were sacrificed on day 14 and serum was analyzed for IgE using an ELISA. At the high dose level, all test materials with the exception of MAc were significantly higher ($p<0.01$) than the VH. OX also produced a positive response. Although the results indicate a robust response for RS, a lack of specificity to distinguish DS vs RS was apparent. Further efforts which may be needed include challenge by the inhalation rather than dermal route and/or evaluation of hapten specific antibodies.

495 ASSESSMENT OF THE SENSITIZING POTENTIAL OF FORMALDEHYDE

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It is well established that formaldehyde is able to cause allergic contact dermatitis. Less certain is the potential of this chemical to induce sensitization of the respiratory tract and allergic asthma. Consistent with skin sensitizing activity formaldehyde was found in the present investigations to induce strong positive responses in the guinea pig maximization and Buehler occluded patch tests and in the local lymph node assay. The mouse IgE test is a novel method for the identification of potential chemical respiratory allergens in which activity is measured as a function of the ability of topically applied materials to stimulate an increase in the serum concentration of IgE in BALB/c mice. At concentrations that stimulated vigorous responses in the local lymph node assay, formaldehyde was inactive in the mouse IgE test. In supplementary experiments the pattern of cytokine production by draining lymph node cells induced by topical exposure of mice to formaldehyde was examined. Responses to this chemical were characterized by the production of comparatively high concentrations of the type 1 cytokine interferon-γ, but only low levels of the type 2 cytokines interleukins 4 and 10; a pattern consistent with the selective stimulation of Th1 T helper cells. These data confirm the skin sensitizing activity of formaldehyde, but indicate the absence of a significant potential to cause sensitization of the respiratory tract.

496 CHARACTERIZATION AND CLASSIFICATION OF CHEMICAL ALLERGENS AS A FUNCTION OF CYTOKINE SECRETION PROFILES

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We have demonstrated previously that repeated topical exposure of mice to chemical contact or respiratory allergens induces characteristic cytokine secretion profiles consistent with the selective activation of T helper 1 (Th1)- and Th2-type cells, respectively. Concentrations of the respiratory allergens trimellitic anhydride (TMA) and toluene diisocyanate (TDI) and the contact sensitizers oxazolone and dinitrochlorobenzene (DNCB) were used which stimulated equivalent levels of immunogenicity with respect to lymph node cell (LNC) proliferation. Under such conditions of exposure, TMA- and TDI-activated LNC expressed high concentrations of the Th2-type cytokines interleukin 10 and interleukin 4, but low levels of the Th1 cell product interferon γ. The converse pattern of cytokine production was observed for oxazolone- and DNCB-stimulated LNC. In subsequent experiments we have examined dose-response relationships for a wider range of chemical allergens. In each case, cytokine production profiles were compared with those observed in LNC derived from animals exposed concurrently to the respiratory allergen TMA, or the contact allergen DNCB. At all concentrations tested, the contact allergens eugenol and isoeugenol provoked a Th1-type cytokine secretion profile while a Th2-type pattern was induced by exposure to the respiratory allergens cyanuric chloride and diphenylmethane diisocyanate. These data suggest that it may be possible to characterize and classify different types of chemical allergen as a function of LNC cytokine production profiles induced following topical exposure.

497 ATTENUATION OF SILICA-INDUCED CYTOTOXICITY BY LAZAROID (U-75412E)

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Lazaroids (21-aminosteroids) are potent scavengers of oxygen radicals (OR) and inhibitors of lipid peroxidation. They have been shown to provide protection from OR induced injury. Crystalline silica (silica) a potent cytotoxic agent is known to cause pulmonary fibrosis in animals and man. We have shown previously that ORs are involved in silica-induced pulmonary injury and inflammation. In the present study, we investigated the effectiveness of lazaroid (U-75412E) in the amelioration of silica-induced cytotoxicity in rat alveolar macrophages (AM). To test the efficacy of lazaroid in attenuating in vitro silica-induced cytotoxicity, we measured lactate dehydrogenase, β-N-acetyl glucosaminidase, superoxide dismutase, glutathione peroxidase, and hydrogen peroxidase release from AMs as indicators of cytotoxicity in the presence and absence of lazaroid. We also studied the ability of lazaroid to scavenge hydroxyl radicals (OH) generated by silica from hydrogen peroxide. Lazaroid protected AMs from silica-induced cytotoxicity and injury. Lazaroid also exhibited a dose dependent ability to scavenge OH. Results of these in vitro studies suggest that administration of lazaroid in silica-induced lung injury may protect the lung against oxidant injury.

