that adapt available approaches from epidemiology, toxicology, and risk assessment to estimate cumulative risk from chemical and nonchemical stressors. This workshop will bring together experts to discuss the latest science aimed at evaluating chemical and nonchemical stressors and incorporating them into cumulative risk assessments. Discussion will encompass a broad range of diseases (cardiovascular disease, neurodevelopmental delay), chemicals (air pollutants, metals), and stress types (maternal stress, chronic stress). Throughout the workshop, speakers will discuss promising approaches, knowledge gaps, and suggested future research. The concerted, multidisciplinary effort embodied in this workshop will help to shed light on the real impact of exposure to chemical and nonchemical stressors on health and disease in our most vulnerable communities. (This abstract does not reflect US EPA policy.)

W 798 Vulnerable Communities: At the Intersection of Chemical and Nonchemical Stressors

E. S. Craft. *Environmental Defense Fund, Austin, TX.*

Analyses of public health data has been used to demonstrate discrepancies in lifespan at a regional and even a zip code level. Questions have arisen regarding the contributing factors responsible for these disparities and often include a discussion of both chemical and nonchemical stressors. Communities comprised of minorities or low income residents have been highlighted as experiencing a disproportionate impact from one or more environmental hazard. Understanding and accounting for the risks from environmental exposures on these communities and identifying areas that represent an intersection of chemical and nonchemical stressors (e.g., port communities of recognized low socio-demographic status) is a difficult task because of the multiple facets of risk present and challenges in measuring and controlling for them. New efforts in evaluating the cumulative risks of chemical and non-chemical stressors are underway to account for and mitigate the disproportionate exposure risks posed to vulnerable communities. This presentation will focus on a few of these initiatives as part of the effort to secure vital environmental and health protections for communities that experience an increased burden as a result of environmental pollution, including efforts by some NGOs to address the science on nonchemical stressors in vulnerable areas, and the increasing use of health impact assessments in policy development within impacted areas. In addition, the presentation will highlight case studies where cumulative risk assessment approaches have been effective in mitigating health risks to vulnerable populations.

W 799 Alterations in CNS Effects of Lead and Methylmercury by Prenatal Stress and Early Behavioral Adversity

D. A. Cory-Slechta. *Environmental Medicine, University of Rochester Medical School, Rochester, NY.*

Important criteria for defining specific mixtures of chemical and non-chemical stressors of potential health significance include their potential co-occurrence coupled with shared biological substrates; the latter can extend beyond single molecular target/receptor sites to include actions on common physiological systems. These criteria exist for the neurotoxic metals lead (Pb) and methylmercury (MeHg), and for prenatal stress (PS), and early behavioral adversity, risk factors that all preferentially impact low socioeconomic status communities and which target the hypothalamic-pituitary-adrenal (HPA axis) and the brain mesocorticolimbic system. When examined in the context of PS, sex-dependent adverse neurotoxic effects of Pb and of MeHg are unmasked and/or enhanced. In rats, effects of maternal Pb exposure initiated 2 mos prior to breeding combined with PS (immobilization restraint on gestational days 16-17) unmasked marked increases in some striatal and frontal cortex catecholamine levels in males, but in serotoninergic functions of females. While combined PS and offspring stress challenge enhanced the behavioral toxicity of Pb in females, PS further enhanced the impaired glucocorticoid negative feedback produced by maternal Pb in males. Combined PS and MeHg (2 weeks prior to breeding through lactation) induced adverse effects not seen with MeHg alone, including enhanced deficits in short term memory in females, and alterations in monoamine levels in brain of both sexes. In mice, early behavioral adversity (forced swim test experience) significantly altered the trajectory of Pb ± PS-induced neurochemical changes as compared to early positive behavioral experience (food rewarded operant responding) measured in adulthood. Thus, non-chemical risk factors such as stress and behavioral experience, can modify the effects of environmental chemicals with which they share biological substrates. These findings underscore the critical need to evaluate effects of chemical exposures in the context of relevant non-chemical stressors in protecting public health.

