asked whether the U.S. Food and Drug Administration (FDA) had examined this study and set a maximum level in all these products. Dr. Sathyanarayana answered that the FDA has evaluated phthalates previously and has not set any concentration levels, but as the results of this study have not been published, the FDA has not examined the data. The FDA did register a warning to health care providers that concentrations might be high in neonatal ICUs because of IV tubing, but the agency has not set any mandatory requirements for testing or RfDs. EPA will be undertaking a larger review soon. Another participant clarified that the FDA receives advice from a separate industry-run organization but does not have authority over cosmetic products. The European Union has banned phthalates in many of these products, which may be pushing U.S. industries to produce phthalate-free products because they market to the European Union. One cautionary note regarding phthalate-free products on the market is that consumer companies still find detectable levels in these products; there must be a higher level of enforcement at some point.

Inner City Toxicants, Child Growth and Development
Mary Wolff, Mount Sinai School of Medicine

Dr. Wolff mentioned a monograph published by *Environmental Health Perspectives* in the 1970s that proved phthalates are not toxic. The issue now is that the levels of phthalates are very high and that some of the newer generations of bioassays have revealed hormonal effects. She summarized preliminary data from the Mt. Sinai birth cohort, a multiracial cohort that included 100 boys and 300 girls from 6–8 years of age. The researchers conducted exposure assessments in mothers during their third trimesters and outcome measurements of the children. In a cohort of school-age children, levels and variability have been assessed to determine feasibility of a single urinary biomarker for these chemicals. Preliminary results showed exposures similar to the Columbia study for MEP. The mothers had higher levels of some phthalate metabolites than the Columbia and NHANES cohorts, but were consistent with NHANES for minorities. Results of temporality studies suggest that some of these biomarkers can be used as predictors of these metabolites for up to 1 year, and of the three families of chemicals studied, phthalates were the most reproducible. The Mt. Sinai team also summed groups of phthalates based on molecular weight and found significant levels of low molecular-weight phthalates among the minority populations and higher molecular weights among whites. Product use questionnaires revealed some borderline associations of the DEHP metabolites with nail polish and hair products, but they were not significant in preliminary data from a small number of subjects.

Because there currently is much interest in body mass index (BMI) and phthalates because of cross-sectional data published by NHANES, the researchers examined gestational age. In relation to phthalate metabolites, the researchers found very weak associations between phthalate exposure and longer gestation. The researchers currently are evaluating these biomarkers with respect to neurodevelopment.

Discussion

Dr. Maida Galvez summarized the presentations before opening the floor to discussion. Phthalate exposures are widespread. In this session, evidence was presented from three different cohorts, ranging from exposures in pregnancy, a particularly vulnerable time period, through early childhood and beyond. The two cohorts of pregnant women from NYC showed similar levels of exposure, despite the fact that the populations were very different in racial and ethnic demographics. This is a contrast to exposures in infancy and early childhood in a predominantly white cohort, with relatively low exposures when compared to the inner city populations. The sources of exposure were varied, from voluntary use of products to contamination of indoor air from dust generated from phthalate products. Through measurement of the available biomarkers, there is now limited evidence from human studies demonstrating possible modulation of gestational age and potential impact on anogenital distance. These cohorts will continue, and effects on body size, particularly BMI and waist-hip ratio; potential associations with asthma; and other developmental outcomes will be examined. What to tell the parents asking for advice is a challenging situation, but it is usually best to give them an action item in the face of clinical uncertainty. Mt. Sinai's Community Outreach Translational Core developed a pocket guide to plastics for easy reference. In the absence of legislation mandating correct labeling of products, these wallet-size cards can help families identify phthalate-containing products. In general, the plastics to avoid are labeled 3, 6, and 7 for recycling purposes. The CEH community needs to work together to determine the best health messages to relay to families and what policy issues to advocate.

A participant asked about the Mt. Sinai study participants' access to results. Dr. Wolff explained that participants were provided with summary data when available on request. Families also would be told how their levels compared to the entire study population on request, but no individual data would be shared with the participants. The researchers were prepared to respond to questions through a potential collaboration with the PEHSUs, but no requests have been received. Study participants did express concern that environmental factors may be related to long-term health outcomes such as obesity and puberty. The same question was posed to Dr. Sathyanarayana, who replied that study participants received a one-page handout of the previously published study because the current study results are not complete. Dr. Wolff's team will not be submitting individual data, but its cohort was educated about group findings versus individual findings at enrollment. The participants were told that if harm is found on a group basis, the entire cohort would be notified about those findings and receive information on what they could do on an individual basis to reduce the exposure.

A participant asked about the issue of potential "sleepers biomarkers" that have been identified in animal models but have not been tested in humans. One of the session speakers answered that some studies are underway, and an issue remains regarding validation involved in anthropological types of markers, such as anogenital distance. Some clinicians successfully use the finger ration with certain conditions (autism, etc.) and the results are very interesting but difficult to measure scientifically. Another participant added that a new mulitcenter cohort study is underway that uses anogenital distance to examine dysmorphology.

A participant asked for clarification on what the focus was of the pocket guide. Dr. Wolff explained that the pocket guide identifies plastics that are associated with phthalates and other chemical exposures from food packaging. Because dietary sources are considered to be the major pathway of phthalate exposure, the card also includes some information about leaching.

A participant questioned the usefulness of cautioning the public about phthalate-free products, because although organic food contains detectable levels of pesticides, it is still considered better because the levels are relatively lower. Dr. Galvez indicated that, from the limited consumer product testing, phthalate-free products do contain relatively lower levels of phthalates, but the study participants received cautioning as a process of full disclosure so they could make informed decisions.

A participant asked, given the relatively small effect size in much of the presented data regarding which plastic containers or which kind of fragrant-free products to use, where clinicians should put this issue on the list of priorities when discussing hazards with parents. A session speaker explained that, although there is no definitive answer regarding humans, it is not a good idea to put phthalates on the bottom of the priority list in a clinic setting. Animal toxicity data exist, and more studies are planned. Full disclosure about what is known and what is not known is better than no disclosure.

A participant commented that the benefit of the CEHCs is that they bring clinicians and the community together in an academic setting where there is integration of mechanistic and animal scientists. Anogenital distance studies were prompted by animal studies. Increased collaboration between animal scientists and human health and environmental researchers will increase opportunities for the CEH community to learn about biomarkers. Perhaps more of the animal models will be adapted to human studies for more definitive purposes.

A participant asked if there is a safer substitute for phthalates. A session speaker explained that there are other plasticizers and other technologies that do not use a plasticizer, but there are enormous data gaps on the substitutes. Nonplasticizers do not leach as much as plasticizers, so that may be a significant advantage. Dr. Wolff's team is preparing to submit a paper examining substitutions in the neonatal ICU because that is where exposures are higher. The paper examines every substitute to date and what is known about them.

SESSION III: THE EVOLVING SCIENCE AND PRACTICE OF ENVIRONMENTAL MANAGEMENT FOR ASTHMA PREVENTION AND CARE

Co-Chairs: Kimberly Gray, NIEHS, and Leyla E. McCurdy, National Environmental Education Foundation

Improving Asthma Outcomes: 2007 NAEPP Guidelines Focus Attention on Education and Environmental Interventions

David Rowson, U.S. EPA

Mr. Rowson provided an overview of the 2007 National Asthma Education and Prevention Program (NAEPP) Guidelines for the diagnosis and management of asthma. The new guidelines focus on monitoring asthma control as the goal for asthma therapy and distinguishing between asthma severity and monitoring asthma control. Treatment should be initiated based on severity assessment and then adjusted based on control. There is a new focus on impairment and risk. Impairment includes the frequency and intensity of symptoms, low lung function, and activity limitations. Future risk includes the risks of exacerbation, progressive loss of lung function, or adverse side effects from medications. Clinicians need to increase the consistency of asthma monitoring, assessment, and care. There are new modifications to the step-wise approach to long-term management of asthma. Treatment is partitioned into three different age groups, and there are six specific steps of care that span from intermittent to severe. The new guidelines incorporate updated approaches to patient education and control of environmental factors and co-morbid conditions that affect asthma. Finally, there are modifications to treatment strategies for managing and classifying asthma exacerbations. The guidelines are built around a framework of four essential components that include: (1) assessment and monitoring of asthma severity and control; (2) education for a partnership in asthma care; (3) control of environmental factors and co-morbid conditions; and (4) medications.

