periods but were not significantly different from controls at 3, 6, and 12 months postexposure. Similarly, morphometric studies measuring alveolar macrophage volume/surface area at BADJs demonstrated a peak at 1 month postexposure but no significant difference thereafter. These results demonstrate that the early fibrotic lesions related to high dose p-aramid exposures are repaired in the absence of continuing exposure, thus indicating reversibility of cellular injury.

622 THE INFLUENCE OF (1→ 3)β -D GLUCAN ON ENDOTOXIN-INDUCED ACUTE PULMONARY INFLAMMATION.

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Organic dust aerosols, known to cause respiratory disease among farmers, are composed of biogenic agents including bacteria, fungi, aeroallergans, excreta, dander, bacterial endotoxins (Etx) and glucans. *Sclerotinia sclerotiorum* (Ss) is an emerging phytopathogenic soybean fungus rich in highly branched, water soluble (1→ 3)β -D glucans to which farmers are exposed. After a first study revealed reduced Etx-induced pulmonary inflammation in mice instilled with Ss extract and Etx, experiments were performed to assess the influence of Ss glucan content in the blunting of Etx-induced inflammation. BALB/cJ mice were intratracheally instilled with 50 μ g of purified scleroglucan (GL) alone, 50 μ g of Ss alone; or 50 μ g of GL or Ss in combination with 0.25 μ g of Etx, or saline (control). Bronchoalveolar lavage (BAL) collected 4 hr postexposure from the Etx group showed an increase in total BAL cells (96% neutrophils) with an increase of MIP-2, TNF-α and IL-6 over controls. GL or Ss exposure alone did not induce changes in BAL cellularity or MIP-2 concentration when compared to controls. However, a reduction of % BAL neutrophils ($p<0.01$) was observed in the GL+Etx group when compared with the Etx group, although total BAL cells remained elevated. The neutrophil response of the Ss+Etx group was similar to the GL+Etx group ($p<0.01$), and total BAL cells were significantly reduced when compared to the Etx group ($p<0.01$). These results suggest that an antagonistic dose-response relationship exists for concomitant GL+Etx exposures and the soluble glucans in *S. sclerotiorum* may be responsible for the reduction of pulmonary inflammation. (Supported by CDC/NIOSH U07/CCU706145 and the Iowa Center for Health Effects of Environmental Contamination.)

623 PULMONARY INFLAMMATORY RESPONSES AFTER EXPOSURE TO OZONE ARE ENHANCED IN ENDOTOXEMIC RATS.

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Inhalation exposure to environmental ozone and systemic exposure to LPS through infection or translocation from the gastrointestinal tract into the circulation are commonplace in people. Acute exposure to ozone causes pulmonary inflammation in rats that is characterized by an early influx of neutrophils (PMNs) into airways. Systemic exposure of rats to small, nontoxic doses of bacterial endotoxin (lipopolysaccharide, LPS) can potentiate deleterious effects of environmental toxicants. To explore effects of a nontoxic dose of systemic LPS on ozone-induced pulmonary inflammation, we evaluated PMN recruitment and inflammatory cytokines in airspaces of Sprague-Dawley rats exposed first to either ozone (1 ppm for six hr) or air and then to either E. Coli LPS (2 mg/kg, i.v. ; $50x10^6$ EU/kg) or its saline vehicle. Three hr after LPS administration, PMNs and cytokines were quantified in bronchoalveolar lavage fluid (BALF). Exposure to ozone alone caused an increase in PMNs and protein recovered in BALF, whereas exposure to LPS alone did not. In rats made endotoxemic after ozone exposure, BALF PMNs were increased compared to rats exposed to ozone alone. Morphometric evaluation of lung tissues showed increased numbers of PMNs in alveolar septa of rats given LPS irrespective of ozone exposure. Examination of inflammatory mediators revealed no or small amounts of tumor necrosis factor-alpha and macrophage chemotactic protein-1 in BALF of rats exposed to LPS or ozone alone, but markedly elevated levels when ozone-exposed rats were made endotoxemic. These results demonstrate that endotoxemia can enhance PMN recruitment into airways of rats exposed to ozone and that this enhancement is associated with markedly elevated release of inflammatory cytokines. (Supported by NIH grant R37ES02581.)

