1122 EFFECTS OF OZONE INHALATION ON RAT ALVEOLAR MACROPHAGE (MP) PRODUCTION OF REACTIVE NITROGEN AND OXYGEN INTERMEDIATES. K Pendino, C Punjabi, C Gardner, J Laskin, D Laskin. Graduate Program in Toxicology, Rutgers University and UMDNJ-RW Johnson Medical School, Piscataway, NJ.

Acute exposure to ozone is associated with the accumulation of inflammatory cells in the lungs which have been hypothesized to release mediators that contribute to lung injury. Nitric oxide is a highly reactive molecule produced via an L-arginine dependent nitric oxide synthase that has been implicated in tissue injury. In the present studies we examined the effects of ozone on production of nitric oxide by lung MP. Alveolar MP were isolated from female SD rats 48 hr following exposure to ozone (2 ppm, 3 hr). Nitric oxide was measured by accumulation of nitrites in the culture medium. Ozone exposure resulted in a 2-fold increase in the number of cells recovered from the lungs. Differential staining revealed that these cells consisted of 89% MP. Cells from ozone-treated rats were found to produce significantly more nitric oxide than cells from control animals. This was correlated with decreased production of superoxide anion by these cells. These data suggest that MP-derived nitric oxide may contribute to tissue injury following ozone exposure. (ES04738)

1123 GENERATION OF FREE RADICALS FROM PHAGOCYTES INDUCED BY OCCUPATIONAL MINERALS. V. Vallyathan, NS Dalal, JF Mega and X Shi. Div. of Resp. Dis. Studies, NIOSH, and Chem. Dept., West Virginia Univ., Morgantown, WV. Sponsor: V Castranova

This study was undertaken to determine and differentiate the potential of occupational dusts to stimulate the production of oxygen radicals by human polymorphonuclear leukocytes (PMN) and rat alveolar macrophages (AM) in vitro using electron spin resonance spectrometry (ESR) and spin trap technique. PMN and AM were exposed to amosite, chrysotile or crocidolite asbestos, to freshly fractured or aged silica, and to an inert dust barite in the presence of a lipid soluble spin trap α-phenyl-t-butyl nitrone (PBN). Free radicals generated during phagocytosis were trapped by the PBN forming a stable PBN adduct. Lipid extract of the reaction medium was subjected to ESR measurement to determine the relative intensities of radicals generated. Amosite and crocidolite asbestos generated greater concentrations of oxygen free radicals than silica and chrysotile asbestos. Catalase, but not superoxide dismutase, inhibited more than 70% of the generation of radicals. Desferoxamine inhibited the radical generation and 1,3-bis(2-chloroethyl-1-nitrosouria (carmustine), an inhibitor of glutathione reductase systems, enhanced radical production four-fold. These data indicate that in vitro exposure of phagocytes to particles will generate significant levels of oxygen radicals.

1124 EFFECTS OF HYPEROXIA ON THE ACTIVITY OF RAT PULMONARY MACROPHAGES. V Castranova, JYC Ma, MW Barger, WH Pailes, HV Dedhia, NS Dalal, M Billie, and V Vallyathan. Div. Respir. Dis. Studies, NIOSH and Div. Pulm. Med., and Dept. of Chem., West Virginia Univ., Morgantown, WV.

This study characterized the activity of pulmonary macrophages after in vivo exposure of rats to 95% oxygen for 64 hrs. Zymosan-induced hydrogen peroxide (H_2O_2) production was decreased by 41% in phagocytes obtained from O_2-exposed rats. Similarly, zymosan-stimulated oxygen radical generation monitored by electron spin resonance was decreased by 53% in phagocytes from hyperoxic rats. This decline in activity could not be accounted for fully by decreased viability, since membrane integrity of exposed cells declined by only 12%. In contrast, zymosan-stimulated chemiluminescence (CL) rose by 540% after O_2-exposure. This high CL could not be explained by lower antioxidant levels (reduced and oxidized glutathione) in O_2-exposed cells. Further, there was no difference in the proportion of CL generated by superoxide, H_2O_2, cyclooxygenase, or lypoxygenase metabolites in O_2-exposed vs control macrophages. Lipid peroxidation of lavaged pneumocytes was elevated by 118% after O_2 treatment. Therefore, high CL may be due to the production of reactive lipids by O_2-exposed pneumocytes. In conclusion, in vivo exposure of rats to hyperoxic conditions results in lipid peroxidation, decreased membrane integrity, and depressed ability of phagocytes to release reactive oxygen species in response to particles.

1125 BRONCHO-ALVEOLAR LAVAGE FLUID ENZYMES AFTER EXPOSURE OF MICE TO RICIN AND RICIN B CHAIN AEROSOLS. D A Creasia, S Bavari*, K A Bostian and D M Walters. United States Army Medical Research Institute of Infectious Diseases, Frederick, MD.

Ricin is a plant toxin, with lectin properties, that is composed of an A chain and a B chain. Ricin binds to cells via the B chain and is internalized. The A chain enzymatically inhibits protein synthesis leading to cell death. When inhaled by mice, ricin causes pulmonary necrosis and death. Systemic administration of ricin causes death but not pulmonary necrosis. Immunization against ricin can prevent death from both inhaled and systemically administered ricin, but does not prevent pulmonary necrosis from inhaled ricin. Since ricin is not a primary irritant, we postulated that the binding of inhaled ricin (lectin) to cell(s) within the respiratory tract was sufficient to trigger the release of inflammatory mediators and produce pulmonary necrosis. To test this hypothesis, we exposed mice to aerosols of either ricin or ricin B chain alone and measured enzyme markers released in brocho-alveolar lavage (BAL) fluid. We found no difference between control and aerosol exposed mice in levels of total protein and albumin, but did find a time dependent, increased release of acid and alkaline phosphatase, lactic dehydrogenase and 5' nucleotidase after aerosol exposure to both ricin and ricin B chain alone. We conclude that either inhaled ricin or ricin B chain alone is sufficient and both are effective in producing the release of enzymes indicative of alveolar macrophage activation and cytotoxicity in BAL fluid.

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