

PS 1159 **PM_{2.5} from a Marcellus Shale Drilling Operation Induces Cardiovascular Toxicity**

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Unconventional natural gas well development (UNGD) of the Marcellus Shale geological formation has continued to be a burgeoning energy driver in the US. Thus, rural communities and regions are experiencing increased industrial activities and air pollutant exposures. Our laboratory has identified increased concentrations of particulate matter (PM) in the fine (<2.5 µm, PM_{2.5}) and ultrafine (<0.1 µm, PM_{0.1}) size ranges near UNGD areas. Furthermore, negative consequences of gas well emissions on health outcomes have been reported in the epidemiological literature. We collected high-volume PM_{2.5} samples onto PTFE filters over 1 week during fracture stimulation at a Marcellus Shale gas well site. Additional samples were taken upwind, and downwind from the well pad during the same time-frame. The samples were liberated from the filters into ultrapure water and dried via lyophilization. Previous *in vitro* data has shown significant cytotoxicity based on distance downwind from the well pad. Young Sprague Dawley rats were exposed to 100 or 300 µg/rat PM_{2.5} from the drill site via intratracheal instillation. PM_{2.5} significantly increased heart rate (HR, Sham 317±8 BPM vs. PM_{2.5} 342±8 BPM). However, separately 100 or 300 µg/rat did not significantly alter HR. *In vivo*, arteriolar responses to metabolic vasodilation, endogenous neurotransmitter vasoconstriction, and endothelial vasodilators were negative. In isolated mesenteric arterioles, there was significant enhancement of phenylephrine-induced vasoconstriction 1 nM (% Max Constriction Sham 2.5±1.0%, PM_{2.5} 8.8±2.6%). Taken together, these data suggest that exposure can significantly increase heart rate, and induce arteriolar vasoconstriction, though the mechanisms are unknown. *Funding: NIEHS R15ES028005.*

PS 1160 **Temporal Differences in Oxidative Potential and Chemical Composition of PM_{2.5}**

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Exposure to fine particulate matter (PM_{2.5}) has well-established systemic human health effects. Oxidative stress is a hypothesized mechanism for the health effects associated with PM_{2.5} exposures. Oxidative potential (OP) is the measure of a substance's capacity to oxidize a target molecule. The OP of PM_{2.5} has recently been suggested as a measure that is more indicative of human health effects than the routinely measured PM_{2.5} concentration. The purpose of this experiment is to analyze the OP of PM_{2.5} collected on air filters and determine if there differences in the OP of PM_{2.5} collected from the same location on different days. PM_{2.5} was collected onto PTFE-coated filters from a monitor placed in a public park in Eugene, OR on different days in the Winter. PM_{2.5} will be extracted from each filter via sonication in methanol. An aliquot of the extraction solution will be used to measure OP using the dithiothreitol (DTT) assay. An additional aliquot will undergo analysis via inductively coupled plasma - mass spectrometry (ICP-MS) to quantify elements (n=30). Correlations between OP, PM_{2.5} mass, and chemical composition will be made. Initial testing of a subset of the filters shows significant differences in elements based on the day that PM_{2.5} was collected, including: Cd, Ce, and Pb (p<0.05, one-way ANOVA). The DTT assay has been optimized and calibration curves for the assay are reproducible with no significant difference observed between replicates and with an r² value consistently above 0.99. PM_{2.5} from the park location collected on different days has shown up to a 2-fold difference in OP for a subset of samples (range of 8.3 to 4.2 nM DTT consumed/µg PM_{2.5} for three filters). We anticipate to see differences in OP for PM_{2.5} collected on different days due to the chemical composition, particularly if redox active elements are in higher concentrations. Correlations will help us identify components of PM_{2.5} that may be impacting the OP more so than the total mass. This research will add to the growing evidence and justification for investigating the OP of PM_{2.5}.