498 LUNG DEPOSITION AND ALVEOLAR MACROPHAGE UPTAKE OF MICROPARTICULATES FROM SUSPENSION AEROSOLS IN GUINEA PIGS

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Size dependency of uptake, disposition, residence time and location of particles is implicated in local inflammatory and chronic diseases of the lungs. Particulate aerosols that deposit in the periphery of the lungs adjacent to alveolar macrophages (AM) will be phagocytosed. Aqueous suspensions of fluorescent polystyrene beads (Dp = 1 or 3μm) were nebulized. Mass median aerodynamic diameters (MMAD) and geometric standard deviations (GSD) were determined by inertial impaction. Aerosols were administered to guinea pigs for 10 or 30 minutes. AM were harvested from bronchoalveolar lavage fluid at 0 and 6 hours. Macrophage uptake of microparticles was assessed by fluorescence microscopy. Aerosols were characterized from the nebulizer (Dp = 1μm, MMAD = 2.1, GSD = 3.4; Dp = 3μm, MMAD = 4.3, GSD = 2.2) and from the inhalation exposure chamber during delivery to the guinea pigs (Dp = 1 μm, MMAD = 1.5, GSD = 2.4; Dp = 3 μm, MMAD = 2.9, GSD = 1.9). The difference between nebulizer and exposure chamber output particle size may be explained by the loss of large droplets in transit through the chamber. These data define the upper and lower limits of aerosol size to which the animals were exposed. Phagocytosis of 1μm particles by AM was evident 6 hours after aerosol exposure. Phagocytosis of 3μm microparticles could not be detected 6 hours after a ten minute exposure to nebulized aerosol, but thirty minutes of aerosol delivery resulted in detectable phagocytosis 6 hours after exposure. These studies demonstrate a size dependency of uptake of microparticles delivered as aerosols to the lungs. Future studies will evaluate the dose and kinetics of disposition of aerosol particles.

499 ACUTE LUNG RESPONSES TO URBAN DUST AND OZONE IN FISCHER 344 RATS

L Bouthillier, R Vincent, P Goegan, S Bjarnason, J Guenette, M Potvin, M Stewart, P Kumarathasan, and R Poon. *Environmental Health Directorate, Health Canada, Tunney's Pasture, Ottawa, Ontario, Canada.* Sponsor: I Chu

We have studied in a short-term animal assay the pulmonary effects of ambient air particles in interaction with ozone. Fischer 344 male rats (n = 5–12) were exposed for 4th by nose-only route to clean air, ozone (0.8 ppm O_3), Ottawa urban dust EHC93 (50 mg/m^3; MMAD = 1.4 μm, GSD = 1.9), or O_3 plus urban dust on a single day or 3 consecutive days. Bronchoalveolar lavage (BAL) was performed after 24h recovery in air. Exposure to O_3 resulted in elevated protein, fibronectin (FN) and alkaline phosphatase (AKP) in BAL fluid, indicating lung injury. EHC93 alone did not increase BAL protein, FN or AKP, nor did it exacerbate these effects of O_3 following co-exposure. However, the BAL neutrophilic infiltration induced by O_3 was increased by EHC93 in the 1-day exposure group. EHC93 alone did not increase BAL neutrophils. BAL macrophages (MAC) were reduced after 3-day exposure to EHC93. MAC viability was not affected by any of the *in vivo* treatments. O_3 inhalation decreased phagocytic activity and TNF-α production by MAC. EHC93 alone decreased TNF-α secretion and the LPS-stimulated nitric oxide production by MAC. While both O_3 and EHC93 separately could alter some aspects of MAC physiology, these cellular effects appeared to be attenuated by co-exposure of the rats to O_3 plus EHC93. There were no clear cumulative effects of 3-day exposure *vs* 1-day exposure. The data indicate that although inhaled urban dust has a low acute pulmonary toxicity, it can depress some key functions of MAC. Toxicological interaction with O_3 appears complex and warrants further investigation. Supported by Health Canada (K281235).

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshops, roundtables, and poster sessions of the 35th Annual Meeting of the Society of Toxicology, held at the Anaheim Convention Center, Anaheim, California, March 10-14, 1996.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 351.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 375.

The abstracts are reproduced as accepted by the Program Committee of the Society of Toxicology and appear in numerical sequence.

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