PS 1976 Health Surveillance Study on MWCNT Manufacturing Workers

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Although many in vivo and in vitro toxicology studies on multi-walled carbon nanotubes (MWCNTs) indicate that exposure to MWCNTs may induce potential human health effect, actual health effect of MWCNTs among exposed workers have not been known. The levels of exposure and internal doses of MWCNT are becoming more and more important for estimating the health effects resulting from exposure to MWCNTs, yet information on biomonitoring and exposure is very difficult to obtain from MWCNT manufacturing workers. We have conducted a health surveillance study in a workplace which manufactures MWCNTs, including the assessment of personal and area exposure levels to MWCNTs, a walk-through evaluation of the manufacturing process, and the collection of blood and exhaled breath condensates from the exposed workers. Additionally, a lung function test was conducted to the MWCNT manufacturing workers and office workers. The workers were exposed to 112-229 μg/m^3 total suspended particulates 6.2-9.3 μg/m^3 elemental carbon near the range recommend exposure level suggested by NIOSH. The workers exhibited normal range of hematology and blood biochemistry values and normal range of lung function parameters. On analysis of EBC, malondialdehyde (MDA), 4-hydroxy-2-hexenal, and n-Hexanal levels in the exposed workers showed a significant increase when comparing with the office workers. The MDA level was significantly correlated with blood molybdenum (Mo) concentration, suggesting usefulness of MDA in EBC and Mo as biomarkers of MWCNT exposure.

PS 1977 The Effects of Pharyngeal Aspiration-Exposure to Zinc Oxide Nanoparticles on Pulmonary Fibrosis Induced by Bleomycin in Mice

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The present study investigated underlying mechanism of pulmonary fibrosis caused by exposure to ZnO nanoparticles, in a mouse model of pulmonary fibrosis induced by bleomycin (BLM). The mouse model was completed by constant subcutaneous infusion of 100 mg/kg bleomycin sulphate using osmotic mini-pumps. Female C57BL/6Jcl mice were divided into BLM and non-BLM groups. In each group, two doses (10, 30 μg/mouse) of ZnO nanoparticles with primary diameter of 20 nm were delivered into the lungs through pharyngeal aspiration. Bronchoalveolar lavage fluid (BALF) and the lungs were collected 10 days after administration under deep anesthesia. Exposure to ZnO nanoparticles dose-dependently increased the lungs weight. Histopathologically, slight and severe thickness was observed within interalveolar septum in low and high dose groups, respectively, which was accompanied by dose-dependent increase in total cells, macrophages, lymphocytes and neutrophils in BALF. The increase in total protein in BALF at high dose indicated increased permeability of air-blood barrier. IL-1 beta and MCP-1 in BALF were significantly higher in all BLM groups as opposed to the low levels in non-BLM groups, indicating lasting inflammation after exposure in BLM groups. Moreover, in BLM groups, ZnO nanoparticles led to dose-dependent increase in IL-1 beta and MCP-1, suggesting higher susceptibility to ZnO nanoparticles in this mouse model. This study suggested severer inflammation was caused by ZnO nanoparticles in the BLM mouse model of pulmonary fibrosis at the early stage.

PS 1978 Effects of Nanoparticle Pre-Exposure Dispersion Status on Bioactivity in the Mouse Lung