W 800 Quantifying "Stress" in Epidemiological Studies

D. B. Miller. *CDC-NIOSH, Morgantown, WV.*

Using animal data in assessing the cumulative risk caused by exposures to chemical and non-chemical stressors requires extrapolation from animal to human. Incorporating epidemiological data in the evaluation obviates this need but requires methods able to quantify the levels of stress and their association with disease. Prolonged exposure to non-chemical stressors of both a psychological and physical nature (i.e., chronic stress) as well as to various pollutants can play an etiological role in disease including cardiovascular disease (CVD). Dr. Miller will discuss the measurement of stress and the most suitable metrics for quantifying stress in epidemiology studies while emphasizing the caveats and limitations in their use. Data from the Buffalo Cardio-Metabolic Occupational Police Stress (BCOPS) study provides information on the body systems (e.g., hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system (ANS)) involved in responding to stressors and their possible relationship to CVD. Police officers are a susceptible and marginalized population who, relative to the general population, suffer greater CVD morbidity and mortality that may be linked to inherent police work stressors. These include long work hours, shift work, trauma, high demand, and pollutant exposure. The longitudinal and multi-factorial design of the BCOPS study will allow us to determine whether stress measures/biomarkers are associated with the chronic progression of subclinical CVD, metabolic derangements and psychiatric disorders. In cross-sectional data a deranged HPA response, as measured by the salivary cortisol response to challenge, is associated with impaired brachial artery reactivity and metabolic syndrome – preclinical indicators of CVD. Self-evaluation of police stressors revealed gender specific associations with poor HPA response and low heart rate variability. Our findings suggest a complex association between these various endpoints that often differ by gender but are potentially interpretable and predictive using allostasis models of causation.

W 801 A Framework for Examining Social Stress and Susceptibility to Air Pollution in Respiratory Health

J. E. Clougherty. *Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA.* Sponsor: C. Rider.

There is growing interest in disentangling the health effects of spatially clustered social and physical environmental exposures and in exploring potential synergies among them, with particular attention directed to the combined effects of psychosocial stress and air pollution. Both exposures may be elevated in lower-income urban communities, and it has been hypothesized that stress, which can influence immune function and susceptibility, may potentiate the effects of air pollution in respiratory disease onset and exacerbation. In this presentation, I will review the existing epidemiologic and toxicologic evidence on synergistic effects of stress and pollution, and describe the physiologic effects of stress and key issues related to measuring and evaluating stress as it relates to physical environmental exposures and susceptibility. Finally, I will identify some of the major methodologic challenges ahead as we work toward disentangling the health effects of clustered social and physical exposures and accurately describing the interplay among these exposures. As this research proceeds, recommendations include careful attention to: the relative temporalities of stress and pollution exposures, non-linearities in their independent and combined effects, physiologic pathways not elucidated by epidemiologic methods, and the relative spatial distributions of social and physical exposures at multiple geographic scales.

W 802 Quantifying Chronic Stress Exposure for Cumulative Risk Assessment: Lessons Learned from a Case Study of Allostatic Load

A. M. Evans[1], G. Rice[2], L. Teuschler[3] and J. Wright[2]. *[1]ORISE/US EPA, Cincinnati, OH, [2]U.S. Environmental Protection Agency, Cincinnati, OH and [3]Linda Teuschler & Associates, St. Petersburg, FL.* Sponsor: C. Rider.

Although multiple methods of quantifying environmental chemical exposures have been validated for use in human health risk assessment, quantifying chronic stress exposure is more challenging. Stress is a consequence of perceiving an "exposure" (e.g., violence, poverty) as more than one can handle (i.e., "stressful"). Humans respond to stressful exposures via measurable physiological changes mediated by the hypothalamic-pituitary-adrenal axis. Chronic stress can result in physiological dysregulation of the stress response, which can be quantitatively estimated via allostatic load (AL). AL has been defined as the number of physiological measures across multiple systems, responding outside of the normal range. While chronic stress has been quantitatively estimated as AL, chronic stress is rarely considered in environmental human health risk assessment. In such assessments, the hazard index (HI) approach is used to estimate risk from multiple stressors. These stressors have

The Toxicologist

Supplement to *Toxicological Sciences*

54th Annual Meeting and ToxExpo™

March 22–26, 2015 • San Diego, California

The Official Journal of the Society of Toxicology

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 144, Issue 1
March 2015

www.toxsci.oxfordjournals.org

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org