The new guidelines have increased attention on self-management and education of family and individuals regarding the environment, noting many potential sites for asthma education and care: homes, schools, and community settings. The guidelines recommend patients receive education in an integrated,

multifaceted method in multiple settings. Written action plans are highlighted as a central component of asthma care, with a focus on multicultural ethnic factors and health literacy to enhance adherence to physician advice and medication regimens. Provider education also is highlighted as an essential component. Automated assistance helps clinicians to adhere to the guidelines, so these systems are being put into place to support them. The most important actions patients should take include avoiding environmental triggers that exacerbate symptoms and cause asthma attacks. The guidelines list potential triggers and a series of steps to follow for controlling individual environments. The guidelines recommend testing individuals for sensitivities so that intervention steps can be tailored to individual needs. The guidelines also stress the importance of an active lifestyle. With proper control, exercise should be possible; if an individual cannot exercise because of symptoms, that should be considered a benchmark for a change in treatment.

Although asthma rates appear to be steady nationally, they remain at an all-time high, and there are significant disparities in morbidity and mortality. *Healthy People 2010* goals contain a range of important indicators; some of those goals are close to being reached, whereas others are farther off. The new guidelines highlight critical areas to help reach those goals. For instance, the guidelines suggest more written asthma action plans, increasing adherence with treatment, and controlling for environmental triggers—all goals of *HP2010*.

To support the delivery of evidence-based care at the community level, EPA is supporting the Communities in Action for Asthma Friendly Environments Network (CAAFE). Grounded in the results of the Asthma Health Outcomes Project and conducted by the University of Michigan, a centerpiece of CAAFE is the Change Package—a compendium of practical, day-to-day best practices program strategies that deliver positive health outcomes. CAAFE is supported by an interactive Web site developed to facilitate real-time learning and sharing of best practices, as well as an annual National Asthma Forum. More information on the CAAFE and the National Asthma Forum can be found at <http://www.asthmacommunitynetwork.org>.

Prenatal and Early Postnatal Exposures and Asthma Risk—How?

Rachel Miller, Columbia University

Dr. Miller provided a review of mechanistic data that begin to address the question of how prenatal and postnatal exposures may affect asthma risk. Asthma is a complex disease mediated by genetic predisposition, environmental exposures, and host factors (e.g., obesity, psychosocial issues, infections). Prenatal and early postnatal exposure (e.g., traffic, diesel, roaches, dust mite allergens, pollens) can modify asthma risk, and there is evidence that exposure during pregnancy is very important in modifying or protecting for asthma. A review of epidemiologic data shows that prenatal exposure can affect asthma risk, and the strongest evidence is related to prenatal exposure to environmental tobacco smoke (ETS). Prenatal ETS exposure is associated with impaired respiratory function, transient wheeze, asthma, and respiratory infections in infants and young children. Additional exposures during pregnancy that appear to be associated with an increased risk of asthma include low maternal intake of vitamin E and zinc during pregnancy, antibiotic use, and several types of maternal infection. Furthermore, respiratory infection during pregnancy has been shown to be an independent factor that may increase later asthma risk. Recent data also suggest that ambient air pollution and polycyclic aromatic hydrocarbons may increase risk later on in life for children. Early postnatal exposure to traffic and combustion-related pollutants has been associated with both dust mite sensitization and impaired pulmonary function in later childhood. There may be, however, other exposures that may help protect against asthma or wheezing illness. These include maternal intake of probiotics during pregnancy, higher birth order, and exposure to dogs and cats during the first year of life.

A review of possible relevant mechanisms implicates immune-mediated processes and epigenetics. For example, multiple studies have shown that cytokine levels differ at birth among those children who may be more likely to develop allergy and wheeze. There also is evidence that the fetus can generate an independent immune response to proteins or allergens that the mother experiences in pregnancy. Epigenetic changes refer to those that influence gene expression without any change in the DNA sequence. They may influence gene expression differentially throughout a lifespan. In conclusion, prenatal and early postnatal exposures do impact risk for later asthma, but more cohort-driven mechanistic research must be done.

The Center for Childhood Asthma in the Urban Environment
Elizabeth Matsui, Johns Hopkins Hospital

Dr. Matsui, co-investigator for the Center for Childhood Asthma in the Urban Environment, provided results of some of the Center's studies. The Center conducted studies of indoor pollutants and asthma in Baltimore row homes. Preliminary data showed no differences between asthmatic children and controls and no differences in levels of other common allergens. Because mouse allergen levels were higher in these homes than in other cities, the researchers investigated whether the allergens were responsible for asthma morbidity among children with asthma who were also mouse sensitized; the results were striking. Across a multitude of asthma outcomes, there was a significant increase in asthma symptoms in children who were mouse sensitized and highly exposed. The findings of this study are an important reminder to conduct community or regional studies in addition to multicenter studies because local signals can be lost when combining data from different regions. The researchers examined indoor pollutants in children's bedrooms; although children with asthma had similar levels of exposure as control children, the causality of environmental exposure to asthma development cannot be ruled out because prevalence rates of asthma in this population were between 25 and 30 percent. In addition, the researchers have not conducted studies of the same asthmatic children in different environments. Surprisingly, indoor pollutant levels are much higher than outdoor levels, and the indoor exposure is likely to play a critical role in the development of asthma, which is compounded by the fact that children today spend more time indoors than outdoors. The researchers also looked at indoor particulate matter (PM) exposure in relation to poorer outcomes in children with asthma and found a strong signal for coarse PM. Coarse PM fraction in bedrooms increased risk in the number of days of symptoms and beta agonist use in children. There were some signals with fine PM also, but results were not as consistent as results with coarse PM.

Clinical Experience with the Environmental Management of Asthma
and the NAEPF Expert Report 2007
James M. Seltzer, University of California at Irvine

Dr. Seltzer presented an overview of his experiences as an allergist/immunologist caring for children with asthma and as a PEHSU Director, who must respond to inquiries from families regarding symptoms and the role of environmental factors in allergy and asthma. As a clinician, he sees patients with environmentally induced illnesses, including asthma, and other allergic disorders. The role of environmental factors as precipitants of allergic disease is not always obvious, especially in children under 5 years of age or where allergens are only one of several types of exacerbating factors. This applies not only to the primary care doctor, but also to the allergist/immunologist who possesses particular expertise in determining the spectrum of allergic sensitivity for a given patient. Allergy testing, especially skin testing, can help identify potentially relevant allergens, whether or not they were suspected from the medical history. Environmental factors can easily be missed and should be confirmed or ruled out in each patient with the possibility of health problems that might be related to environmental exposures. As a PEHSU Director, Dr. Seltzer responds to inquiries from parents, schools, the media, and other entities or persons regarding environmental factors, and the questions typically are focused on high-profile exposures, such as mold and diesel, but not other common exacerbants, such as dust mite or cockroaches.

