despite similarities in metal profile. ROA causes a less severe pulmonary inflammatory response perhaps mediated through a molecular pathway different from ROFA.

1994 PULMONARY TOXICITY OF RESIDUAL OIL FLY ASH IN THE RAT: INHALATION VERSUS INTRATRACHEAL INSTILLATION.

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Controversy exists as to the appropriateness of intratracheal instillation (IT) of particulate matter (PM) into the rodent lung as a surrogate for inhalation exposure (IH). The artificial nature of bolus dosing versus time- and ventilation-dependent interlobar distribution of PM, probable disparate intralobar dosimetry, and the impact of fluid vehicle co-administration undermine the acceptability of the IT methodology. However, a validated IT approach would allow the screening of relative PM toxicities, the study of PM samples of limited availability (e.g., ambient PM), and would diminish the necessity of IH for acute testing. To evaluate the value of the IT approach, residual oil fly ash (ROFA) (an emission PM) was administered to groups of rats by nose-only IH (12 mg/m^3 × 6 hrs; 1.9 um MMAD) followed by assessment of airway reactivity, bronchoalveolar lavage (BAL), and histopathology at 24, 48, and 96h. The dose of ROFA to each of the five dissected lung lobes was assayed (via neutron activation of V / Ni content) in cohorts immediately after exposure and summed for the total lung dose (~110ug). An identical study was then performed using this IT dose (110ug in 0.3 ml sterile saline). The interlobar distribution of ROFA was similar (<15% variation) between IT / IH with the exception of the diaphragmatic lobe dose (IT >INH ~25%). The kinetics and quantitation of inflammation (BAL protein, LDH, and neutrophils) in the two groups was virtually identical over all time points. Airway reactivity in the IH group showed a definite, but not statistically significant increasing trend (~25%) over the 96th period whereas the IT group exhibited a significant increase (~40%) at 24, 48, and 96h. These findings will be compared to the morphometric distribution of injury. Thus, a low dose of IT-PM appears to mimic the IH-derived injury in terms of lobal distribution and inflammatory biomarkers over 96h, while airway reactivity, though showing a similar response, is somewhat exacerbated by the bolus IT challenge. (*This abstract does not reflect EPA policy.*)

1995 CAPSAICIN RECEPTOR ANTAGONIST AND C-FIBER DEPLETION REDUCE PULMONARY RESPONSES TO PARTICULATE MATTER IN BALB/C MICE.

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Several clinical and experimental studies associate tachykinin neuropeptides with pollutant-induced airway inflammation. Recent cell culture studies have demonstrated that cytokine release by human bronchial epithelial cells (BEAS-2B) in response to the emission source particulate residual oil fly ash (ROFA) can be diminished by preincubation with neuroreceptor antagonists. We investigated whether disruption of tachykinin function inhibits pulmonary inflammation and airway hyperreactivity in mice exposed to ROFA. Six groups of 10 wk old male BALB/c mice (n = 6–7 per group) were compared. Capsaicin was administered (50 mg/kg i.p.) to postnatal day 2 mice to denervate sensory C fibers. As 10 wk old adults they were then intratracheally instilled (IT) with saline (CAP/0) or ROFA (3 mg/kg; CAP/ROFA). Other 10 wk old mice received IT capsazipine (CPZ; 100 µl, 10^{-4} M), a selective antagonist of the vanilloid (i.e., capsaicin or irritant) receptor, immediately before IT saline (CPZ/0) or ROFA (CPZ/ROFA). Control mice received only IT saline (0/0) or ROFA (0/ROFA). Twenty-four hr after exposure, numbers of bronchoalveolar lavage (BAL) neutrophils were 27-fold greater in 0/ROFA mice compared with 0/0 mice, and other significant increases in BAL protein and lactate dehydrogenase (LDH) were found. Compared with 0/ROFA mice, CAP/ROFA mice had 37% fewer neutrophils, 34% lower LDH, and 25% lower protein; in contrast, CPZ/ROFA values were similar to 0/ROFA. 0/ROFA mice were hyperreactive to i.v. methacholine challenge compared with 0/0 mice (methacholine dose inducing 75% increase in resistance (ED75) was 38% lower in 0/ROFA mice; $P = 0.015$). CAP/ROFA and CPZ/ROFA mice were less reactive than 0/ROFA mice (ED75 was 21% greater in both groups). Although these latter differences were not significant, these trends suggest that tachykinins contribute to particulate-induced airway inflammation and hyperreactivity. (*This abstract does not reflect EPA policy.*)

1996 EXPOSURE TO DIESEL EXHAUST PARTICLES (DEP) ALTERS THE RESPONSIVENESS OF RATS TO BACTERIAL LIPOPOLYSACCHARIDE (LPS) INSULTS.

