Mn, and Ni. Particle size distribution analysis indicated the mass median aerodynamic diameter to be 0.24 μm. Lactate dehydrogenase and albumin were significantly elevated ($p<0.05$) in the SS group at both doses compared to air controls. Interestingly, less than 10% of the cells recovered from the lungs of the SS group were PMNs. Lung bacteria clearance and macrophage production of reactive oxidants were significantly reduced ($p<0.05$) in the SS group. In summary, acute exposure of rats to SS welding fume caused significant lung damage, suppressed lung defense responses to bacterial infection, but had little effect on pulmonary inflammation. Additional chronic inhalation studies are needed to further examine the lung effects associated with SS welding fume exposure.

1058 SOLUBLE CHROMIUM IN WELDING FUME INCREASES SUSCEPTIBILITY TO PULMONARY BACTERIAL INFECTION IN RATS

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Frequency, duration, and severity of pulmonary infections have been shown to be increased in full-time welders. Animal studies have shown that manual metal arc, stainless steel welding fume (MMA-SS) increased susceptibility to lung infections. MMA-SS is primarily composed of iron (Fe), chromium (Cr), and nickel (Ni). The objective of this study was to determine which component of MMA-SS may alter lung defense. At day 0, male Sprague-Dawley rats were intratracheally instilled with MMA-SS at a concentration of 2 mg per rat or saline (vehicle control), or the metal constituents Fe_2O_3 (insoluble, 0.82 mg), NiO (insoluble, 0.06 mg), $Cr_2Na_2O_7$ (soluble, 0.60 mg) at the concentration at which they are present in the dose of MMA-SS. Another group of rats received a mixture of the three metals. At day 3, rats were intratracheally inoculated with 5×10^3 *Listeria monocytogenes*. At days 6, 8 and 10, left lungs were homogenized, cultured overnight, and colony-forming units counted to assess pulmonary bacterial clearance. At day 3 (prior to infection) and at days 6, 8 and 10, right lungs were lavaged to recover cells and fluid from the airspace. Cell differentials were performed and the production of reactive oxygen species by phagocytes was measured. Lactate dehydrogenase and albumin levels were measured in lavage fluid as indicators of lung damage. Exposure to MMA-SS, the soluble Cr, or the mixture of metals before infection significantly slowed the pulmonary clearance of the bacteria and increased lung tissue damage when compared to control, and animals treated with NiO or Fe_2O_3 did not differ from control. Animals pre-treated with soluble Cr or the mixture of all three metals had increased cell numbers of macrophages, neutrophils, and eosinophils, and oxidant production by phagocytes was increased at all time points when compared with the saline group. The results of this study indicate that the soluble Cr present in MMA-SS is likely to be the primary component responsible for the suppression of lung defense in rats.

1059 COMPARATIVE INFLAMMATORY LUNG RESPONSE IN A/J AND C57BL/6J MICE EXPOSED TO STAINLESS STEEL WELDING FUME

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Several epidemiology studies suggest that inhalation of welding fume (WF) increases lung cancer risk in welders. Stainless steel WF in particular contains both chromium and nickel, two known human carcinogens. However, controlled animal studies are undoubtedly needed to conclusively link WF exposure to increased lung cancer risk. Thus, we initiated a multipart study to compare the inflammatory and tumorigenic responses to WF in a lung tumor susceptible (A/J) and resistant (C57BL/6J) mouse strain. Mice were exposed by pharyngeal aspiration to a total of four doses, one every three days, of 5mg/kg manual metal arc-stainless steel WF (MMA-SS), 1.5 mg/kg soluble chromium (S-Cr), or saline vehicle. Bronchoalveolar lavage (BAL) was performed postmortem at one and four weeks after the final dose. Indices of lung cytotoxicity (lactate dehydrogenase release) and air-blood barrier damage (albumin) were measured in the acellular BAL fluid. The cellular BAL fraction was used to assess inflammation via polymorphonuclear leukocyte (PMN) infiltration. One week post-exposure, MMA-SS WF caused a slightly greater lung cytotoxicity compared to S-Cr, which was more pronounced in A/J versus the C57BL/6J mice. MMA-SS WF, but not S-Cr, caused greater air-blood barrier damage in A/J versus C57BL/6J mice. PMN infiltration was significantly elevated compared to control in both mouse strains one-week post-exposure to MMA-SS WF. S-Cr elicited a significant PMN response in A/J mice only at one week post-exposure. By four weeks post-exposure to MMA-SS WF or S-Cr, lung injury in both mouse strains returned to control. PMN infiltration decreased, but remained elevated in both strains exposed to MMA-SS WF, with the A/J mice showing greater inflammation. In conclusion, exposure to MMA-SS WF or S-Cr elicited greater lung injury and inflammation at one versus four weeks in both mouse strains. The A/J strain showed increased susceptibility to lung injury and inflammation compared to the C57BL/6J mice following exposure to MMA-SS WF or S-Cr.