He discussed the significance of the assessment of environmental factors in each clinical case; the importance of taking a careful, extensive history; determining if exposures are relevant; and, if relevant, teaching the parent and child how to reduce exposure and to monitor future exposures and clinical responses to exposure reduction. Reducing factors contributing to asthma severity can be accomplished by environmental control measures for clinically relevant precipitants, such as reducing sources and reservoirs of allergens and airway irritants in the child's environment. Dr. Seltzer also discussed the hygiene hypothesis: early life exposures to certain allergens may provide protection from the development of asthma and other allergic disorders later in life. Although early life exposure appears to have more effect than exposure later, there are not enough data to recommend early exposure as a method to reduce future risk. Education is important. Patients and physicians can learn how environmental factors affect children's health, thereby improving recognition of these disorders as well as how to institute effective environmental control measures. Finally, he outlined the goals of asthma therapy. For control of asthma to be effective, it must be recognized, its nature defined, and the roles of all relevant environmental factors identified and addressed for any given child. With successful environmental control, pharmaceutical therapy and, if indicated, immunotherapy (desensitization), the need for clinician intervention ultimately can be minimized. Lastly, to be effective, asthma therapy must be practical, affordable, and convenient.

Discussion

A participant asked Dr. Matsui whether any composition studies have been done to identify PM. The Johns Hopkins Children's Center had examined the composition of ambient PM previously, but composition studies for indoor PM have yet to be performed. Animal particles, however, are much more readily airborne than insect particles. It will be difficult to measure cockroach PM, because these larger particles settle quickly and it is difficult to disrupt the dust to become airborne. The other session speakers contributed to the discussion in regard to outdoor air pollution, including pollen, mold, traffic emissions, and ozone, and all agreed that individual sensitivities and time of day need to be considered. Ozone levels generally are highest during middle to late afternoon, and some outdoor molds sporulate at different times of the day. Additionally, there is difficulty separating the effects of indoor pollutants from the effects of outdoor air pollutants. Often, allergen and irritant concentrations are higher indoors. The complexity of allergen and pollutant exposures, which occur in both indoor and outdoor environments, combined with individual differences in susceptibility to these exposures, makes it challenging to provide guidance regarding optimal environmental control measures to patients. In fact, recommendations in the new NAEPP guidelines are more general than specific for this very reason. It was mentioned that the guidelines are directed at the delivery of asthma care and what clinicians should do when interacting with and educating the patient. EPA regulations affect outdoor triggers but do not regulate indoor exposures, so patients who are advised to reduce particular indoor exposures are responsible for implementing the environmental control practices. For those who are not homeowners, appealing to landlords to make necessary modifications to the home or provide pest extermination is needed. Regarding outdoor exposure to pollutants, ORD is examining school sites and athletic fields near roadways to better understand this issue. A session speaker invited participants to become actively engaged in the process of updating the guidelines, because the guidelines are posted for public comment during development.

A participant asked Dr. Miller for clarification of her lab's work on inhaled allergen and diesel exposure on DNA methylation and immunoglobulin E (IgE) production in mice. The question was whether the exposures in her studies were mixed or single. Dr. Miller responded that the effects on DNA methylation and IgE production in mice were measured after combined exposures to the mold *Aspergillus* and diesel administered chronically by inhalation over 3 weeks.

A participant asked Dr. Seltzer whether there is a lower boundary for which to diagnose asthma in children and what the place of skin testing is in immunotherapy. Dr. Seltzer responded that the diagnosis

of asthma in a 1- or 2-year-old is problematic, because young children typically have recurring episodes of wheezing with viral infections. Children in families where other members have asthma or allergic disorders are at increased risk of developing asthma or recurring reactive airway disease. Although these and other risk factors can be identified, in a given child it is more a function of how often symptoms occur, what they are associated with, and how persistent they are that helps to make the diagnosis. Among 1- and 2-year-olds, although a wheezing child may have asthma, the clinician must be concerned about other diagnoses associated with recurring wheeze as well. Treatment usually involves a therapeutic trial of bronchodilator, with or without inhaled steroids delivered by nebulizer or a pediatric mask attached to a spacer, depending upon age and ability of the child to use a spacer. As far as skin testing, Dr. Seltzer has tested down to 6 months. Typically, there is less skin reactivity and less IgE in younger children, but testing can be performed at any time, even at birth.

SESSION IV: EARLY LIFE EXPOSURES TO METALS AND NEUROTOXIC OUTCOMES

Co-Chairs: Isaac Pessah, University of California at Davis, and Nigel Fields, U.S. EPA

Neurodevelopment, Autism, and Mercury: Biomarkers and Epidemiologic Approaches **Irva Hertz-Picciotto, University of California at Davis**

Dr. Hertz-Picciotto discussed mercury and its relation to neurodevelopment and autism. The effects of mercury are complex, but it is known to cause developmental delays and deficits in the mental, muscular, visual/spatial, social, and sensory domains. Autism is a pervasive developmental disorder characterized by deficits in three domains: (1) social interaction, manifested in lack of eye contact, lack of response to name, failure to engage in joint attention, and so forth; (2) communications/language, including lack of language or odd use of language; and (3) repetitive behaviors or restricted interests. The current prevalence estimate of autism is about 1 case in 150 individuals and the ratio of males to females is 4:1. There is a strong genetic component to autism, but environment also may play a role. Autism is a multifactorial condition with a wide severity curve, yielding high-functioning individuals and individuals who cannot function independently. Historically, autism was thought to be a result of poor parenting. It now is generally accepted that it is a neuropathologic condition, but this legacy has led to a general mistrust of the medical community by parent and advocacy communities. Brain imaging studies have shown that facial recognition processing is one of the most affected areas and a hallmark of the condition. When looking at faces, areas of the brain that are used in typically developing individuals are much less activated in autistic individuals, and there is no one area of the brain that is affected by autism. Lesions from autopsies are very widespread; this suggests that the insults occur very early in development, most likely during gestation. The most replicated finding anatomically is the loss of Purkinje cells.

In the 1950s and 1970s, several high-profile mercury contamination episodes led to mass poisonings in Iraq and Minamata Bay. Children exposed *in utero* appeared to be the most vulnerable. Severe impairments, deficits, seizures, abnormal neuronal migration, and disorganized cerebral cortex were seen in some autopsies. Studies followed birth cohorts in communities with high fish consumption. More than 1,000 mother-child pairs in the Faroe Islands were used to relate development to prenatal exposure, which was measured through maternal hair, cord blood, and cord tissue levels. The results showed deficits in attention, language, memory, and visual/special domains in children at 7 years. Similar findings and motor deficits were evident at age 14. The Seychelles Islands study found no deficits, and it has been difficult to reconcile the conflicting findings. Project VIVA (Venue-Intensive Vaccines for Adults), which involved maternal hair mercury measurements, controlled for the benefits of fish consumption. Results clearly showed the benefits of fish consumption, and harm from mercury was measured in a dose-response fashion. Dental amalgams are a source of an inorganic form of mercury, which is broken down into the methylated form and travels more easily across the blood-brain barrier. A randomized study examining children who received mercury amalgams found no mental deficits, suggesting that

susceptibility to mercury neurodevelopmental toxicity may be greater when exposure occurs prenatally as compared with mid-childhood.

Studies regarding the link between mercury and autism are mixed and controversial. Several studies were conducted on thimerosal, a vaccine preservative introduced in the 1930s. Thimerosal breaks down into ethyl mercury and thiosalicylate. It was removed from many child vaccines in 2002 but remains in some vaccines (e.g., hepatitis B virus and influenza). Most studies examining the link between thimerosal and autism have been in the form of ecologic studies comparing before and after removal or introduction. Very few studies have individual data, and multiple factors related to better diagnosis make the data difficult to interpret. Vaccines, however, are not the only source of mercury. Home sources can include nasal sprays, contact lens solutions, ear wax removal products, damaged batteries and light bulbs, and skin lightening creams.

