tency comparisons with other fiber types. *In vitro* dissolution provides a rapid way to compare fiber durability and persistence in the respiratory tract. (This abstract does not represent US EPA policy.)

PS 1567 Effect of Metal Composition and the Use of Adhesive and Anti-Spatter Chemicals on Lung Responses in Rats after Inhalation during Spot Welding

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Spot welding (SW) is common in the automotive industry. Adhesives are used as sealers to the seams of metals that are joined. Anti-spatter compounds are sprayed onto metals to be welded to improve the weld surface finish. SW produces complex aerosols composed of metal and volatile compounds (VOCs) which have caused lung disease in workers. The goal was to evaluate the effect that different components of SW fumes may have on lung responses in an animal model. Sprague-Dawley rats were exposed by inhalation to 25 mg/m^3 of aerosol for 4 h/d x 8 d during SW of mild steel or galvanized Zn-coated steel in the presence or absence of an adhesive or anti-spatter spray. Controls were exposed to air. Particle size distribution and chemical composition of the generated aerosol were determined. Particle size distribution was tri-modal with a MMAD of 0.25 μm. The metal fraction of the mild steel fume was >99% Fe, whereas the Zn-coated steel was 90% Fe, 7% Zn, and 2% Mn. VOCs (e.g., siloxanes, benzene, toluene) were present when an adhesive was used. After exposure, bronchoalveolar lavage (BAL) was performed to assess lung toxicity. Lung resistance (R_L) was evaluated before and after challenge with inhaled methacholine (MCh). Lung toxicity and BAL neutrophils were significantly elevated compared to controls 1 d after exposure to the fumes from Zn-coated steel but not mild steel, indicating the development of acute lung inflammation. All markers of lung toxicity for the Zn-coated group returned to control values by 7 d. Immediately after exposure, baseline R_L was significantly elevated in the group exposed when VOC levels were high. Basal R_L returned to control level by 1 d. Reactivity to MCh was not affected at any time point after SW fume exposure. The use of an anti-spray compound had no effect on lung toxicity or function. Inhalation of SW fumes caused acute lung toxicity due to the presence of specific metals (e.g., Zn) as well as increase R_L due to the use of adhesives.

PS 1568 Comparison of Inhaled Dose vs. Postexposure Time Period in Silica-Induced Pulmonary Toxicity in the Rats

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Occupational exposure to respirable crystalline silica results in silicosis, cancer, autoimmune diseases, tuberculosis, and renal diseases. Currently, we have investigated and compared the effect of dose vs. post-exposure time period in the pulmonary toxicity induced by inhalation exposure of rats to crystalline silica. Rats were exposed by inhalation to respirable crystalline silica (Min-U-Sil 5 Silica, U.S. Silica, Berkeley Springs, WV) at a concentration of 15 mg/m3, 6 hours per day, 5 days/week for one week or 12 consecutive weeks. The rats exposed to silica for 1 week were maintained under standard animal housing conditions for 44 weeks following termination of their exposure to silica and euthanized. The rats exposed to silica for 12 weeks were euthanized soon after termination of the silica exposure. The total amount of silica inhaled by the 12-week exposure group of rats was roughly 12-times more than that of the 44-week post-exposure group. Silica-induced pulmonary toxicity was determined in both groups of rats on the basis of bronchoalveolar lavage fluid (BALF) parameters of toxicity [lactate dehydrogenase (LDH) activity, albumin content, total number of alveolar macrophages (AMs) and polymorphonuclear leukocytes (PMNs), and inflammatory cytokine levels], lung histology, and global gene expression changes in the lungs. Induction of significant pulmonary toxicity was identified in both groups of rats based on the various pulmonary toxicity parameters analyzed. However, the magnitude of changes in the majority of the pulmonary toxicity parameters determined was significantly higher in the rats belonging to the 44-week post silica exposure time period group compared to the 12-week silica exposure group. These results collectively suggested that the post silica exposure time period is more critical to silica-induced pulmonary toxicity than the inhaled dose of crystalline silica in the rats.