1060 EXAMINING THE INFLAMMATORY RESPONSES OF HAPS: THE ROLE OF OZONE AND OTHER PHOTOCHEMICAL TRANSFORMATION PRODUCTS

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The chemistry and health effects of individual hazardous air pollutants (HAPS) have been studied for many years. Once released into the atmosphere, HAPS interact with hydroxyl radicals and ozone (created by photochemical processes), to produce many different products, whose toxic potential is currently unclear. In this study, three common HAPS (methanol, isoprene(ISO) and 1,3-butadiene(BD)) underwent photochemical transformations using real sunlight, generating a range of photochemical transformation products, including organic carbonyls such as formaldehyde and ozone. The objective of this study is to determine the role of ozone in the effects caused by the photochemically active HAPS mixtures. Using the UNC outdoor smog chambers interfaced with an in vitro exposure system, A549 cells were exposed to dynamic atmospheric mixtures. Exposure to the photochemically generated products of BD or ISO significantly increased cytotoxicity and cytokine gene expression compared to their injected primary photochemical transformation products, such as acrolein, formaldehyde and ozone for BD and methacrolein, methyl vinyl ketone, and ozone for ISO. Interestingly, exposure to the equivalent levels of ozone generated during the photochemical transformation of BD or ISO did not induce the same level of inflammatory cytokine release, suggesting that ozone alone is not the sole inducer of inflammatory responses in this system. However, for the photochemical transformation of methanol, generating primarily ozone and formaldehyde, ozone was the main inducer for both inflammation and cytotoxicity. Taken together these results indicate, that unlike simplistic atmospheric models such as methanol, ozone does not significantly account for the effects seen in more complex atmospheric mixtures, such as those generated by BD and ISO, and therefore full photochemical transformations and interactions must be carefully evaluated when investigating adverse health effects induced by exposure to HAPS.

1061 A GENETIC BASIS FOR INCREASED SENSITIVITY OF THE NEONATAL MOUSE LUNG TO OZONE

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Formed by the action of sunlight on nitrogen oxides and reactive hydrocarbons, ozone (O^3) is a powerful oxidant and respiratory irritant that leads to airway inflammation and pulmonary dysfunction. Studies have not established whether children are susceptible to ozone, even though animal studies have shown that neonates are more sensitive than adult rodents. Although it is postulated that children's potential for heightened susceptibility results from an underdeveloped respiratory system coupled with higher outdoor activity, the biological mechanisms underlying the predisposition of children to pollution-induced adverse pulmonary effects are unknown. Using a murine model, we tested the hypothesis that there is a genetic basis for the differential response of neonatal and adult lungs to inhaled pollutants. In this study, we exposed male and female adult and neonatal mice (15 to 16 d old) to 0.8ppm O^3 for 5 h from 8 inbred mouse strains. To insure that differences were due to biological responses, and not dose, mice from sensitive and resistant strains were exposed to ozone generated with ^{18}O and the lung burden of ^{18}O was determined. Inflammation and pulmonary injury were evaluated in lung lavage fluid recovered 24-hours post-exposure. Clear inter-strain differences in response to ozone, independent of dose, were seen in neonatal mice: SJL/J, C3H/HeJ, and Balb/cJ mice being the most sensitive while A/J, AKR/J, and 129x1/SvJ mice were the most resistant. Also, the neonatal response was greater than that observed in O^3-exposed adult mice, particularly in the SJL/J and C3H/HeJ strains. These results strongly suggest that genetic determinants do play an important role in the enhanced sensitivity of the young mammalian lung to ambient air pollutants. Further research will enable us to determine which genetic factors contribute to the heightened susceptibility of the juvenile lung to ozone, and to quantify the relative contribution of genes vs. the environment in the adverse effects of inhaled ozone.

1062 DISEASE-SPECIFIC SUSCEPTIBILITY TO ACUTE OZONE-INDUCED INJURY AND INFLAMMATION IN EIGHT RAT STRAINS

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Susceptibility to environmental pollutant-induced injuries may be influenced by presence of disease and genetic make-up. To identify disease-specific susceptibility phenotype, we used eight rat strains with or without genetic cardiovascular disease.

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 45th Annual Meeting of the Society of Toxicology, held at the San Diego Convention Center, San Diego, March 5–9, 2006.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 500.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 534.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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