Dr. Hertz-Picciotto ended her discussion by presenting an overview of the Childhood Autism Risks from Genetics and the Environment (CHARGE) Study, which is examining the causes and contributing factors of childhood autism risk and the mechanisms of susceptibility, including those that are genomic, immunologic, and metabolic. Many possible mechanisms may affect neuronal maturation, regulatory genes, immune signaling, and endocrine processes. She discussed the catchment area, assessment measures, study design and laboratory methods, and some preliminary results. A multiple linear regression model was used to predict blood mercury. Preliminary findings showed that fish consumption is predictive of mercury, and the use of nasal spray or ear wax removers or amalgam fillings was associated with blood mercury level. There were no associations found with autism.

Future work will include multivariate analyses on baby hair locks, 483 newborn blood spots, and mothers' hair that may represent the prenatal period. Other subsets will be analyzed regarding the heterogeneity, metabolizing genes, and xenobiotics that may affect the immune system.

Genetic and Social Modifiers in Environmental Neuroepidemiology: The Role of Context in Chemical Exposure

Robert Wright, Harvard School of Public Health

Dr. Wright discussed the variance found in studies of chemical exposure and health outcomes and possible explanations for the different susceptibilities to certain neurotoxicants. A broad biological framework for the reasons children are more biologically susceptible was presented. Fundamentally, because the CNS is developing, there is ongoing activity (largely absent in adults) on generating cells, differentiating cells, and cell migration. Finally, those processes that determine synaptic architecture and the ability to develop acquired memory are dominant during early childhood. Environmental stimuli drive whether a given synapse is kept or regresses. This is a form of natural selection and mimics evolution. Synapses that serve an adaptive purpose are preferentially kept, and those that do not, regress. Environmental chemicals may interrupt these processes and send them down different developmental pathways. For example, at low doses, lead causes neurons to fire in a stochastic fashion, thereby mimicking inappropriate environmental stimuli and the natural process of natural selection for synapses. Over time, the resulting underlying synaptic architecture with prolonged exposure to toxic chemicals will be less efficient. Like chemicals, social factors can be either maladaptive or adaptive. Neurohormones such as cortisol are critical to synaptogenesis, and their metabolism changes in response to chronic stress. Chronic stress, which is a nonchemical toxicant, is known to impair memory and learning capacity. Because both chronic stress and lead share properties that can modify synaptogenesis, the joint or sequential presence of lead and stress can be interactive. If instead of being stressful, social factors are adaptive, animal studies demonstrate they will mitigate the effects of lead. On the other hand, if they are maladaptive (i.e., produce stress), they may increase its toxicity. There may be ways to treat lead toxicity beyond chelation. In animal studies, an enriched environment appears to mitigate the effects of lead

poisoning. Following lead poisoning, animals that are socialized perform better than those in isolation (stress environment). Self-esteem also may modify the effect of lead, as indicated by the results of one human study. Maternal self-esteem is not stress, but it may be considered a buffer to chronic stress. Mothers with higher self-esteem develop adaptive responses to chronic stress. Another pilot study in humans showed that teens exposed to prenatal tobacco smoke and high levels of exposure to violence as children (i.e., neurotoxicant and stressor) had worse performance on the Wisconsin Card Sorting Test than teens with high tobacco smoke exposure and low violence exposure.

Genes also regulate synaptic formation. The process of synaptogenesis and synaptic pruning is an interplay between genetics and the environment. At least three studies demonstrate that variants in the *apoE4* gene, which is critical to synaptogenesis, are associated with better cognitive performance. Further, results suggest that the *apoE4* gene variant might have a protective effect against lead. Blood manganese also may be a predictor of neurodevelopment, and there is some evidence that manganese is neurotoxic. Just as exposure does not occur in a social vacuum, it does not occur in a chemical vacuum. Some people exposed to lead also are exposed to other chemicals. Animal studies show that joint exposure is more neurotoxic than individual exposure to either lead or manganese, and human studies are being conducted to address this finding as well.

Ongoing work in Mexico City will examine a birth cohort, in terms of metal mixtures and neurodevelopment and also, with respect to stress as a modifier of lead poisoning, iron-deficiency anemia. The studies will measure prenatal and postnatal contributions, genetic susceptibility, mixtures of metals, and social modifiers and toxicity. The long-term goals are to identify those factors that increase or decrease metal toxicity, understand the biology of metal toxicity to prevent toxicity, and treat toxicity after it has occurred.

Criminal Behavior as a Late Outcome of Early Exposure to Environmental Lead
Kim Dietrich, University of Cincinnati

Data from previous cross-sectional and ecological studies suggest that there is an association between exposure to lead and antisocial behaviors, including delinquency and adult criminality, and data from the Cincinnati Lead Study show an association between prenatal and postnatal exposure and delinquent and criminal behavior. Lead exposure associated with a higher risk for engaging in criminal activity is not a new observation, but it is one that has resurfaced with some recent epidemiological studies. One 1996 study examined bone lead levels and the relationship of child scores on the Achenbach Child Behavior Checklist. Clinically significant high scores on delinquency, aggression, and attention problems were measured in those with high bone lead levels. An observational ecological study examined the correlation between homicide rates and air lead contamination levels in more than 3,000 counties in the United States and found a four-fold increase in homicide in counties with the highest rates of air lead concentrations. Another study reported a statistically significant relationship between trends in sales of leaded gasoline and violent crimes. Strong causal inferences cannot be made with ecological studies, but the results of these studies are very suggestive. Although there are limitations, these pioneering studies clearly suggest an association between environmental lead exposure in childhood and development of behavioral problems.

The Cincinnati Lead Study, funded by NIEHS since 1979, is a prospective longitudinal study that examines early and late effects of childhood lead exposure on growth, development, and neurobehavioral outcomes. There are many lead paint residues in the catchment area of this cohort study, and the researchers have a dense collection of blood lead determinations. Blood is collected prenatally and every 3 months through the first 6–7 years of life. From questionnaire data from study adolescents, there was a statistically significant relationship in terms of the number of total reported delinquent behaviors with respect to their blood lead levels. To determine relationships of early exposure to lead and adult

criminality, criminal arrest records from the State of Ohio were used. Prenatal and 6-year blood lead levels were significantly associated with total arrests, particularly for violent offenses. Lead increases antisocial behavior through the direct route; it affects brain systems that are important in regulating control. Gene-environment interactions also may play a role. It affects behavior through an indirect route as well. Early lead exposure is associated with high rates of school failure and reading disabilities, and children who perform poorly in school are more likely to engage in delinquent and criminal activities. Volumetric magnetic resonance imaging was used to examine the brains of study participants. When looking at the relationship between blood lead levels in these subjects, there was a significant association to gray matter loss in the frontal regions of the brain (i.e., those areas that are involved in attention, executive function, and regulation of social behaviors).

Discussion

A participant asked Dr. Dietrich about separate effects of blood lead at various ages to identify particular ages that are more important, higher late blood levels as an indicator of sustained exposure, and the temporal relation across the lifespan. Dr. Dietrich responded that the Cincinnati study did not address critical periods, but there are many intra-individual tracking data. Blood lead levels remained fairly consistent over the lifespan. When examining intra-individual blood lead levels in relation to IQ, measures of executive function, and criminality, the later the blood lead, the more robust the parameter estimate was in relationship to late outcomes. The higher late blood levels measured could be an accumulated effect, but genetic factors related to excretion or retention of lead in the blood may be involved.

A participant asked Dr. Hertz-Picciotto what advice she gives parents regarding consumption of fish. Dr. Hertz-Picciotto replied that communication is the key issue with respect to complicated messages. There is much variability across fish species, and not all fish have mercury. Several papers show that many fish species do not have high mercury, so it is best to emphasize consumption of low-mercury fish; consuming no fish is counterproductive because of the benefits of fish consumption, including during pregnancy.

