and their lungs lavaged to provide pulmonary macrophages. Inhalation of RO emissions reduced bacterial killing *in vivo* and diminished *in vitro* phagocytosis by macrophages recovered 1 and 2 h post-exposure. Results demonstrate that acute inhalation of woodsmoke generated from a model system that produces emissions comparable to those produced in homes using woodburning devices, compromises important immune defense mechanisms of the lung. Supported by Center Indoor Air Research. Contract No. CIAR 94-03.

1374 IMMUNOTOXIC EFFECTS IN THE RAT LUNG FROM INHALATION OF VANADIUM

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Male Fisher 344 rats (10 wk old, 200–250 g) were exposed to atmospheres containing 2 mg vanadium (V)/m^3 (as ammonium metavanadate NH_4VO_3, 0.32 μm diameter particles) for 8 hr/d for 4 d in a nose-only exposure system. In exposed rats, lung burdens of V increased in a time-dependent fashion. Nearly all (88%) V-exposed rats displayed markedly increased levels of bronchus-associated lymphoid tissue (BALT) after each exposure, though the effect was only transitory. Analysis of lung cells and lavage fluid 24 hr after the final exposure suggested that a strong inflammatory response was elicited; levels of free neutrophils and immature monocytes, as well as of lavage protein and lactate dehydrogenase, were greatly elevated as compared with levels observed in air-exposed controls. Vanadium also affected the capacity of pulmonary macrophages (PAM) to both produce and respond to important immunoregulatory cytokines. PAM production of tumor necrosis factor-α in response to lipopolysaccharide was significantly inhibited, as was their ability to synthesize/express MHC Class II/Ia molecules in response to interferon-γ (IFNγ). The PAM from V-exposed hosts were also inhibited in their ability to be primed by IFNγ to produce superoxide anion and hydrogen peroxide in response to opsonized zymosan stimulation. These studies indicate that subchronic exposure of rats to workplace levels of atmospheric V can cause strong immunomodulatory effects in the lungs, with a major effect occurring at the level of cytokine-related functions. These alterations may be underlaying mechanisms for the well-documented increases in bronchopulmonary infections and cancers in workers chronically exposed to V-containing atmospheres. This study was supported by NIOSH (Grant No. OH03064-01).

1375 VANADIUM ALTERS MACROPHAGE INTERFERON-γ-INTERACTIONS AND -INDUCIBLE RESPONSES

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Vanadium (V) impairs host resistance overall, and the antimicrobial activity and function of several intracellular enzymes of macrophages (Mø) in particular. Mouse WEHI-3 Mø-like cells were exposed overnight to subcytotoxic concentrations of ammonium metavanadate (NH_4VO_3) to determine whether this observed immunomodulation might be due, at least in part, to altered Mø interactions with interferon-γ (IFNγ) or IFNγ-inducible responses, i.e., increased reactive oxygen intermediate (ROI) production, Ca^{2+} ion influx, and surface Class II/Ia antigen expression. Binding studies performed at 22°C indicated that V-treated cells had ≅50% fewer actively-binding receptors, but binding affinities 450-times greater than that of control receptors. At 4°C, V-treated cells had 98% fewer functional receptors, but again higher (145-fold) affinities. IFNγ-receptor complex internalization was unaffected by V, although significantly higher in cells incubated at temperatures which minimize uptake. ROI production in IFNγ-stimulated V-treated (either NH_4VO_3 or V_2O_5 [vanadium pentoxide]) cells was decreased relative to spontaneous production, while control cells showed consistent increases due to IFNγ priming. Vanadium also reduced the Ca^{2+} ion influx rate into stimulated cells without affecting final cell Ca^{2+} burdens. Although V did not affect IFNγ-induced Ia expression, exposures resulted in increased numbers of Ia-bearing cells with lower maximal antigen densities than control cells. The results of this study show that V exposure may alter Mø-mediated functions by modifying cell interactions with IFNγ and subsequent IFNγ-dependent parameters. This study was supported by NIOSH (OH03064-01) and by EPRI (RP2155-1).

1376 EFFECTS OF INHALED NITRIC OXIDE (NO) ON RAT LUNG

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Inhaled NO has been shown to be a potent pulmonary vasodilator clinically useful in adult respiratory distress syndrome and persistent pulmonary hypertension of the newborn. However, little is known about the potential toxicity of this agent. In the present studies, we analyzed the effects of inhaled NO on the lungs. Exposure of female SD rats to 80 ppm NO for 3 hr resulted in a small increase in polymorphonuclear leukocytes in lung lavage fluid 24 hr after exposure. Superoxide anion production by lung lavage cells was also elevated, an effect which persisted for 48 hr. In contrast, although exposure of rats to 80 ppm NO for 3 days (6 hr/day) had no major effect on superoxide anion production, cells isolated from these animals produced significantly increased levels of NO *in vitro* in response to lipopolysaccharide. Interestingly, inhalation of NO prior to ozone resulted in partial reversal of ozone-induced increases in lavage protein levels and decreases in superoxide anion release. Taken together, these data suggest that inhalation of NO activates lung lavage cells to release increased quantities of reactive intermediates. Furthermore, NO may modify the response of the lung to pulmonary irritants. (ES04738) and a fellowship from the American Lung Association (ALA).