624 ACUTE SMOKE-INDUCED LUNG INJURY IS RELATED TO TUMOR NECROISIS FACTOR-α mRNA GENE AND PROTEIN EXPRESSION IN ALVEOLAR MACROPHAGES.

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Acute inhalation of diesel fuel-polycarbonate plastic (DFPP) smoke causes severe lung injury, leading to acute respiratory distress syndrome (ARDS) and death. It has been reported that the initiation of acute lung injury is associated with activation of pulmonary alveolar macrophages (PAM). To further explore the pathogenesis, PAM of New Zealand rabbits ventilated and exposed to a 60 tidal volume of DFPP smoke *in vivo* were recovered at 1 hour post-smoke. Smoke exposure induced a significant increases in both mRNA and protein levels for PAM tumor necrosis factor-α (TNF-α), when compared to smoke control. Smoke also induced a biphasic response (inhibited at 2 hours, enhanced at 24 hours after cell isolation) in the production of superoxide (O_{2^-}) by PAM. However, aerosolized lazaroid U75412E (1.6mg/kg body weight) significantly attenuated smoke-induced expression in PAM TNF-α at the protein level, but not at the mRNA level, and smoke-induced changes in PAM O_{2^-}. These changes were paralleled with lung cellular morphological alterations and gas exchange function. This study suggests that highly expressing PAM TNF-α following smoke may be a key contributor to the cascade that establishes an acute injury process and exacerbates oxidant-derived cell injury. Whereas, the lazaroid may ameliorate smoke-induced lung injury by attenuating PAM TNF-α release, in addition to its primary antioxidative mechanism. (Supported by DAMD 17-94-J4001 and NIH ES06694.)

625 PHYSICAL AND CHEMICAL DEGRADATION OF SYNTHETIC VITREOUS FIBERS IN THE LUNG AND IN VITRO.

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Recent rodent inhalation studies of synthetic vitreous fibers (SVFs) and asbestos show a correlation between fiber biopersistence in the lung and fiber toxicity. Inhaled fibers longer than 20 μ m cannot be efficiently cleared by macrophages and therefore can be eliminated only by dissolution or by fragmentation into short segments. In rodent inhalation studies, the fast-clearing, non-toxic fibers demonstrated the following over time in the lung: long fibers cleared more rapidly than short fibers; surfaces became pitted; chemical composition changed; and mean length but not necessarily mean diameter decreased. The slower-clearing, toxic fibers did not show these changes to the same extent or at all. This suggests that incongruent dissolution (leaching) and transverse fragmentation were more pronounced in the non-toxic fibers and enhanced their clearance from the lung. The degradation of 18 fiber glasses was studied in vitro; a correlation between rate of leaching and transverse breakage was found. Additionally, two models of dissolution were demonstrated: (a) constant velocity (CV), the most popular model, which assumes a constant dissolution rate and simple dissolution (all components dissolve at the same rate); (b) diffusion controlled (DC), in which dissolution is incongruent and a hydrated, diffusion-limiting silica gel forms on the fiber surface. 901 fiber glass (MMVF10), which was non-toxic to rodents, fit the DC model. Fibers that fit the DC model underwent rapid transverse fragmentation long before they dissolved completely. Fiberization process (flame vs. air attenuation) strongly influenced in vitro leaching and dissolution rates. Taken together, these studies suggest that biopersistence is an important determinant of fiber toxicity and that, in addition to fiber length and dissolution, leaching and transverse breakage may be important mechanisms of fiber biopersistence.

626 STYRENE METABOLISM BY MOUSE AND RAT ISOLATED LUNG CELLS.

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Styrene has been shown to be pneumotoxic in mice. Rat and mouse pulmonary microsomes are capable of metabolizing styrene to styrene oxide (SO). To determine which cell types in lung are responsible for this metabolism, enriched cell fractions were obtained from mouse and rat lung and comparisons made. The rates of formation of both enantiomers of SO were

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