PS 1569 A Single Exposure to Photochemical Smog Causes Airway Irritation and Cardiac Dysrhythmia in Mice

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Smog, which is a complex mixture of particulate matter and gaseous irritants (ozone, sulfur dioxide, reactive aldehydes), as well as components which react with sunlight to form secondary pollutants, has recently been linked to increased risk of adverse cardiopulmonary responses. We hypothesized that a single exposure to photochemical smog would cause cardiac electrical and ventilatory changes in mice. Female C57BL/6 mice were surgically implanted with radiotelemeters for the measurement of heart rate (HR), electrocardiogram (ECG) and heart rate variability (HRV). Following recovery mice were exposed whole-body to either smog or filtered air (FA) for 4hrs. A photochemical reaction chamber was used to generate smog from a precursor mixture of hydrocarbons and nitric oxides which achieved concentrations of 337 μg/m3 secondary organic aerosol, 0.072 ppm O3, and 0.131 ppm NO2. Ventilatory function was assessed before, and one and 24hrs after exposure in a plethysmograph while HR and ECG were measured continuously. Mice exposed to smog experienced a significant increase in HR during exposure when compared to FA; however, there were no differences or changes in ECG or HRV. Exposure to smog caused a significant increase in breathing frequency and decreased inspiratory time (i.e. rapid shallow breathing) and a significant decrease in HR 1hr post-exposure; these effects were gone 24hrs later. Mice exposed to smog also had cardiac dysrhythmia as well as non-conducted p-waves, which were not present in the FA group. The results of this study show that a single exposure to smog causes acute cardiac and ventilatory effects, which reverse over time. Although these responses likely do not represent serious or permanent underlying deficits, they clearly indicate the potential toxicity of complex multipollutant mixtures, particularly for those with cardiopulmonary disease. (This abstract does not reflect USEPA policy)

PS 1570 The Role of Oxidized Low-Density Lipoprotein Receptors in Matrix Metalloproteinase Activity and Tight Junction Protein Expression in the Cerebral Microvasculature of Mice Exposed to Traffic-Generated Air Pollutants

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Epidemiologic studies report a positive correlation between environmental air pollution exposure and deleterious effects on the central nervous system, including neuroinflammation and onset/exacerbation of stroke. While the mechanisms involved have not been fully elucidated, one pathway may be through disruption of the blood brain barrier (BBB). We have reported that oxidized LDL (oxLDL) and its receptor, the lectin-like oxLDL receptor (LOX-1), are significantly elevated in the systemic vasculature of Apolipoprotein KO (ApoE-/-) mice exposed to mixed exhaust (ME). ME-exposure also increased BBB permeability, associated with matrix metalloproteinase (MMP)-9 activity and decreased tight junction (TJ) protein expression. To determine whether ME pollutants mediate disruption of the BBB through an oxLDL-LOX-1 pathway, 10 wk old male ApoE-/- mice on a high fat diet received either mouse IgG (control) or the neutralizing antibodies to LOX-1 (LOX-1 Ab) at 16 μg protein/ml, 0.1 ml/ i.p. every other day. Mice were randomly assigned to inhalational exposure of either filtered-air (FA: n=12 LOX-1 Ab, n=12 IgG) or 30 μg PM/m3 diesel exhaust + 70 μg PM/m3 gasoline exhaust (ME, n=12 LOX-1 Ab, n=12 IgG) for 6 hr/d for 7 d. Treatment with the LOX-1 Ab led to a significant decrease of LOX-1 expression in the cerebral microvasculature. Exposure to ME resulted in a significant increase in MMP-9 and -2 expression and activity, which was attenuated by LOX-1 Ab treatment. Histological analysis showed that ME-exposure resulted in decreased expression of BBB TJ proteins occludin and claudin-5, which were normalized with LOX-1 Ab treatment. Such findings indicate that inhalation exposure to traffic-generated air pollutants results in BBB disruption associated with MMP activity and decreased TJ protein expression, which are mediated (at least in part) through the LOX-1 receptor. Funded by NIEHS R00ES016586 (AKL).

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