trophils/cytokines and bronchus-associated lymphoid tissue compared to that in infected air-exposed control rats. Moreover, exposure of infected rats to PM increased the extent of pneumonia-associated lung lesions, as well as the incidence of septicemia in rats for up to 18 hr following PM exposure. Taken together, these findings suggest that exposure of rats with fulminating *S. pneumoniae* infections to concentrations at or somewhat greater than the promulgated 24 hr NAAQS of 65 μg PM2.5/m3 can exacerbate the disease process and compromise host ability to adequately "handle" an ongoing pneumococcal infection. These changes, in turn, could possibly contribute to the increased incidence of pneumonia-related deaths observed in PM-exposed elderly populations. (Supported by HEI #94-03A.)

1221 RESIDUAL OIL FLY ASH (ROFA)-INDUCED PULMONARY INFLAMMATION AND MUCOUS CELL METAPLASIA IN RATS CORRELATES WITH LEACHABLE VANADIUM CONTENT.

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Increases in particulate air pollution are linked with increased hospital admissions and emergency room visits for cardiopulmonary diseases. Intratracheal instillation of residual oil fly ash (ROFA), an emission source particulate, induces pulmonary inflammation, cytokine/chemokine expression, and airway epithelial injury. F344 rats were intratracheally instilled with 0, 50 or 200 μ g of ROFA containing high (ROFA6) or low (ROFA2) amounts of leachable Vanadium to examine the effect of this transition metal in ROFA-induced inflammation and mucous cell metaplasia. Rats were sacrificed 3 d and 7 d after instillation. Right lung lobes were lavaged and recovered fluids analyzed for inflammatory cells, LDH activity, and total protein content. RNA from right lung lobes was analyzed for MIP-2 and MCP-1 mRNA levels. The left lung was processed for light microscopy and morphometric quantitation of intraepithelial mucosubstances in pulmonary airways. Both ROFA2 and ROFA6 induced dose-dependent increases in recovered neutrophils and lymphocytes that were greatest 7 d after instillation. All ROFA6-instilled rats had significantly more neutrophils than ROFA2-instilled rats. Only ROFA6 induced an increase in LDH activity and total protein levels in lavaged fluids. Both ROFA6 and ROFA2 induced dose- and time-dependent increases in MCP-1 and MIP-2 mRNA levels. ROFA6, but not ROFA2, induced mucous cell metaplasia with significant increases in stored mucosubstances in the surface epithelium lining main axial pulmonary airways. These data suggest that ROFA-associated inflammation and mucous cell metaplasia is dependent on the amount of Vanadium associated with the particles and emphasizes the need to consider the chemical/physical characteristics of ambient air particulates when assessing potential pulmonary toxicity.

1222 RESIDUAL OIL ASHES WITH DIFFERING COMPOSITION ELICIT PRO-INFLAMMATORY CHEMOKINES IN THE LUNG AND HEART.

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Residual oil ash (ROA) is a significant environmental hazard and contributes to airborne particulate matter. In the present study, toxicity profiles for two ROAs differing in composition were examined. Residual oil ash 1 (ROA1) had a lower carbonaceous component and high vanadium content; ROA2 was rich in carbon and included high amounts of nickel and manganese. HYPOTHESIS: The greater presence of vanadium in ROA1 will result in more severe pulmonary injury. METHODS: Rats were lightly anesthetized and intratracheally instilled with 2.5 mg/kg ROA1 or ROA2 or PBS. Animals were sacrificed at 4, 24, and 48 hours (hr) post-instillation (PI). Bronchoalveolar lavage (BAL) was performed and BAL cells as well as lung and heart tissues were retained for RNA isolation and Northern analysis. RESULTS: Significant ROA-induced pulmonary inflammation was observed in BAL samples at all time points with neutrophil and eosinophil influx and increased biochemical markers of inflammation ($p < 0.05$). These changes were significantly more severe in the ROA1 group for several parameters, particularly at 4 hr. Macrophage inflammatory protein (MIP)-1α and MIP-2 mRNA levels were markedly increased in ROA-exposed BAL cells at 4 hr; expression was present but declining at later timepoints. Lung and cardiac tissue exhibited very low MIP-1α and -2 mRNA levels at 4 hr PI only. There was no difference in the level of mRNA expression of these chemokines between the two ROA groups. CONCLUSION: ROA1 appears to be a more toxic pro-inflammatory particle indicating that composition is an important determinant of pulmonary response. The presence of vanadium or lack of carbon content may play a role in this differing response. Secondly, these data indicate that ROA induces pulmonary inflammation by induction of pro-inflammatory chemokines. (Supported By: ES00002, ES08129, HL05947, and HL54958.)

