root ganglion (DRG) sensory neurons, which enervate the upper and lower airways, were cultured from BALB/c and B6 fetal mice. These cultures were exposed (4 hr) to ROFA (25-50 μg/ml), coal fly ash (25,50 mg/ml), capsaicin (1-3 μM) or acid (pH 5.0 and 6.5 for 15 min, then culture medium for 4 hr). In all instances, DRG neurons from BALB/c mice released significantly higher levels of the proinflammatory cytokine, IL-6 into their nutrient media compared to B6 mice. Finally, single cell recordings of intracellular calcium were taken from cultured DRG, loaded with the fluorescent calcium indicator dye Fluo-3 AM, in response to pH 6.5 and capsaicin (0.5 μM). These data indicated that significantly higher numbers of BALB/c neurons responded with increases in intracellular calcium compared to B6 neurons, but that qualitatively the responses (i.e., peak amplitudes) were equivalent between strains. Taken together these data suggest that irritant receptors (i.e., capsaicin, acid sensitive) located on sensory nerve fiber terminals subserve PM-induced airway inflammation and are quantitatively different in responsive and non-responsive mouse strains. (This abstract does not reflect EPA policy.)

1462 PARTICULATE MATTER AND CHARGED SYNTHETIC POLYMER MICROSPHERE ANALOGUES ACTIVATE BRONCHIAL EPITHELIAL CELLS AND SENSORY NEURONS THROUGH CAPSAICIN AND ACID RECEPTORS.

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Residual oil fly ash (ROFA), an industrial particulate pollutant, causes airway inflammation and hyperresponsiveness in rodents. Recent data showed that exposure of BEAS-2B bronchial epithelial cells to ROFA elicited inflammatory effects (e.g. increases in intracellular calcium, cytokine transcript and release), which were inhibited by capsazepine (CPZ), an antagonist of capsaicin receptors, and by amiloride, an antagonist of acid receptors (Veronesi et al., Toxicol. Appl. Pharmacol., *in press*). In this study, we examined whether physico-chemical characteristics of particles contributed to the inflammatory changes recorded in culture. Electrophoresis showed that 'field' ROFA particles carry a negative surface potential, as indicated by their zeta potential of -25 - -35 mV. Synthetic polymers microspheres (SPM) were synthesized, that resemble ROFA particles with 2-6 μm diameter and a zeta potential of -29 mV. The effects of ROFA and SPM were examined on BEAS-2B cells and sensory dorsal root ganglion (DRG) neurons. ROFA and SPM caused an immediate increase in intracellular calcium which was inhibited by CPZ and amiloride, respectively. In addition, exposure of BEAS-2B cells and DRG neurons to ROFA or SPM caused the release of IL-6, which was completely blocked by CPZ and partly blocked by amiloride. In both cell types capsaicin and pH 6.5 increased intracellular calcium and caused the release of IL-6 in a receptor-mediated fashion. These data suggest that the acidic environment associated with the negative zeta potential of the particles can activate capsaicin and acid receptors. We propose that activation of these irritant receptors triggers the subsequent release of inflammatory cytokines and neuropeptides which initiate and sustain neurogenic inflammation in the airways. (This abstract does not reflect EPA policy.)

1463 PHYSICOCHEMICAL COMPONENTS OF PARTICULATE MATTER CONTRIBUTE DIFFERENTIALLY TO INFLAMMATORY RESPONSES IN SENSORY NEURONS.

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Airborne particulate matter (PM) consists of complex aggregates of elemental and organic carbons, metals, sulfates and microbial contaminants. Its heterogeneous composition has complicated identifying the mechanism(s) which underlie the symptoms of airway inflammation. We examined the physicochemical characteristics of various urban and industrial PM in relation to their inflammatory effects in cultured sensory dorsal root ganglion neurons (DRG). The components of PM were separated by centrifugation and filtration, and characterized in terms of particle size, surface charge and pH in buffered solutions. The results show that most PM remain acidic in solution, even after multiple washings. The different PM contained particles of variable sizes, including ultrafine particles. The 'field' PM particles, their washed particle core and the ultrafine particles, obtained after 22 μm filtration, contained a variable surface charge as indicated by their zeta potentials. Exposure of DRG to PM caused a differential release of the proinflammatory cytokine IL-6 depending on the source and on the fraction of PM tested. Finally, pretreatment of DRG with antagonists of capsaicin receptors (i.e., capsazepine) or acid-sensitive receptors (i.e., amiloride or benzamil) inhibited the PM-induced IL-6 release in a differential manner. Collectively, these data support our hypothesis, that PM initiate inflammation by activation of capsaicin and acid-sensitive irritant receptors located on various airway target cells. In addition, the data indicate that soluble, acidic and charged particle components of PM contribute differentially to the inflammatory effects. (This abstract does not reflect EPA policy.)

