

**S** 17 **Effects of Acrolein or Concentrated Ambient Particulate Matter Exposure on Plasma Lipids and Vascular Targets**

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Acute exposure to the inhaled carbonyl, acrolein, or to fine (concentrated) ambient particulate matter (CAP) leads to alterations in plasma lipids, oxidized lipids, circulating progenitor cells and vascular insulin resistance but how these divergent endpoints are related to each other is not clear. Because vascular dysfunction and vascular insulin resistance are two early events associated with metabolic syndrome and the progression to diabetes (and in order to interrogate mechanistic relationships between disparate endpoints), we studied whether changes induced in lipids and the vasculature were shared across different pollutant exposures (gas or CAP) and to similar degrees dependent on exposure level to reveal potential common mechanisms of action.

**S** 18 **Vehicle Emissions-Exposure Results in Increased Cerebrovascular Lipid Peroxidation Associated with Altered Blood Brain Barrier Permeability**

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Traffic-generated air pollution-exposure has recently been associated with adverse effects in the central nervous system (CNS) including neuroinflammation and neurodegeneration. While alterations in the blood brain barrier (BBB) have been implicated as a potential mechanism of air pollution-induced CNS pathologies, there is currently little known about the pathways involved. Lipid peroxidation and oxidative stress are known to regulate air pollution-mediated effects in the systemic vasculature resulting in progression of vascular disease states; therefore, we investigated their role in altered signaling, transport, and permeability in the cerebral vasculature after inhalation exposure to vehicle emissions. We observed significant increases in lipid peroxidation in the cerebral vasculature of mice, resulting from exposure to vehicle emissions, which was associated with increased BBB permeability. Additionally, we measured increased matrix metalloproteinase-9 activity and decreased tight junction expression in the cerebral vessels from exposed animals. Further studies using plasma from exposed vs. control mice in an *in vitro* BBB co-culture model suggest that a circulating "reactive factor" may mediate the observed alterations in BBB permeability and transport. Collectively, these data suggest that lipid peroxidation may mediate alterations in signaling and structural proteins responsible for maintaining BBB integrity.

**S** 19 **Air Pollution, Lipid Peroxidation, and Alterations in HDL Functionality**

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Exposure to ambient particulate matter (PM) lead to enhanced atherosclerosis in experimental animal models. Particle size and composition play a role in the extent how atherosclerosis is promoted. We have reported that inhalation of concentrated fine and ultrafine ambient particles led to alteration of plasma HDL anti-inflammatory capacity in ApoE null mice that correlated with their ability to enhance atherosclerotic lesion formation. In addition, we have also shown that exposures to diesel exhausts result in alteration of HDL anti-oxidant capacity. This presentation will focus on our studies that have evaluated whether HDL functional changes, induced by air pollutants, are related to effects on lipid peroxidation in the lungs, circulating blood and systemic tissues.

**S** 20 **Carbon Nanotubes Are Toxic in Experimental Models: What's Next, Who's Being Exposed, and Should We Be Concerned?**

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Engineered nanomaterials have vast potential with applications in medicine, electronics, and composites. Carbon nanotubes (CNT) represent one such material with broad applications, but this material also has the propensity for significant toxicity. Toxicities include pulmonary and systemic inflammation, fibrosis, immunosuppression, and cardiovascular dysfunction, and evidence is growing that CNT may have properties that influence carcinogenicity. Over the past decade there has been a significant investment in research to examine the *in vivo* and *in vitro* toxicity of CNT. Conversely, very little is known about the exposure level and chemical and physical properties of airborne CNT that humans are exposed to, especially in the workplace. These deficiencies make the interpretation of the vast number of

experimental studies to human relevance difficult. Initial findings from epidemiological studies of workers handling engineered nanomaterials, recent advancements in detailed facility exposure assessment, pertinent *in vivo* toxicology studies with dosimetry-based human health implications, regulatory aspects, and risk assessment based on results from animal inhalation studies will be included. The outcome of this session is to provide the most recent human exposure assessment and epidemiological findings and to gather perspective on *in vivo* toxicology studies involving risk estimates and potential carcinogenicity. This data should have direct influence on the course of newly designed studies and add perspective on previous studies of CNT-induced toxicity.

**S** 21 **Epidemiological Study of Workers Handling Carbon Nanotube and Engineered Nanomaterials**

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The aim of this study was to investigate the health hazards of workers handling nanomaterials. Study population was 206 nanomaterial-handling workers and 108 unexposed workers recruited from 14 manufacturing factories in Taiwan and were followed up for no less than 2 times. For each participant, a self-administered questionnaire was used to collect personal habits, work history, potential confounding exposure, and detailed information of work conditions and nanomaterials handled after informed consent. Since there was still a lack of personal sampling methodology and summary index for heterogeneous exposure, we adopted the control banding nanotool risk level matrix proposed by Dr. Paik to categorize the risk level for each participant as a surrogate of exposure. There were 108 workers in risk level 1, 91 workers in risk level 2, and 7 in risk level 3. The markers of health outcomes include pulmonary and cardiovascular disease markers, inflammation markers, oxidative stress markers, antioxidant enzymes activity, and genotoxicity markers in blood, urine and exhaled breath condensate (EBC). Generalized Estimating Equation (GEE) model was applied to analyze no less than 2 repeated measurements in 4-year follow-up. Increase and a risk level gradient of antioxidant enzymes, superoxide dismutase (SOD), were found in nanomaterials and carbon nanotube handling workers with compare to controls. But cardiovascular dysfunction, lung inflammation and lung function, oxidative stress, and genotoxic markers were not associated with nanomaterials handling in this four-year follow-up study. Pilot environmental study indicates that the exposure level of nanoparticles in the workplace was low. Nanomaterials handling in current negligible emission scenario may not have health impact on the workers, except for increase of antioxidant enzyme.

**S** 22 **Carbon Nanotube Exposure Assessment: An Evaluation of Workplace Exposures in the US**

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Just as there has been much advancement in the field of toxicology over the past decade relative to health outcomes from carbon nanotube (CNT) exposures, similar strides are being made in the field of exposure assessment. Recent developments in sampling methodologies have led to more accurate estimates for worker exposure levels as compared to preliminary studies, which may have overestimated exposures. As part of an ongoing NIOSH exposure assessment and epidemiologic study, worker exposure to CNT has been examined by sampling 14 different worksites across the US over a three year period. Personal breathing zone exposure levels were measured using a chemical specific marker for the mass concentration of elemental carbon (EC) at both the inhalable and respirable size fractions. The sampling methodologies are in accordance with the NIOSH Current Intelligence Bulletin on CNTs and carbon nanofibers which set a mass based Recommended Exposure Limit at 1 µg/m<sup>3</sup> of EC at the respirable size fraction. Overall, personal workplace exposures at the respirable size fraction to EC ranged from 0.02 – 1.47 µg/m<sup>3</sup> with an 8 hr time weighted geometric mean of 0.16 µg/m<sup>3</sup>. Inhalable personal breathing zone exposures ranged from 0.003 – 22.40 µg/m<sup>3</sup> with a geometric mean of 0.38 µg/m<sup>3</sup>. Concurrent personal breathing zone samples were also collected and analyzed by electron microscopy using methods similar to the asbestos counting convention. CNT structure agglomerate sizes averaged > 4 µm while few single CNT fibers were found. This study also focused on how exposure level and type change within the various industries in which CNTs are being applied (composites, electronics, production), between types of materials (multi-walled vs. single-walled), and under varying work conditions. The detailed information from these exposure assessment findings bring awareness to industries with higher

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