the airways. We used a mouse model to elucidate inflammatory effects of nano-sized titanium dioxide (TiO2) particles in the lungs of BALB/c mice that were exposed to intranasally administered fine (particle size ca. 1μm) or nano-sized (diam. x length ca. 10nm x 40nm) TiO2 at three different concentrations (1, 100, and 1000 μg/ml) twice a week for three weeks. Inflammatory cell infiltration was defined in the bronchoalveolar lavage (BAL) fluid. Expression of cytokines and chemokines relevant to inflammation in the lung tissue was assessed by using real-time PCR. Bronchial responsiveness to methacholine was determined by whole body plethysmography. An increase in the expression of chemokine MIP-2, a potent chemotactic factor for neutrophil recruitment, in the lung tissue of mice exposed to high concentrations (1000μg/ml) of nano-sized TiO2 particles, when compared with mice exposed to the same concentration of coarser particles, was detected. In addition, increased infiltration of macrophages and neutrophils in the BAL was seen after the installation of high concentrations of TiO2. The increase was lightly higher in mice exposed to nano- sized than to coarser particles. These data suggest that nano-sized particles of titanium dioxide may be more potent than larger particles in evoking inflammatory responses in the lungs of mice.
Supported by The Finnish Work Environment Fund, project no 105097.

1109 A TWENTY-EIGHT DAYS INHALATION TOXICITY STUDY OF SILVER NANOPARTICLES IN SPRAGUE DAWLEY RATS.

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Silver nanoparticles (SNP), second most widely used nanomaterials, have been used in health, electronic, and home products. Although previous studies on silver dust, fume and silver compounds suggested some insights on their toxicity, the toxicity of SNPs, in which size and surface area are recognized as important determinants for toxicity, is little known about. Especially inhalation toxicity of SNPs is foremost information to protect workers and consumers'health, despite difficulties in inhaltion study of NPs. Accordingly, we have designed a device to generate SNPS by evaporation/condensation, using a small ceramic heater. The generator was able to distribute desired concentrations of SNP to chambers containing experimental animals. The concentrations and distribution of the NP with respect to size can be measured directly by a differential mobility analyzer and an ultra condensation particle counter. SNPs were tested for 28 days for inhalation toxicity. Eight-week-old rats weighing about 283 g for male and 192 g for female were placed in to four groups (10 rats in each group); fresh air control, low (1.73×10^4), middle (1.27×10^5), and high-dose (1.32×10^6 particles/cm^3, 61 μg/m^3). The animals were exposed to SNPs 6 hours each day, 5 days per week, for a total 4 weeks. The male and female rats did not show any significant changes in body weight depending on the concentration of SNPs during the 28-day of the experiment. There were no significant changes in hematology and blood biochemical values either both in male or female rats. Our initial results indicated that SNPs at a concentration near to current ACGIH silver dust (100 μg /m^3) may not have significant health effect.

1110 PULMONARY AND CARDIOVASCULAR TOXICITY OF MULTIWALL CARBON NANOTUBES IN MICE.

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Manufactured nanoparticles possess unique properties and may have a potential to cause toxicity. In the present study, pulmonary and cardiovascular toxicity of multi-wall carbon nanotubes (CNT) was studied in apoE-deficient mice maintained on standard mouse diet. CNT (>95% purity, diameter 20-30nm and length ~50 micron) were suspended in sterile PBS and introduced into mice lungs @ 40μg/mouse, once/wk for 16 consecutive weeks by pharyngeal aspiration. Age-matched mice receiving sterile PBS served as controls. Twenty four hour urine samples were collected from animals after the 1st and 15th CNT treatment to assess oxidative stress. Animals were sacrificed on day-1 and day-7 after the last CNT treatment. Markers of pulmonary toxicity and inflammation were measured in bronchoalveolar lavage (BAL) by standard techniques. The formation of atherosclerotic lesions in the aorta was evaluated by *en face* lesion planimetry. The results showed significant increases in total BAL cells and polymorphonuclear neutrophils in CNT-treated mice on day-1 and day-7 post treatment. Analyses of cell-free BAL fluids showed significant increases in total proteins, LDH and mucin levels in CNT-treated mice given multiple treatments suggesting toxic and inflammatory responses. The lung tissue levels of CuZn-SOD and Mn-SOD proteins did not differ significantly in the control and CNT-treated groups. However, a significant increase in the urinary levels of 8-OHdG in mice within a day after the first CNT treatment indicated development of oxidative stress. Yet, multiple weekly exposures to CNT for 16 wks failed to influence the plasma cholesterol and the area of atherosclerotic lesions covering aortic intima of apoE-deficient mice. The results suggest that multiple exposures to CNT evoke a toxic and inflammatory response in the pulmonary system but are unable to promote atherosclerosis for up to 16 weeks in a susceptible mouse model of human atherosclerosis.