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Exposure to DEP has been associated with increased susceptibility to pulmonary infection (Environ Res 37:44, 1985). Our hypothesis is that the functional activity of alveolar macrophages (AM) in response to bacterial LPS insults is diminished after DEP exposure. Male Sprague-Dawley rats (~250 g) received a single intratracheal instillation of DEP (5 mg/kg) or saline, then were challenged intratracheally with LPS (1.0 mg/kg) or saline 3 days later. Rats were sacrificed 3 h after this second treatment and underwent bronchoalveolar lavage (BAL). BAL cell differentiation, protein and lactate dehydrogenase (LDH) in BAL fluid were measured. Macrophage inflammatory protein 2 (MIP2, ELISA), tumor necrosis factor-alpha (TNF-α, ELISA) and nitric oxide (NO, Greiss assay) were monitored in both AM-conditioned supernatant and BAL fluid. Exposure to DEP resulted in increases in protein, LDH, neutrophil influx, lymphocyte influx and the production of MIP2, TNF-α and NO by AM. Exposure to LPS alone increased the infiltration of both neutrophils and lymphocytes and the production of MIP2, TNF-α and NO in AM supernatant and BAL fluid. Pretreatment of rats with DEP decreased the production of TNF-α, MIP2 and NO by AM in response to subsequent treatment with LPS below levels expected if the DEP and LPS responses were additive. In summary, both DEP and LPS caused inflammation. However, pre-exposure to DEP decreased the secretory function of AM in response to subsequent LPS exposure, which may, in part, be responsible for the increased morbidity of infectious diseases after DEP exposure.

1997 COMPROMISED PULMONARY AND SYSTEMIC IMMUNE RESPONSES IN THE RAT MAY HELP EXPLAIN INCREASED PULMONARY INFECTIONS OBSERVED IN WOODSMOKE-EXPOSED CHILDREN.

J T Zelikoff, Y Li, K Fang, L C Chen, M D Cohen. *New York University Med. Ctr., Tuxedo, NY.*

Epidemiological studies suggest that chronic inhalation of woodsmoke (WS) increases the incidence, duration, and, possibly, severity of infectious respiratory disease in children. This study seeks to examine whether acute high-dose and/or long-term low-dose exposure to inhaled WS compromises host resistance against bacterial infections. Rats were exposed nose-only for either 4 d (1 hr/d) or 1 mo (3 hr/d) to WS generated from the burning of red oak. Smoke was characterized in terms of particulates, CO, NOx, metals, and BaP. Under the current burning conditions, particulates were generated at a level of either 750 or 100 µg/m^3 for the short and long-term studies, respectively. Following exposure, rats were intratracheally-instilled with *Staphylococcus aureus* to assess effects upon bacterial clearance; these same animals were also used to study effects upon thymic cellularity, blood cell profiles, and lymphoproliferation. Lungs from uninfected rats were lavaged to assess effects upon macrophage (Mø) function and biochemical markers. Both short and long-term WS exposure reduced bacterial clearance 5 d post-exposure; effects from short-term exposures persisted for up to 11 d. Mechanistic studies suggest that compromised host resistance may be associated with changes in Mϕ function. Inhalation of WS for 4 d reduced Mϕ production of superoxide anion, while exposure for 1 mo significantly reduced thymic cellularity and proliferation of blood lymphocytes 3 d following the final exposure. Results from these toxicological studies demonstrate that altered pulmonary immunity may, at least in part, explain particular health effects observed in WS-exposed children. Supported by CIAR #94-03.