A participant asked Dr. Hertz-Picciotto if her research collaborators have observed any co-morbidities between immune responses, mental disorders, and autism spectrum disorders. The participant asked for comment on the biological pathways by which environmental triggers may be causing some susceptibility to immunological responses and mental disorders or whether the environmental triggers are triggering immune responses that causes brain development to go awry, thus exhibiting the phenotype of autism spectrum disorders. Dr. Hertz-Picciotto replied that, in regard to co-morbidities, the research team is examining fatty acid screens in children in the CHARGE Study, and one of the findings is that certain fatty acids appear to be related to disorders that may be dysregulating. There may be a pathway where there is an accumulation of long-chain fatty acids that are not being metabolized to the shorter chain down the pathway. The team also is attempting to identify additional clinical signs of these disorders because they are not always present, indicating that there may be subclinical issues in a subset of the autism cases. One of the intriguing findings is of mothers of children with autism who make antibodies to fetal brain tissue. The CHARGE Study is being followed up by a prospective study called the MARBLES Study, which stands for Markers of Autism Risk in Babies—Learning Early Signs. Mothers of autistic children are being recruited during or before subsequent pregnancies. Regarding the question of biology versus environmental factors, all researchers would like to have insight on this issue.

A participant asked Dr. Wright about environmental treatment in humans, the current marker for stress in his cohort, and chemical water pollution and exposure assessment. Dr. Wright explained that he is not aware of any prospective human studies measuring whether the environment changes outcomes, but cross-sectional studies have been conducted that examine whether the social environment modifies

toxicity of lead or other neurotoxins. Because the brain is developing, there is no reason to think that an insult that occurs at age 2 necessarily has to be permanent. His study is utilizing a variety of questionnaires to assess stress that examine exposure to violence, negative life events, and perceived stress measured longitudinally. He also is collecting biological markers of stress, such as salivary cortisol. By collecting it multiple times over a random day, the diurnal rhythm of mothers during pregnancy and their children at age 2 can be measured. The NCS also is measuring salivary cortisol at various time points throughout the day in addition to collecting questionnaire data. Regarding water pollution, not all forms of lead are bioavailable today but may become bioavailable in the future; therefore, a critical issue in preparing long-term management plans at contaminated sites, particularly mining sites contaminated with the relatively inert lead sulfide, is to ensure that nonbioavailables remain so. As an example of what may develop, he cited the tragedy in Bangladesh in the 1980s. To counter the effects of a diarrhea epidemic, shallow wells were dug for cleaner drinking water. But the digging changed the reducing conditions in the soil so that the nonbioavailable form of arsenic in the soil changed to a bioavailable form, which was dispersed in the ground water and poisoned the population. Land and the environment may be stagnant, but human activity may change the bioavailability of chemicals.

OCTOBER 12, 2007

SESSION V: TRANSPORTATION, THE BUILT ENVIRONMENT, AND CHILDREN'S HEALTH

Moderator: Joanne Rodman, U.S. EPA

Development Patterns and Children's Health

Tim Torma, U.S. EPA

Mr. Torma presented background on development patterns, health, and the implications of the built environment. Contemporary community design has a tremendous impact on public health, particularly children's health, and the environment. There have been three macro trends during the last 50 years: (1) Employment and population growth heavily favored medium and large metropolitan regions versus nonmetropolitan areas. (2) Within metropolitan regions, most growth has occurred in low-density development at the fringe of urbanized areas. (3) There has been an emphasis on automobile travel at the expense of other modes. During the past 20 years, vehicle travel increased as a result of how and where populations are growing, not just because there are more people. Much has been known about this pattern and its impacts on the environment for a long time. The health impacts of these trends, however, have not been a focus of attention until recently.

The recent book *Urban Sprawl and Public Health* reveals that health outcomes are linked with land use and community design, including air pollution and related illnesses; a decline in physical activity; obesity and its attendant diseases; injuries related to auto dependence; threats to water quantity and quality; mental illnesses; and erosion of social capital. The authors cited the precautionary principle, "When an activity raises the cost of human health, precautionary measures should be taken even if some of the causes are not scientifically proven." Another message from this book is that urban planners are public health officials, whether they realize it or not. The public health community has been largely absent from and now needs to engage in the conversation on built environment and development patterns because how and where building occurs makes a difference.

Mr. Torma's presentation then focused on one particular aspect of the built environment—the size and location of schools. In 1969, 48 percent of children walked to school; in 2002, that percentage dropped to 16 percent. Today, there are far fewer schools than in the 1930s, but more students. Schools are now bigger, and these "mega-schools" are not accessible by foot. Many states have rules and policies that mandate or favor large schools; some local districts have even banned walking and biking access, citing

safety issues. Some argue that driving children to school protects them from predators, but the CDC performed a study to determine barriers to walking to school and learned that distance, not “stranger danger,” was the main reason given by parents whose children did not walk to school. Many recently built residential subdivisions have no sidewalks and are built as pods that require driving to arterial roads to leave the neighborhood. There are multiple health implications as a result of the built environment in general, and unwalkable schools in particular. For public health professionals, school siting decisions are a logical place to start engaging on the built environment. Mr. Torma ended his presentation by showcasing The Safe Routes to School Program and the “Regulatory Blueprint for Healthy Community Design” handout.

Traffic, Trade, Air Pollution and Land Use Decisions
Andrea M. Hricko, University of Southern California

The Children's Environmental Health Center based at the University of Southern California has scientists who study air pollution. The Center's Community Outreach and Translation Core is responsible for translating science for the public, including policy-makers, and the Center's investigators testify frequently in front of local, state, and federal elected officials.. They also serve on public scientific committees and working groups at the local, state, and federal levels, with a focus on ensuring that the research is delivered to the scientific, transportation, and urban planning committees as it relates to traffic, trade, air pollution, and land use decisions. Studies by Center investigators show that children who live within 500 meters of a freeway have a greater risk of reduced lung function than children who live further away and that there is a greater probability of asthma in children who live close to busy roads. Local air pollution exposure has adverse effects on children's lung function, independent of air quality measures. Lung function at age 18 is 3–7 percent lower than expected for children living within 500 meters of a freeway. Asthma prevalence is greater than 15 percent for children living within 50 meters of a busy road their entire life, which is nearly double the prevalence for children living at least 200 meters away, according to Center studies. Real estate developers need to be informed of these statistics and should be encouraged to reconsider their development plans. School budget committees should be informed as well, but conflict can occur with parents who would prefer to have their children go to a school in their own neighborhood, even if it is situated close to a freeway, rather than have them be bused to another location. Some California schools still are being built close to freeways, despite state guidelines and laws; developers cite “overriding considerations” for not following these guidelines and laws. Another potential conflict includes economics; land is very valuable in certain areas, and the only affordable land may be in close proximity to freeways.

Ms. Hricko raised the following question: Should the Federal Highway Administration (FHWA) be advising state transportation agencies to consider the latest research findings in their freeway expansion decisions? Several years ago, EPA issued “hot spot rules” requiring mobile source air toxics analyses, but currently FHWA states that it cannot validate the proximity-to-traffic studies and is waiting for an upcoming Health Effects Institute evaluation.

Dr. Jonathan Samet, in a recent article in *Inhalation Toxicology*, suggests that: (1) control will require both reduced emissions and increased separation of people from emissions; (2) there is a need for further research to refine our understanding of the health consequences of traffic exposures (and as a basis for formulating mitigation policies); and (3) a “no-regrets” strategy should be instituted to reduce exposures while further evidence is obtained.