1111 INFLAMMATION AND FATE OF QUANTUM DOTS FOLLOWING PULMONARY TREATMENT OF RATS.

J. R. Roberts, R. R. Mercer, S. Young, D. W. Porter, V. Castranova and J. M. Antonini. *HELD/PPRB, NIOSH, Morgantown, WV.*

Inhalation of nanoparticles may affect the respiratory, cardiovascular, and central nervous systems. The mechanism by which nanoparticles translocate from the airspaces into the bloodstream is unknown. The goal was to investigate the fate and inflammatory effects of fluorescent quantum dots (30-50 nm; coated with carboxyl terminal groups) after pulmonary exposure. To monitor phagocytosis of quantum dots by non-primed and primed alveolar macrophages (AM) *in vitro*, AM were collected by bronchoalveolar lavage (BAL) from untreated rats or rats that had been treated by pulmonary inoculation with *L. monocytogenes*. AM were incubated for 2 hr with 0 (control), 2.5, or 25 μg/ml of quantum dots and mounted for laser scanning confocal microscopy (LSCM) or analyzed by flow cytometry to quantify phagocytosis. For *in vivo* studies, male Sprague-Dawley rats were intratracheally instilled with saline or quantum dots on day 0 at a dose of 12.5 μg/rat. At 2 hr post-instillation, and on days 1, 3, and 5, the left lungs were cryopreserved and sectioned for LSCM. BAL was performed on right lungs, and indicators of lung damage were measured. Collected lavage cells were differentiated to assess inflammation. Recovered AM also were mounted onto slides and analyzed by LSCM to assess uptake of the quantum dots *in vivo*. A concentration-dependent increase in the phagocytosis of the quantum dots by AM *in vitro* was observed. A greater number of quantum dots were phagocytized by the primed AM. At 2 hr post-instillation, quantum dots were located in the AM and airspaces, as well as on the epithelial surfaces, in the alveolar region. By 24 hr, most of the quantum dots had been phagocytized by AM, and localized areas of quantum particles were observed in interstitial areas of lung parenchyma. Lung injury and inflammation were found to be elevated in the BAL of animals treated with quantum dots on 1, 3 and 5 days post-exposure compared to saline controls. Due to their high intensity fluorescent signal, quantum dots appear to be appropriate for studying the pulmonary deposition and fate of nanoparticles.

