67 DEPOSITION AND DISPOSITION OF LARGE, HUMAN-RESPIRABLE PARTICLES IN THE LUNGS OF RATS.

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The predictions of a recently developed multiple-path computer model for lobar deposition of inhaled particles (S. Anjilvel and B. Asgharian, Fundam. Appl. Toxicol. 28, 41-50,1995) were evaluated in the rat for particles with an aerodynamic diameter larger than 2 μm. Two groups of 6 Long-Evans rats were exposed by endotracheal inhalation once for 30 min to an aerosol mixture of 3-, 6-, and 9-μm polystyrene latex beads. Approximately 24 hr after the exposure, the lungs were harvested, and each lobe was dissolved with strong base (TEAH) overnight. Particle counts were made using a hemacytometer viewed through a standard light microscope. The endotracheal inhalation exposure system was capable of delivering particles 3, 6, and 9 μm in diameter into the lungs of rats. The lobar distribution pattern of the 3-μm particles was fairly consistent among animals. The distribution of 3-μm particles in the alveolar region of the left lobe appeared to be underestimated by the dosimetry model with marginal significance. The model significantly overestimated the alveolar deposition of 3-μm particles in the right diaphragmatic and intercostal lobes. The 6-μm bead deposition pattern was very similar to the 3-μm bead deposition pattern. There were not enough 9-μm diameter particles present to compare among samples.

68 COMPARISON OF PULMONARY RESPONSE TO INHALED AND INTRATRACHEALLY INSTILLED DIESEL EXHAUST PARTICULATE.

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Diesel exhaust particulate (DEP) is a complex mixture of polyaromatic hydrocarbons, ash, transition metals, and carbon core. Exposure levels of DEP up to 2 mg/m3 has been documented in underground mines, railroad, construction, and auto repair industries. Such exposures have been associated with pulmonary inflammation, fibrosis, lung cancer, increased rate of respiratory infections, and enhanced allergic sensitization. The purpose of this study was to compare the effect of the inhaled (4hr exposure, 17mg/m3) and intratracheally instilled (IT) DEP (5mg/kg b. wt.) and carbon black (CB, 34 mg/m3) particulate on pulmonary inflammation, pulmonary associated lymph node cells (LNC) and alveolar macrophages (AM) in a Brown Norway rat model. Carbon black was used as a surrogate of the non-extractable carbon core of DEP. Cellular Cysteine (CYS) and glutathione (GSH) levels were analyzed by conjugation to monobromobimane and subsequent HPLC-fluorescent analysis. Alveolar macrophage IL-1 and TNF- production were also assessed three days post exposure. Both, DEP and CB were generated by nebulizing suspended particles through a diffusion dryer into a nose-only chamber. Greater than 90% of the particles generated were in the submicron range. The microscopic evaluation of the DEP and CB particulate revealed similarities in shape and size between them. Inhaled DEP caused a significant increase in the levels of glutathione and cysteine in the LNC, but not AM. LNC thiols were unchanged following IT DEP, but AM GSH was elevated. A significant decrease of AM TNF- of DEP exposed rats after ex vivo endotoxin challenge was also observed in both IT and inhalation groups. Instillation of DEP caused pulmonary inflammation as noted by the increases in neutrophils count, and lavage protein and LDH levels. Inhaled DEP did not produce measurable pulmonary inflammation. The cause of the differences observed between acute inhalation vs IT DEP in pulmonary inflammation and thiol content is not known, but may be due to dose deposited in the lung.

69 CHRONIC INHALATION OF ROOM-AGED CIGARETTE SIDE-STREAM SMOKE (RASS) AND DIESEL ENGINE EXHAUST (DEE) IN RATS - EFFECTS ON LEUKOCYTE SUBPOPULATIONS IN BLOOD AND BRONCHOALVEOLAR LAVAGE FLUID (BALF).