Ms. Hricko pointed out that the Los Angeles/Long Beach area is the epicenter for current international trade and health debates in the United States. The volume of containers coming through West Coast ports has increased dramatically since the 1970s (and U.S. ports have increased their international trade), and imports continue to grow. Los Angeles ports are the gateway for 40 percent of U.S. imported products

today, and imports through these two ports are expected to double or triple by 2030. California suffers the air and noise pollution and damage to infrastructure, while the rest of country benefits from inexpensive goods. The environmental impacts, however, also travel with the goods. Ships (with unregulated air emissions) bring millions of imported containers into California ports, which adds to regional pollution. Each container then becomes a truck on the freeway or is placed onto a train. Train and truck traffic creates local problems in communities throughout the country because rail yards often are located in immediate proximity to homes and schools, increasing the risk of health effects. Traffic, noise, and diesel pollution increase, and the sense of community is decreased. In California, Ms. Hricko pointed out, the proposed solution to the current congestion is to expand the infrastructure to accommodate three times as much cargo and trucks by 2030. California elected officials, government staff, and leaders in the transportation industry argue that expanding freeway infrastructure will reduce congestion and improve air quality. California bond money for infrastructure projects include budgets for bridges, rail lines, freeways, and possibly adding truck-only lanes to the I-710 Freeway. The governor's current high-priority projects are a new BNSF rail yard and an expanded Union Pacific rail yard located about 5 miles from the ports in residential areas. Community, public health, and environmental groups argue that it would be better to have rail yards at the ports so that containers are moved directly from ships to trains (and on to the rest of the country), rather than to have rail yards in local communities, where residents and school children have to breathe the diesel exhaust emanating from them.

Discussion

A participant asked about economic power as the driving consideration in the school development and siting. Ms. Hricko responded that there is significant literature that disputes the claim of expected savings of consolidated schooling. One study showed that costs are reduced in larger schools if costs are measured per student year, but smaller schools are less expensive if cost per student who graduates is measured; the issue is complicated. Often public policy dictates spending the money on a stadium in a prime area versus building a school there. Segregation is another issue. How is building bigger schools for integration addressed with well-intentioned public policy? Smaller neighborhoods and schools tend to segregate. In the long term, however, economic desegregation needs to be included in public policy.

A participant asked about hot zones and the options for building schools elsewhere when a full 40 percent of available land in Los Angeles may be adjacent to major roads and freeways. Ms. Hricko replied that there are other studies that examine school construction and configurations and that look at siting parking lots close to freeways, with the playgrounds and athletic fields farther away (to reduce exposure to pollutants). Air filtration and air quality management are being tested as other considerations.

A participant commented on the complexity of planning. Ms. Hricko responded that when scientists, physicians, and others in the public health community inject themselves into policy-making, a difference can be made. It would be a great model for participants to return to their communities and resolve to go to a zoning or planning meeting and offer health-based information in the planning process, said the discussant. He asked session speakers to speak more about how these complexities could be incorporated into practice. Mr. Torma explained that more reports and research are needed to provide evidence for take-home messages at these planning meetings, but he believes that attending these meetings with questions and concerns can be more effective than trying to provide all the answers. Merely mentioning health issues increases considerations from everyone involved in the planning process; the public health community needs to raise the questions. Another participant suggested developing a fact sheet of obstacles from the health care professional standpoint and including possible solutions to those obstacles. Participants can bring these fact sheets with them to the zoning meetings as a more effective contribution.

A participant commented about the fear factor in parents, with regard to children walking to school. "Stranger danger" needs to be factored into the equation, whether it is substantiated by the statistics or

not. Researchers must be proactive in obtaining and translating these data in a public forum when discussing school sitings.

One participant asked about cost considerations with building new schools versus updating old ones. Adaptive reuse is a great method to manage this issue, especially for buildings that were built in the 1920s and 1930s and stand for civic pride. Some of these schools are being turned into lofts instead of being demolished, but, if possible, the participant suggested, they should be kept as schools. There is a great amount of literature showing the relative costs of renovating versus replacement. It often is not cheaper to build new, but to bring the existing schools up to standards, depending on the age and condition of the schools. Private schools may be more amenable to some of these arguments because they operate under a different set of constraints and drivers.

A participant asked how lifestyle choices are considered when parents have a host of arguments against walking to school, including time. Mr. Torma agreed that time is an issue, but people need opportunities to engage their children; parents could be encouraged to walk their children to school and engage them in discussions along the way. It is about prioritizing and interacting with children in a manner that does not occur when driving them or spending time with them at night. A participant suggested that the global warming issue is beginning to encourage thinking about these issues.

A participant asked about replacing diesel engines in school buses and if that will change the proximity issue. A session speaker responded that there are attempts in many cities to replace diesel buses with cleaner fuel, although it may take some time to replace all of the diesel buses. The EPA Clean School Bus USA Web Site can be found at <http://www.epa.gov/cleanschoolbus>.

THE NATIONAL CHILDREN'S STUDY: ADJUNCT STUDIES

Marion J. Balsam, NIH

The NCS is an interagency, interactive study led by NICHD in partnership with CDC, EPA, and NIEHS. It was authorized by the Children's Health Act of 2000 to study the effect of the environment on child health and development. Environments to be studied include chemical, physical, biological, and psychosocial. Gene-environment interaction is an important aspect of the study. The sample will include 100,000 children from across the United States from before conception through age 21. The goal is to determine which environmental effects on children are harmful, harmless, or helpful. Another goal is to find preventable causes of health-related conditions and provide evidence-based data to guide children's health care, as well as health-related policy. Participants will be drawn from 105 sites across the country, and 40 Study Centers will perform the research. The priority is to determine environmental exposures (physical, chemical, biological, psychosocial) and their effects on specific outcomes. Priority outcome areas include: pregnancy outcomes, neurodevelopment and behavior, injury, asthma, obesity, physical development, and specific illnesses and disorders. Results from the core study are expected to spawn further research with different research questions.

Adjunct studies will draw upon a subset of the parent study participants and/or their biospecimens or environmental samples. These will be modular-focused studies, utilizing NCS infrastructure and samples. Anyone with a good idea can initiate adjunct studies. Specifically, it is expected that many adjunct studies will be initiated by government scientists or study center scientists. Independent researchers, research advocates, and industry can initiate adjunct studies as well. The focus of these studies can be about any topic, but there will need to be some mutual benefit to their leveraging the NCS. The adjunct studies will rely on outside funding, not on the core NCS funding source. Reviewers evaluating proposals for adjunct studies will rate such factors as scientific value to the NCS, public health importance, and proper fit with the NCS. Also considered will be the burden on participants regarding time or discomfort, the burden on the study infrastructure and logistics, human subject issues for any ethical or legal considerations,

appropriate institutional review board (IRB) review, and proof of funding. A brief electronic preliminary application is required. After the preliminary application is approved, a full application will be available for submission. The review process is aimed at facilitating the timely review of proposals. The NCS currently is expected to start in July 2008, which is the onset of a 1-year, Vanguard Center pilot year. The full national study will begin with enrollment 1 year later. Adjunct studies can begin with the full study. Proposals regarding preconception, delivery, and early infancy could be submitted soon. Opportunities will continue to arise for additional research by leveraging the NCS, and adjunct studies will broaden and enhance the NCS contribution to children's environmental health. More information can be found on the NCS Web site at <http://www.nationalchildrensstudy.gov>.

Discussion

A participant asked whether funding is required prior to applying for adjunct studies. Dr. Balsam replied that funding is not required, but the application asks about funding plans. After preliminary approval for adjunct studies pending IRB decisions and so forth, the studies can obtain funding.

A participant asked whether there will be an opportunity to develop gene expression analysis and arrays from the NCS. Dr. Balsam responded that the core protocol is very broad and will include specimen samples and questionnaires. The NCS will be obtaining, storing, and analyzing the specimens, and the data will be made publicly available. The research plan is available on the Web site now, so if others are planning to do similar studies, they may not want to repeat efforts. The protocol draft is not very specific about what gene expression analyses are planned, so if participants have specific questions, they can be submitted by e-mail to ncs@mail.nih.gov.