1998 WORKER EXPOSURE TO HEAVY METALS IN PRESSURE-TREATED WOOD DUST.

P Decker, B Cohen, and T Gordon. *NYU Medical Center, Tuxedo, NY.*

Pressure treatment with chromium, arsenic, and copper enables relatively non-resistant wood to be used in a number of outdoor construction projects including marine pilings, foundations, playgrounds, and recreational decks. This study examined the airborne concentration and particle size distribution of wood particles, chromium, copper, and arsenic at outdoor and indoor work sites. The mean total dust concentration for the outdoor area and personal samplers were 0.73 and 0.57 mg/m^3, respectively. Personal impactor sampling demonstrated that over 80% of the outdoor wood dust was greater than 15 µm in diameter. Indoor wood dust concentrations were much greater than the outdoor values and were job category-dependent. For an indoor sanding operation, the mean total dust concentration, as determined by personal

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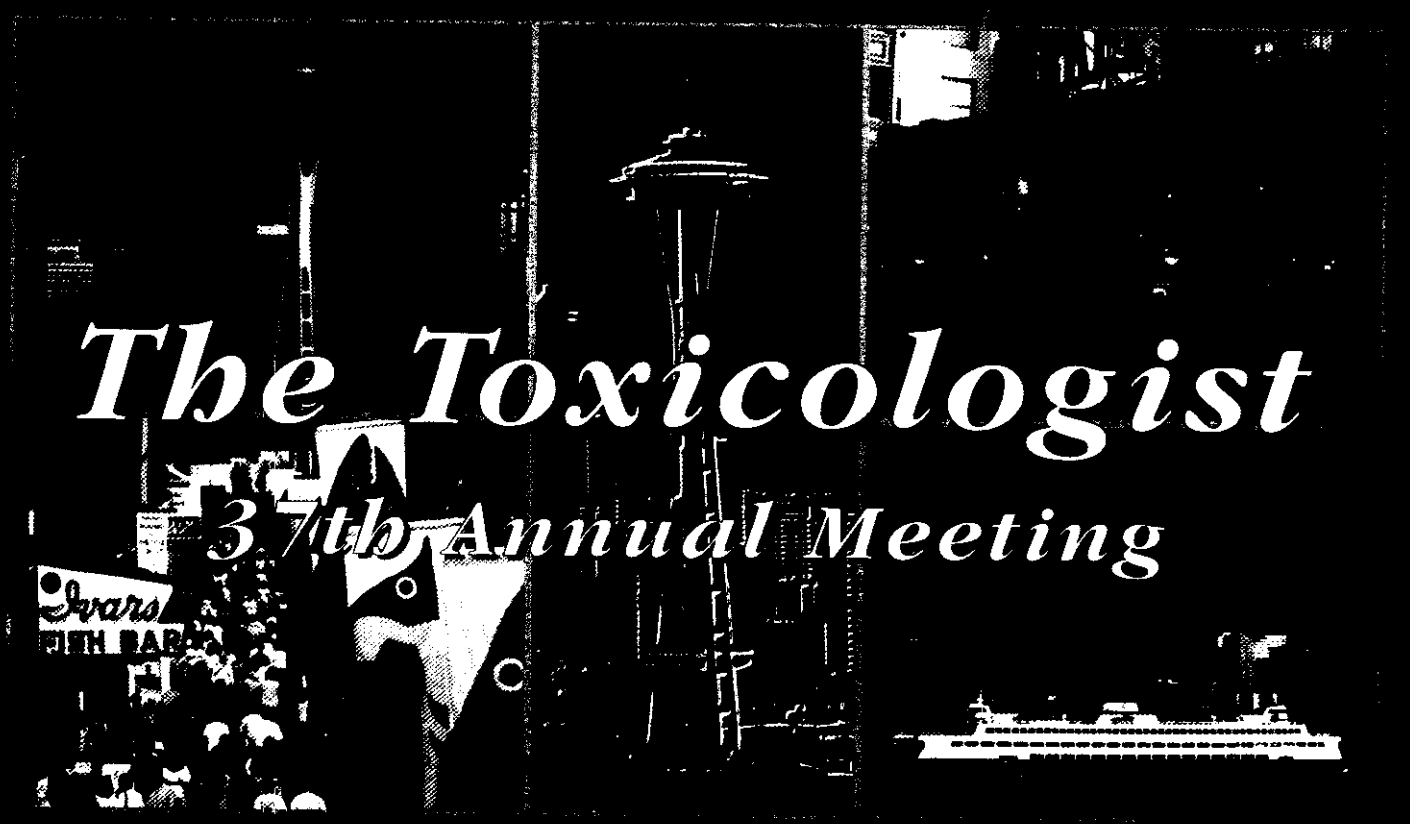

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Preface

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 37th Annual Meeting of the Society of Toxicology, held at the Washington State Convention Center, Seattle, Washington, March 1-5, 1998.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 407.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 433.

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