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The immuno-modulating effects of RASS, an experimental surrogate for environmental tobacco smoke (ETS), and DEE were investigated in a 24-month inhalation study in rats. The particulate matter concentrations chosen (3 and 10 μg/l) exceed the upper limit of typical ETS and DEE exposure concentrations for humans by approximately 100-fold. Leukocyte and lymphocyte subpopulations in blood and BALF were analyzed by microscopic and flow cytometric analysis. The following changes were observed in DEE-exposed, but not in RASS-exposed rats: In blood, there was a small increase in the (absolute and relative) number of neutrophils and a corresponding decrease in the percentage of lymphocytes, but no changes in blood lymphocyte subpopulations. In BALF, there was an increase in relative and absolute numbers of neutrophils from 1% or 1E5 cells in sham controls to up to 60% or 8E7 cells in the high DEE group. Corresponding lymphocyte numbers were 1.5% or 2E5 in sham controls, 8% or 3E6 in the low DEE group, and 5% or 6E6 in the high DEE group. These changes indicate a massive pulmonary inflammation. Within the BALF lymphocyte population, the T suppressor/cytotoxic cells were slightly increased. These results show that leukocyte subsets are more sensitive than lymphocyte subsets to chronic DEE inhalation. The major effects are restricted to the lungs as the port of entry and do not have relevant systemic consequences. RASS, which has an organic composition relatively similar to DEE, did not produce any immuno-modulating effects at the same particulate matter concentration. The immuno-modulating effects seen in DEE-exposed rats are considered as to be associated with the pulmonary accumulation of elemental carbon particles which was not seen in RASS-exposed rats. (Sponsored by Philip Morris USA.)

70 AHR AND PM10.

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Ah receptor mediated activity associated with PM10 extracts from the Paso del Norte airshed.The Paso del Norte airshed, which includes El Paso, TX, Ciudad Juarez, Mexico, and Las Cruces, NM, has historically high levels of PM10. The extensive use of wood and scrap material for fuel, an aged vehicular fleet, and rapid urban development associated with maquiladoras and NAFTA, have contributed to this problem, which is compounded by winter inversion layers. As a first step in an effort to identify biomarkers that reflect contaminants in this airshed, PM10 filters were collected from six monitoring sites located in El Paso and Ciudad Juarez. Filters from Jan. 1999 were extracted with dichloromethane for 24 hours in a Soxhlet apparatus and extracts were concentrated with a Kuderna-Danish per EPA method 3540C. To assess the biological effects of Ah receptor ligands associated with PM10, H4IIE rat hepatoma cells were exposed in 6-well plates to extracts containing the equivalent of 1 and 4 weeks of respirable air (air equivalents) for 24 hours and ethoxyresorufin-O-deethylase (EROD) activity was measured in the post-mitochondrial supernatant. Control activity was 1.55 pmol-1min-1mg prot; 1 μM b-naphthoflavone (BNF), the positive control, caused a 6½ fold increase. Variability in EROD activity was greatest in cells exposed to 1-week air equivalents from a brickmaking district, where as great as a 4 fold difference in enzyme activity (2.76-11.65 pmol -1min-1mg prot.) was observed on different dates. These differences are likely to be associated with varying patterns of activity in this cottage industry. Greater than 1-week air equivalents from this site inhibited enzyme activity by 50%. At sites primarily associated with car and truck traffic, EROD activity remained fairly constant (2.4-4.8 pmol-1min-1mg prot.) regardless of date. Filters from all winter months, are presently being analyzed for EROD activity and Ah receptor ligands with a luciferase reporter system.

71 DEPOSITION OF MONODISPERSE AEROSOLS IN YOUNG BEAGLE DOGS.

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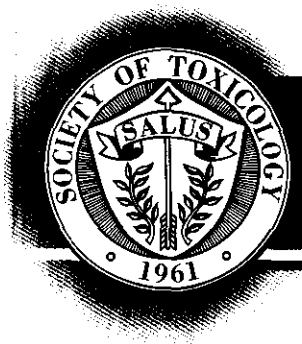
The effects of inhaled particles are determined by chemical composition and sites of deposition. The shape, density and size of the particles determine not only sites of deposition in the respiratory tract but also the fraction of inhaled particles that are deposited. Deposition of monodisperse aerosols (1 to 9 microns Mass Median Aerodynamic Diameter (MMAD)) was measured in young unsedated 4 and 7 month old Beagle dogs using mouth-breathing and nose-breathing models. Iron oxide aerosols, with ^{99m} Technetium tracer, were produced using a spinning top aerosol generator (STAG). Particle size was controlled by varying the concentration of the iron oxide suspension and the speed of the STAG rotor. Satellite particles were removed by adjusting the exhaust flow. Animals were acclimated to the mouth-breathing and nose-breathing masks prior to aerosol exposures and were exposed to aerosols of approximately 1, 3, 5, 7 or 9 microns MMAD for up to ten minutes. Deposition was determined using gamma camera scintigraphy. Scintography images were taken immediately after exposure. Areas of interest in the images were delineated and data reported for both total and regional deposition as a function of particle size. For the 7 month old Beagle dogs lung deposition was



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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, roundtable, and poster sessions of the 39th Annual Meeting of the Society of Toxicology, held at the Pennsylvania Convention Center, Philadelphia, Pennsylvania, March 19-23, 2000.

An alphabetical Author Index, cross referencing the corresponding abstract number (2), begins on page 423.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 448.

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