A participant asked about the funding status of the NCS. Dr. Balsam answered that the NCS is funded for Fiscal Year (FY) 2007 and anticipates funding for FY 2008. NCS is funded yearly.

A participant asked about the process for obtaining existing data and whether it will be similar to NHANES. Dr. Balsam replied that the policy and procedures dealing with data access currently are being developed.

A participant asked whether any of the people involved with the data warehousing for NHANES also are involved with the NCS. Dr. Balsam replied yes, the CDC is involved with sampling, information management, and laboratory and repository aspects.

A participant asked whether local sites have to wait for national data or whether access is available at the local level prior to full data. Dr. Balsam responded that data distribution currently is being developed. The NCS anticipates, however, that first access will be to government, followed by study centers, adjunct studies, and then public use. When communities can have access is part of the process being developed now.

SESSION VI: CHILDREN'S PROTECTION IN THE AFTERMATH OF A NATURAL DISASTER: TOOLS FOR RECOVERY AND COMMUNICATING RISKS

Chair: Debra Cherry, University of Texas Health Center at Tyler

Dr. Cherry opened the session with a brief overview of the topic: tools for recovery and communicating risks after hurricanes. The objectives of this panel were to describe the collaborative PEHSU response to Hurricanes Katrina and Rita, provide experience and feedback from a Gulf Coast pediatrician at ground zero, and describe the NIEHS Hurricane Response Portal. Hurricane Katrina was one of the most devastating natural calamities to affect the United States. More than 354,000 Gulf Coast homes were

destroyed; more than 200 sewage treatment plants and 140 oil and gas platforms were damaged; and multiple health risks increased as a result of rampant mold growth, mountains of debris, widespread demolition and reconstruction projects, and through exposure to toxicants in temporary housing. The Tyler, Texas, PEHSU was the closest Center to ground zero and was called to help with communication issues. The project involved multidisciplinary collaboration, and cleanup required the expertise of scientists, engineers, volunteers, health care workers, and safety training professionals.

The potential hazards included returning to home sites too soon, sludge, structural damage, and lack of respiratory protection. Joint documents and recommendations for dealing with environmental issues and returning children to previously flooded areas were created and distributed to officials and parents. The Center also answered calls from parents through a toll-free line.

Tales from Ground Zero: Hurricane Katrina and Pediatric Environmental Health in Coastal Mississippi

Scott Needle, Formerly of Bay St. Louis Pediatrics

Dr. Needle joined the workshop by telephone to share his experiences with the aftermath of Hurricane Katrina, including the logistical issues, the health effects, and the communication issues that he encountered, particularly as they related to the formaldehyde problem in Federal Emergency Management (FEMA) trailers.

He was in private practice in Bay St. Louis, Mississippi, when the hurricane made landfall. Between 50 and 90 percent of the local housing was damaged or destroyed, including his office and other public health spaces. Although the medical community was prepared for some of the expected problems, they did not anticipate the mental health issues that occurred including short-term memory problems, confusion, and disorganization. Trauma was anticipated but not chronic stress.

The Sierra Club found significantly elevated levels of formaldehyde in one FEMA trailer, which led to the finding that 29 of 30 trailers had elevated levels. Formaldehyde is a known respiratory irritant and is classified as a carcinogen; it was found in the particle board in the trailers. The manufacturers voluntarily had taken it out years before, but the boards were still circulating. There are no government levels regulating formaldehyde in travel trailers and no standard for levels of safety for children. Dr. Needle noted that many families reported recurring respiratory problems in their children when they had been in good health before staying in the trailers. FEMA explained that a small number of cases were being monitored, and no major problems were anticipated. No government resources were available through the summer of 2006 to analyze formaldehyde, but the Sierra Club still was finding elevated levels. In February 2007, the media investigated the manufacturer of the trailers and discovered respiratory problems with the factory workers and particle board sheets that were still wet with formaldehyde. In May 2007, the *CBS Evening News* ran a story of results of the 2-month investigation, which prompted the Department of Homeland Security to contact Dr. Needle to determine how best to study the issue. The next month, the House Committee on Oversight and Government Reforms announced that they would hold hearings and invited Dr. Needle to testify. FEMA workers testified that they had voiced formaldehyde concerns about the trailers as early as March 2006. FEMA finally announced last month that they are now taking steps to move people out of these trailers. But what about the families still living in these trailers? The fundamental question remains unanswered: Is the formaldehyde the cause of the health problems, and if not, what is? Researchers must work hard to find out. Almost every agency failed to take ownership and responsibility for public health, and the CDC cannot just launch an investigation. The providers on the ground are the ones providing public health the first few months following a natural disaster. These providers rely on the experts for advice and need government agencies to listen to their concerns. Will we be able to handle future problems that weren't anticipated?

NIEHS Environmental Health Sciences Data Resource Portal
Marie Lynn Miranda, Duke University

Dr. Miranda presented satellite imagery of the New Orleans area from pre- and post-Hurricane Katrina perspectives. These images showed the scale of persistent flooding in an expansive area to help gauge the potential environmental health effects. The group was tasked with setting up work for the entire Gulf area, not just New Orleans. The key health consequences questions that arose involved mold, respiratory health, contaminant transfer, solid waste management, and mental health, and the NIEHS chose to develop the Hurricane Response Web Portal to build and maintain an extensive data file and archive. This archive allows many different environmental health questions to be examined and provides a collaborative work space and working tools that allow people from all over the country to work together on a long-term living resource. Data from the Web portal can be accessed directly from the NIEHS Web Site. The portal is user friendly and provides maps and imagery, query tools, measurement tools, data manipulation tools, potential contamination sources, water quality information, and sediment information. There is free and open access to these data. She demonstrated examples of how to make specific queries and how to download data by geographic and other variables and provided navigation instruction. A customizable research environment and custom reports are available.

Discussion

A participant recommended a book called *One Dead in Attic* by Chris Rose for a more information about how New Orleans has been coping since Hurricane Katrina.

KEYNOTE ADDRESS: THE NATIONAL FORUM ON CHILDREN AND NATURE

Speaker: Lawrence A. Selzer, The Conservation Fund

Introduction and Discussant: Howard Frumkin, CDC

Mr. Selzer explained that he wanted to challenge researchers to broaden their investigations to include the health effects resulting from communing with nature. There is a growing body of evidence pointing to the benefits of nature, but more data are needed to effect positive change with respect to children's health and the environment. As the nation becomes more urban and the demographics continue to change, reconnecting children to nature will be less about bringing them to nature and more about bringing nature to them. Nature must be brought to children in a manner that makes sense to them. This requires a more strategic vision of reconnecting children and nature; it is a mission that cuts across sector, status, and geography. This is the challenge, and leadership is needed to succeed.

One in five American children is considered obese, and one in three with diabetes has the type II form; 25 years ago, doctors did not even have a name for it. Children in the United States now gain three to five times more weight during the summer than they do during the school year. There are classes in urban schools where as many as one-third of the boys are on Ritalin or similar medicines. Pediatricians do not see as many broken bones anymore, and one of the most common ailments among children eight to 18 today is repetitive motion disorder. Fifty percent of Hispanic boys in this country drop out of school by the eighth grade. Some states now project their future prison needs based on third grade reading scores. If this trend continues, the first generation since World War II will exist that will have a shorter life span than its parents. Sensationalist media coverage and fearful parents have scared children right out of the woods while promoting a litigious culture of fear that favors safe, regimented sports over imaginative play outdoors. This anxiety can feed on itself, and those who watch more television have more sense of the potential dangers and less engagement with their community. The result is the perception that the outside has become more dangerous and thus the freedom to explore and improvise is reduced dramatically. The radius beyond which children are not allowed to roam has shrunk by 89 percent during

the past 20 years. During the past 30 years, children of the digital age have become increasingly alienated from the natural world with disturbing implications for their physical fitness, their long-term mental and spiritual health, and the environment. Young people who grow up without spending time in nature are much less likely to be strong champions for the environment when they reach voting age, thereby jeopardizing the land legacy that the nation has spent the last 200 years setting aside.