PS 1161 **Effect of a High-Fat Diet and Occupational Exposure in Different Rat Strains on Lung and Systemic Responses: Development of an Animal Model to Examine the Exposome**

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The exposome is the measure of all exposures of an individual in a lifetime and how those exposures relate to health. Important components of the exposome include lifestyle (diet), environmental and occupational exposures, and individual genetic predisposition. Mapping of the exposome could improve the understanding of disease and aid in prevention strategies and pos-

sible cures of many diseases. The goal was to develop an experimental model of the exposome by collecting biological samples during critical life stages of an exposed animal that are applicable to worker populations. Genetic contributions were assessed using strains of male rats with different genetic backgrounds [Fischer-344 (F344), Sprague-Dawley (SD), Brown-Norway (BN)] maintained on a regular (REG) or high fat (HF) diet for 24 wk. At wk 7 during diet maintenance, groups of rats from each strain were exposed to welding fume (WF; 20 mg/m³ x 3 hr/d x 4 d/wk x 5 wk) or filtered air until wk 12, at which time some animals were euthanized. A separate set of rats from each strain were allowed to recover from WF exposure until the end of the 24 wk period. Bronchoalveolar lavage fluid and serum were collected at 7, 12, and 24 wk to assess general health indices. Exposure to WF during maintenance on a HF diet caused specific adverse health outcomes directly after exposure as well as after a 12-wk recovery phase. Depending on the animal strain, there was evidence that WF exposure and HF diet together worsened lung toxicity and kidney function as well as altered different serum enzymes and proteins. The exposomal factors of diet, exposure, and strain were all important, depending on the health outcome measured. Exposure had the most significant influence on the pulmonary responses, whereas strain and diet were the most significant contributors regarding parameters related to extrapulmonary responses. Principal component analysis further confirmed the influence of strain on the responses measured, indicating the importance of genetic predisposition as an exposomal factor. In summary, this study showed that an animal model can be useful in the assessment of the exposome as external lifetime exposures can be easily controlled and adverse health outcomes measured.

PS 1162 **Differential Responses of Murine Alveolar Macrophages to Elongated Mineral Particles of Asbestiform versus Non-Asbestiform Varieties**

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Occupational exposures to asbestiform elongated mineral particles (EMP) may lead to diffuse fibrosis, lung cancer, malignant mesothelioma and autoimmune diseases. Cleavage fragments (CF) are chemically identical to asbestiform varieties of mineral, but there is no consensus on whether to treat them as asbestos from the toxicological and regulatory standpoint. Alveolar macrophages (AM) are the first-responders to inhaled particulates, participating in clearance and activating the other resident and recruited immunocompetent cells, which has an impact on the long-term outcomes. In the current study we are addressing the question of how differences in EMP crystal growth habit (asbestiform vs. non-asbestiform) affect AM responses. MPI cells, a non-transformed line that closely mimics AM phenotype, were treated with mass-, surface area- (s.a.), and particle number- (p.n.) equivalent doses of respirable asbestiform and non-asbestiform riebeckite/tremolite EMP (median lengths 4.5-5.5 µm) for 24 h with or without LPS (5 ng/ml). We assessed viability and apoptotic response, lactate dehydrogenase (LDH) and cytokines in cell supernatants. Riebeckite/tremolite asbestos and CF were taken up and induced similar LDH leakage and decrease in viability at the s.a. equivalent doses. At the equal mass, asbestiform EMPs were clearly more cytotoxic. When treated with equal p.n., CF had more pronounced cytotoxic effects. Apoptosis induction was more pronounced in asbestos-treated cells, compared to CF in all comparisons (mass/s.a./p.n.). There was an increase in chemokines and elevated pro-inflammatory cytokine secretion compared to control. Principal component analysis of the cytokine/chemokine secretion showed close clustering for the s.a. and p.n. equivalent treatments. LPS stimulation shifted the cytokine profiles towards inflammation compared to non-LPS-stimulated cells, with more IL-1β and TNF-alpha secretion in asbestos-treated cells compared to CF. In conclusion, murine AM initial responses to respirable EMP of similar lengths, but different growth habit depend on the s.a. metric rather than the mass or the p.n. The study also confirms that asbestiform habit itself is an important determinant of some signaling pathways, i.e. apoptosis. Finding out what metric is critical for the mineral fiber toxicity is a complex task and the *in vivo* study with the same EMP is underway to further address the issue.

PS 1163 **Multimodal Mass Spectrometry Analysis following Repeated Intratracheal Instillation of Dispersed Silver Nanoparticles in Rats**

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Silver nanoparticles are among the most widely manufactured nanomaterials and have been incorporated into a wide variety of consumer products such as textiles, detergents, medical devices, drug delivery products, anti-microbial



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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and Scientific Sessions of the 59th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 15–19, 2020.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 542.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 580.

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