1464 NUCLEAR FACTOR–KAPPA BETA (NF-KB) ACTIVITY IN RAT ALVEOLAR MACROPHAGES EXPOSED TO RESPIRABLE ORGANIC PARTICLES AND ANTIOXIDANTS.

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Activation of the transcription factor NF-kB by respirable organic particles (ROP) facilitates oxidative damage in lung through increased expression of pro-inflammatory genes. In previous studies, we found that NF-kB in alveolar macrophages was activated maximally at 2 hours following <I>in vitro</I> treatments with ROP. Because of the recent interest in identifying oxygen radical pathways of NF-kB activation, we have investigated inhibitory effects by specific antioxidant agents. NR8383 rat alveolar macrophage cells were treated with ROP, with and without antioxidants, and analyzed for NF-kB activation employing the electrophoretic mobility shift assay (EMSA). Densitometry analysis of EMSA gels revealed the following reductions in NF-KB activation (reported as % of positive control). 200 units/ml superoxide dismutase reduced activation by 51%, whereas catalase had no inhibitory effect, strongly suggesting a primary role for the superoxide anion radical, but not hydrogen peroxide, in the activation of NF-kB in alveolar macrophages. Furthermore, only a 27% reduction in NF-kB activation was observed following cell treatments with 1 nM melatonin, an efficient scavenger of hydrogen peroxide. A series of vitamin E species, alpha-tocopherol succinate, vitamin E acetate, and Trolox, a vitamin E derivative, at 100 uM reduced NF-kB activation 63%, 33%, and 38%, respectively, clearly indicating that vitamin E analogs differ in their potencies of NF-kB inhibition. One uM pyrrolidinedithiocarbamate and 20 mM N-acetyl cysteine, which have effects on diverse oxygen free radical pathways, reduced NF-kB activation 54% and 66%, respectively, providing further support for a general role of reactive oxygen species in NF-kB activation. Ongoing studies are exploring the role of lipopolysaccharide receptors and calcium regulatory pathways on NF-kB activation in lung cells following exposure to particulate matter. (Support from NIOSH and USACEHR.)

1465 FREE RADICAL GENERATION BY WOOD SMOKE PARTICLES AND IN VITRO DNA DAMAGE.

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As a component of our investigations into the pathophysiology of smoke inhalation, the present study characterizes the free radicals generated by combustion of Western bark (fir and pine), using the technique of electron spin resonance (ESR) . Smoke was generated by heating the wood chips in a crucible furnace at a constant temperature of 400°C and an air flow of 6 L/min. Smoke was filtered through Whatman 1 filters or bubbled through saline over a 1 min period beginning at 0, 5, 10, 15 and 20 min after generation of the smoke. ESR analysis of the particles trapped by the filters revealed the generation of carbon-centered free radicals similar to those generated by coal or diesel particles. These radicals were observed at all time points and may be associated with the surface or the core of the particles. Addition of H_2O_2 generated hydroxyl radicals (•OH). There was no direct correlation between the generation of •OH and the level of carbon-centered free radicals. In aqueous media, wood smoke particles also generated •OH. Incubation of wood smoke particles with DNA, in vitro, caused DNA strand breaks as measured by gel electrophoresis. The H_2O_2 scavenger, catalase, the •OH scavenger, formate, and the iron chelator, deferoxamine, inhibited the DNA strand breaks, while H_2O_2 enhanced them. These data suggest that free radical reactions mediated by wood smoke particles may play an important role in the cellular injury associated with smoke inhalation.

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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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