Mr. Selzer provided an overview and history of The Conservation Fund, which has protected more than 6 million acres of America's outdoor areas during the past 21 years. Leadership and new ideas, resources, partners, research, and data are needed urgently. Reconnecting children with nature is the passion of our time. The National Forum on Children and Nature is a new initiative, a collaborative effort launched in June. The 2-year effort is to identify and implement signature projects across America that serve to reconnect children and nature. Individually and collectively they will be a most powerful form of advocacy for change, for a new direction in the products that are made, the services that are delivered in communities that are built, and the education that is provided. They will help to elevate this issue to the highest levels of society so it becomes a national priority. Reconnecting children with nature cannot be legislated or regulated; it must be done by changing the culture of the country and to do that we need to better understand the connection between children, nature, and health.

Two examples are being pursued through the Forum. The first is in the area of technology. The world is technological, so children's attraction to technology must be used to get them outdoors. One idea of the National Forum is to work with a new organization called the Serious Games Initiative, which was created by an independent group of game developers who view video games as an opportunity for social good and achieving social purpose. A national competition to make state-of-the-art technology that has to be played outdoors is being launched. The next example deals with the built environment, especially how the environments are built where Americans will live tomorrow.

The modern America of obesity, inactivity, depression, and loss of community has occurred because of legislation, subsidy, and planning. A subgroup of the National Forum consisting of some of the most progressive developers in the country has been formed. This group is focusing on understanding children and nature design elements, identifying best practices, and alternately arriving at a national certification standard for child-friendly developments. This is the kind of energy that the National Forum is channeling. The real value of the projects is the opportunity they provide to investigate what happens as a result. This chance to gather primary data that will help to influence policy and practice across the country must not be lost. Forum collaborators are building a solid component as part of each of these national projects. They will conduct research on what happens as a result and make these data available.

Beyond the allure of technology, beyond the isolating design of new development, beyond the fear of stranger danger, there is another fundamental issue that requires our immediate attention: the increasing lack of places to be outdoors and the lack of leadership at the federal level to address this issue in a meaningful way. America loses more than 3 million acres a year in development and sprawl. The current administration has proposed twice to permanently terminate the Land and Water Conservation Fund, the most powerful land protection program in this country. There also is a crisis in creativity. It is known that protecting watersheds is one of the methods by which to assure clean, safe drinking water, so protecting the sources of drinking water protects public health. It is known that air pollution contributes to cardiovascular disease, respiratory disease, and allergies. Therefore, protecting air quality and land protects public health.

Protecting natural landscapes is a powerful form of preventive medicine, but only 5 percent of the money spent on health care in the United States is allocated to preventing disease and promoting health and a healthy lifestyle. Nature needs to be viewed as the first prescription. People do not want less environmental protection; they want smarter protection that balances economic and environmental

objectives. It is this dynamic that is driving the tremendous force and support of the environment at the state and local levels. More than 30 billion dollars in just the last 5 years in state and local bond money were allocated by taxpayers to protect open spaces across the country, including natural areas and neighborhood parks. Recent election results show that a wide variety of Americans care about these issues. No one among us wants to be a member of the last generation to pass on to its children the joy of playing in nature.

Discussion

A participant asked for clarification about bringing nature to the children versus taking them to nature. Mr. Selzer responded that redefining what nature means (redesigning alleys to replace lost park land) is part of this, but he cited a National Geographic Society program that brings children to national parks. Children expressed fear of the dark, of quiet, and of nature. It was too foreign for them to continue interest in it. Children must be moved along a continuum to help them identify what represents nature in their own neighborhoods in a manner in which they can connect and continue with sustained investment. This improves school performance and increases the number of students who continue to secondary education; many of them have a lifelong interest in the natural world.

A participant asked about the issue of people who view nature as having a big backyard. Mr. Selzer explained that people tend to show a preference for a house and big yard as a sign of success, comfort, and quality of life. It is a cultural issue, but it has an ecological impact. It represents a loss of land and loss of migration and native species. The human health impacts of those kinds of sprawling developments have just begun to be understood. The impacts of changing those patterns of development must be considered and documented through research. For example, only 30 percent of people who live on a golf course play golf, but they all paid a higher premium to purchase the lots because they like the open green space. Developers should build housing developments on open land and charge the higher premium but they will not because it is an unfamiliar idea. Change must occur slowly, the success stories must be highlighted, and the results documented to effect cultural change.

A participant commented about the disconnect that she has seen in some of the nature programs; most of them failed or the children could describe the environment but could not see themselves in it. She asked for a description of a better way to design these programs. Mr. Selzer explained that what it means to experience nature must be redefined. Researchers need to come together and promote one curriculum on environmental education, because there are too many competing factions. Obesity rates are rising, but participation in structured sports is the highest it has even been; therefore, there is something about unstructured time and play outdoors that matters. It has to do with engaging with nature first hand. Environmental education must include being outside in a less structured way.

A participant described a recently convened a group of state and environmental directors that dealt with the issue of how to collaborate on smart growth and asked what can be done in the early stages. Mr. Selzer replied that all that can be achieved with legislation has been achieved, and now the power of the marketplace is needed to drive things forward. The developers must be encouraged to change.

A participant suggested that participants should consider running for local office to make changes. If researchers sit on local planning agencies or the school board, environmentalists and the local health community will help fund the campaign. Mr. Selzer added that a recent study showed that children who emerge as leaders in the gray playgrounds (blacktops) are the most physically mature. The children who emerge as leaders in a green playground are the most creative. Green space is not needed in an urban setting because sometimes it is not available; some schools put it on their roofs. He described a school of the future in downtown Manhattan. Regarding running for office, the only thing protecting the land is the will of the public officials; 20 years from now if the elected officials do not have a stake in the land, it is

in jeopardy, which is why we need to engage children today because it takes a lifetime to build a commitment like that.

A participant expressed a sense of personal frustration and lack of creativity and mentioned children who are afraid to go outside because of drive-by shootings. Mr. Selzer agreed that one of the central issues is safety. He described an initiative called America's Promise, started by Colin Powell. It is an umbrella organization designed to improve the quality of the lives of the 30 million children who are most at risk in the United States. One of the central directions is based on the concept of school as the center of community. Many inner city schools are barren and lacking in programs. Maybe, school can be the place where education takes place, not just in the classroom, and where children spend a lot more time. This will take time, budget, policy, and creativity; and schools as the center of community is the direction in which this program is headed.

Dr. Frumkin stated that now is the time to submit proposals through the National Forum on Children and Nature. Information can be found at http://www.conservationfund.org/children_nature.

CLOSING REMARKS

William H. Sanders III, U.S. EPA

Mr. Sanders thanked the presenters and expressed his appreciation for their quality talks. He specially thanked Mr. Fields and Dr. Frumkin, whose comments complemented the theme today of thinking in broader terms. The community is at a point of opportunity to think more broadly about CEH to demonstrate and measure the results. He thanked participants for engaging the speakers in each of the sessions and thanked the planning committee and coordination teams for their efforts in bringing about this workshop. Because this workshop was enlightening and a great opportunity to connect and discuss ideas, another workshop may be planned in the future. He anticipates great response to this workshop.

Mr. Sanders adjourned the meeting at 12:30 p.m.