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From a toxicology perspective, nanoparticles possess two features that promote their toxicity. The first involves physical-chemical characteristics, including particle surface area. The second is the ability of the nanoparticle to traverse cell membranes. These two characteristics are influenced by placing nanoparticles in liquid medium prior to animal exposure. Nanoparticles tend to agglomerate in suspension, making it difficult to accurately deliver them for in vivo or in vitro experiments. Thus, we hypothesize that the nanoparticle dispersion status will correlate with the in vivo bioactivity/toxicity of the particle. The proposed questions of this study are of great importance to the nanotechnology/toxicology community, namely the highly debated question of whether nanoparticle dispersion status (pre-exposure) is of importance. To test our hypothesis, nano-sized nickel oxide was suspended in four different dispersion media (PBS, dispersion medium (DM), Survanta, or Pluronics). At each respective dose, well-dispersed and poorly dispersed (suspensions were sonicated utilizing a Branson Sonifer 450, 25W continuous output, 20 min or 5 min, respectively) suspensions were created. Mice (male, C57BL/6J, 7 weeks old) were given 0-80 μg/mouse of nano-sized nickel oxide in the different states of dispersion via pharyngeal aspiration. At 1 & 7 days post-exposure, mice underwent whole lung lavage (WLL) to assess pulmonary inflammation and injury as a function of dispersion status, dose, and time. Results show that pre-exposure dispersion status correlates with particle bioactivity. In fact, the particle/media combination that produced the smallest hydrodynamic particle size (nano-NiO2 suspended in DM & sonicated for 20 min. = 7.5 nm) produced a greater increase in PMNs, LDH activity, as well as albumin levels in WLL fluid than the other nano-nickel/suspension media combinations. These results indicate that a greater degree of pre-exposure dispersion increases particle bioactivity/toxicity in the lung. This work was supported by NIH grant F32 ES021341.

PS 1979 Effects of Multiwalled Carbon Nanotube Solubility on Inflammation and Lung Function

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Multi-walled carbon nanotubes (MWCNTs) have high ξ potential, are relatively insoluble in aqueous solvents, and interact with hydrophobic materials. These properties are altered by functionalization. Due to complexity of MWCNTs it is important to study organ level effects. To study effects of MWCNTs on the lung we use a suspension method involving native surfactant. This method is effective at keeping MWCNTs in suspension despite functionalization. We hypothesized that increasing solubility of MWCNTs in the aqueous environment would shift the organ level response to inflammation from interaction with the lung lining fluid. C57Bl6J mice were intratracheally instilled with MWCNTs (30-50nm OD, 0.5-2μm length) at 1.5μg/g body weight. 2 types of MWCNT were examined—functionalized by carboxylation or acid-purified. 1 day post instillation, the functionalized MWCNT treated mice showed neutrophilia (147.1 ± 105.67 v 2.5 ± 0.92 x10^3) and increased cell count (196.5 ± 113.02 v 57.0 ± 8.25 x10^3) vs control. Purified MWCNT mice did not display significant inflammation (18.5 ± 15.62 v 2.5 ± 0.92 x10^3 neutrophils; 63.0 ± 15.09 v 57.0 ± 8.25 x10^3 total cells). Lung function was not affected by functionalized MWCNTs but purified MWCNTs increased lung stiffness, consistent with surfactant disruption. 3 days post instillation, neutrophilia resolved in functionalized MWCNT treated mice, but protein concentration increased vs control (0.2 ± 0.03 v 0.1 ± 0.02 μg/μl total protein). Purified MWCNT mice do not show increased tissue stiffness. Both MWCNT treated groups demonstrated significant decrease in collectin content. These data are consistent with functionalization "revealing" the MWCNTs to inflammatory system and reducing effect on lung function. Supported by NIH Grants 5U19ES019536-02 & 5T32ES007148

PS 1980 Pre-Exposure to Nontoxic Levels of Magnetite Nanoparticles Sensitizes Mice to Pulmonary Infection by *Streptococcus pneumoniae*

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Two major forms of iron oxide are preferred for medical applications due to their perceived biocompatibility. Pretreatment of cultured macrophages with non-cytotoxic doses of superparamagnetic iron oxide (SPIO) reprogramed ~500 genes in response to subsequent challenge by endotoxin, suppressing activation of both pro- and anti-inflammatory pathways and diminished bacterial phagocytosis (Kodali et al. 2013). Herein we characterize and confirm the potential impaired clearance of bacteria by mice pretreated with SPIO. We administered 0 or 1.0 μg SPIO/gbw to C57BL/6 by oropharyngeal aspiration (OPA) and evaluated the pro-inflammatory response by measuring cytokines in BALF collected 1-28 d post-dosing. No statistical changes in cytokine levels were observed at 1-28 d post-dosing confirming that

The Toxicologist

Supplement to *Toxicological Sciences*

53rd Annual Meeting and ToxExpo™

March 23–27, 2014 • Phoenix, Arizona

An Official Journal of the Society of Toxicology

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OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 138, Issue 1
March 2014

www.toxsci.oxfordjournals.org