1112 PULMONARY INFLAMMATORY AND SYSTEMIC IMMUNE RESPONSES TO INHALED OIL NANOCONDENSATES.

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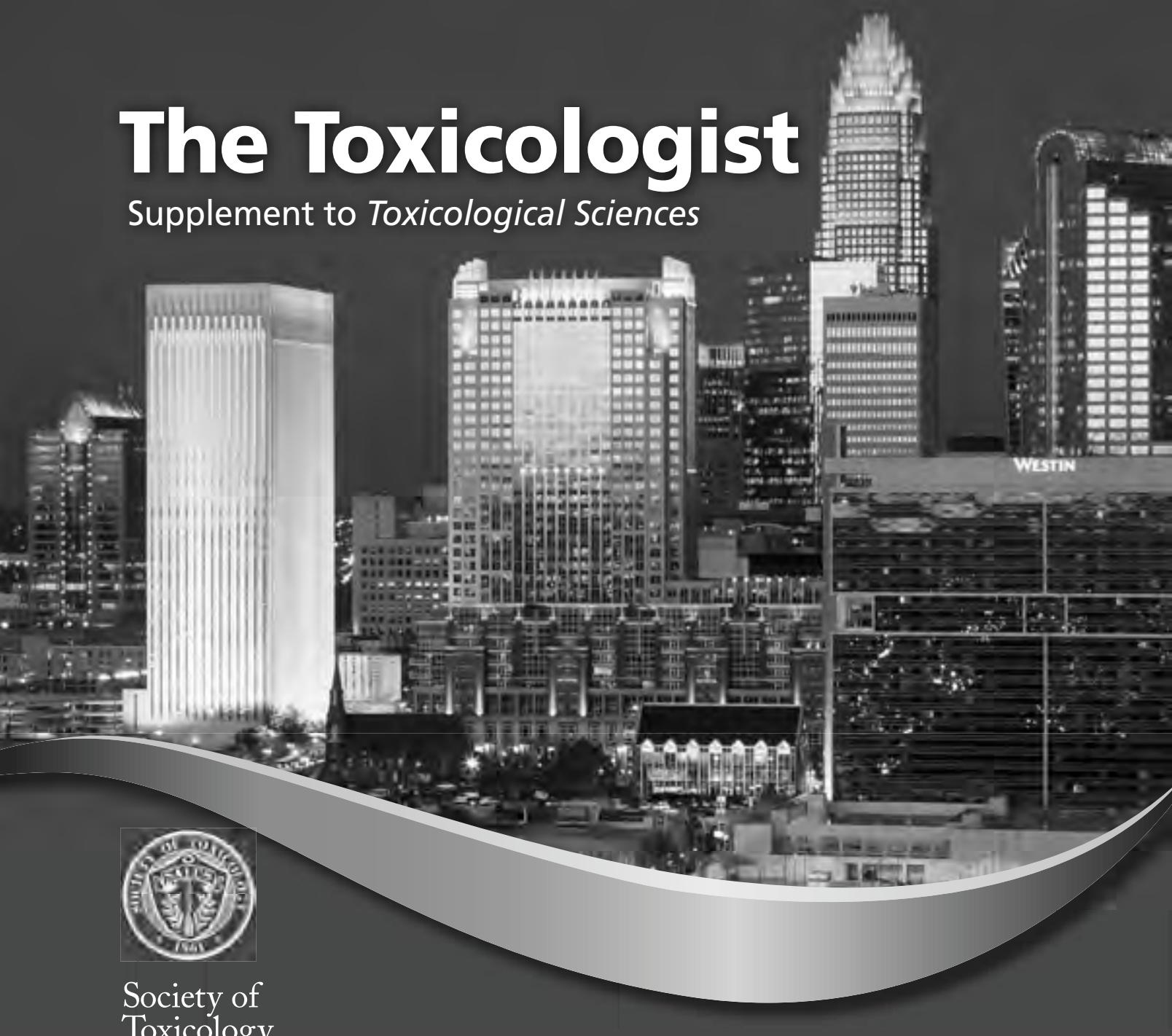
This study was conducted to follow up on our previous finding of a statistical association between chemical components of oil and pulmonary toxicity of collected automobile and diesel exhaust that was extracted and instilled into rat lungs. Organic condensates derived from unburned or partially burned oil and fuel account for the majority of the particle emissions, especially nanoparticle emissions, from motor vehicles. Despite significant interest in the toxicity of nanoparticles in the environment, this class of materials has not been well studied. We report results from a recent study that characterized the pulmonary inflammation and systemic immune effects of inhaled organic condensates of used engine oil. Used 15w/40 (Shell, Rotella T) motor oil was obtained after 200 hours of operation in a 2000 Model Cummins 5.9L diesel engine operated on a slightly modified (no motoring) FTP engine cycle. Organic aerosol condensates of oil were generated by evaporation and condensation. C57Bl/6 mice (n=7) were exposed to oil droplets of approximately 20 nm in size in a nose-only inhalation exposure system. An equal number of mice were exposed to clean air as controls. Mice were exposed for 7 consecutive days, 6 hr/day at a particle mass concentration of 300 μg/m3 and number count of ~1 x 106 particles/cm3. On day 7, the mice were sacrificed. Lungs were lavaged for determination of total and differential inflammatory cell populations and indicators of toxicity. Lung tissue pathology was assessed by light microscopy of hematoxylin/eosin stained sections. Biochemical indicators of inflammation and oxidant stress were analyzed in lung tissue. Immunotoxicity was analyzed by splenic B and T cell proliferation in response to mitogens. We observed modest to no response in most of the pulmonary indicators of toxicity and oxidant stress. However, we did observe significant changes in B and T cell proliferation. Supported by DOE FreedomCar and Vehicle Technology Program.

The Toxicologist

Supplement to *Toxicological Sciences*



Society of Toxicology

46th Annual Meeting and ToxExpo™

Charlotte, North Carolina

An Official Journal of the Society of Toxicology

www.toxsci.oxfordjournals.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 96, Number 1, March 2007

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 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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

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