1223 DISTRIBUTION OF RETAINED PARTICULATE MATERIAL IN RAT AND HUMAN LUNGS.

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Rats and monkeys differ in patterns of particle retention in the lungs after identical exposures to diesel exhaust (DE) or coal dust at a single concentration (2 mg respirable material/m³) resulting in moderate lung burdens. Here we extend the morphometric studies of particle retention to humans and examine the influence of exposure concentration on retention patterns in rats and humans. Histologic lung sections from a previous study in rats and from the National Coal Workers' Autopsy Study were examined morphometrically to estimate the volume percentage of particulate material in defined anatomic compartments. The rats had been exposed 7 h/day, 5 days/wk for 24 mo to DE at 0.35 (low), 3.5 (medium), or 7.0 (high) mg soot/m³; the 24-mo soot lung burdens were 0.6, 12, and 21 mg, respectively. The human lungs sections were from 1) nonsmokers who did not work as miners, 2) nonsmoking coal miners who worked under the current standard of ≤ 2 mg dust/m³ for 3 – 20 y (mean = 13 y), and 3) nonsmoking coal miners who worked under the former standard of < 10 mg dust/m³ for 33 – 50 y (mean = 40 y). The volume percentage of the lung occupied by particulate material was 0.2, 1.6, and 3.7% in the low, medium, and high exposure concentration rats, respectively. The particulate material was predominately retained in macrophages in the alveolar and alveolar duct lumens, with 82, 81, and 85% of the material being in lumens and 18, 19, and 15% of the material being interstitial in the low, medium, and high exposure concentration rats, respectively. The volume percentage of the lung occupied by particulate material was 0.3, 1.8, and 10.3% in the non-miners, coal miners under the current standard, and coal miners under the former standard, respectively. Fifty-seven, 68, and 91% of the particulate material was interstitial, and the remainder was in lumens, in the non-miners, coal miners under the current standard, and coal miners under the former standard, respectively. These results show that chronically inhaled diesel soot is similarly retained predominately in lumens of rats over a wide range of exposure concentrations and resultant lung burdens. In non-miners and coal miners, chronically inhaled particulate material is retained primarily in the interstitium, and the percent of the material in the interstitium is related to dose (exposure concentration, years of exposure, and/or lung burden). (Research sponsored by the Assoc. of German Car Manufacturers (VDA).)

1224 RESPONSE TO ULTRAFINE AND FINE PARTICLES IN THE LPS-PRIMED LUNG.

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Bacterial endotoxin (LPS) is an environmental contaminant and product of infection which has potent inflammatory and priming effects in organs such as the lung. Low levels of urban particles are associated with increased morbidity in susceptible populations. We hypothesize that ambient ultrafine particles are more effective than fine particles in causing adverse effects. To test this, we have compared the response of young (8 wks) and old (20 mos) F344 rats to two different sizes of TiO_2 both with and without prior exposure to LPS. Rats were exposed to LPS (0.02 μ g deposited for young rats; 0.01 μ g for old rats) via inhalation and then immediately to particles via intratracheal instillation (50 μ g ultrafine TiO_2 (~20 nm) or fine TiO_2 (~250 nm)). Animals were sacrificed 24 hrs after exposure and inflammatory parameters in bronchoalveolar lavage fluid were assessed. Priming with LPS resulted in a significantly greater PMN response in the lungs of particle-exposed rats as compared to LPS or particle exposure alone; this was true for both young and old rats. Additionally, the ultrafine particles produced greater inflammation by themselves and with LPS priming as compared to the fine particles. We conclude that inhaled LPS can act to prime the lung to subsequent particle exposure and that ultrafine TiO_2 has greater inflammatory potential than fine TiO_2.

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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 38th Annual Meeting of the Society of Toxicology, held at the Ernest N. Morial Convention Center, New Orleans, Louisiana, March 14-18, 1999.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 419.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 444.

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