1377 MODIFICATION OF AIRWAY EPITHELIAL PERMEABILITY AND NITRIC OXIDE RELEASE UPON OZONE EXPOSURE

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Results from epidemiological and laboratory animal studies have demonstrated that ozone (O_3) is an inducer of lower airway inflammation and nonspecific airway hyperreactivity. The airway epithelium is the first cell type inhaled O_3 will encounter. The production and release of mediators such as reactive oxygen intermediates (ROI) and nitric oxide (NO) as well as of chemotactic factors (i.e. IL-8) by epithelia in response to ozone might be contributory to these two observed responses. The present study was designed to investigate the effects of O_3 exposure on epithelial NO release, IL-8 production, as well as disruption of the epithelial permeability barrier. A Human type II-like cell line (A549) was grown to a monolayer in Costar Transwells (Costar, Cambridge, MA) and exposed to 0.4 ppm O_3 for 1 hour. Epithelial resistance was measured using a "chopstick" voltohmmeter (World Precision Instruments, Sarasota, FL). Resistance was decreased 72 hours after exposure (91.4 Ω cm^{2-1}) as compared to before the O_3 exposure (193.2 Ω cm^{2-1}) in unstimulated cells. No change was observed in non-exposed cell. Additionally, the effect of O_3 on NO release by epithelial cells was assessed. Immediately after exposure, A549 cells were stimulated with cytomix (IL-1β, TNFα, IFNγ, all at 10 ng/ml) for 72 hours and the nitrite content was determined in the basolateral media. O_3 exposed A549 cells showed an increased nitrite content (1.338 μM) as compared to non-exposed cells (0.846 μM). These results indicate the airway epithelium as a target as well as an effector cell of ozone toxicity in the lower airways. (Sponsored by EPA R819342).

1378 AIRWAY INFLAMMATION AFTER EXPOSURE TO OZONE — CYTOKINE mRNA PRODUCTION IN LUNG CELLS

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Animal and human studies have shown that acute inhalation of ozone causes airway inflammation and tissue damage, lung function decline, and airway hyperreactivity. Although these responses are also considered as important components in the pathogenesis of asthma, spirometric data following ozone exposure do not show that asthmatics are more susceptible than healthy people. Cytokines are thought to play a role in ozone-induced airway inflammation and structural tissue damage. Therefore, studies were initiated to investigate the airway inflammatory cell and mediator response to ozone and to develop (early) markers for (asthmatic) susceptibility.

In cells from lung lavages as well as in lung tissue from ozone exposed rats (6 hours, 2400 μg/m^3 O_3), changes in cytokine mRNA levels (IL-1α, IL-6, IL-12p40, TNF-α, TGF-β, and the chemokine KC) were assessed upon exposure by a semiquantitative RT/PCR using GAPDH as internal control. In cells from lung lavages increased levels were found for IL-6, IL-12p40, and KC mRNA, whereas decreased levels were found for IL-1α mRNA. No changes were found in TNF-α and TGF-β mRNA levels. In lung tissue increased levels were found for IL-1α and IL-6 mRNA, whereas decreased levels were found for IL-12p40 mRNA. No changes were found in TNF-α, TGF-β, and KC mRNA levels.

Data show that acute ozone exposure is able to induce pulmonary inflammatory mediator signals involved in cellular and immunological defense.

Future studies will include mRNA production of additional cytokines, in situ hybridization, and protein measurements.

SOCIETY OF TOXICOLOGY

34th Annual Meeting

THE TOXICOLOGIST

Volume 15, No. 1, March 95

FUNDAMENTAL AND APPLIED TOXICOLOGY

THE TOXICOLOGIST

An Official Publication of the Society of Toxicology

and

Abstract Issue of

FUNDAMENTAL AND APPLIED TOXICOLOGY

An Official Journal of the Society of Toxicology

Published by Academic Press, Inc.

Abstracts of the
34th Annual Meeting
Vol. 15, No. 1, March 95

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 34th Annual Meeting of the Society of Toxicology, held at the Baltimore Convention Center, Baltimore, Maryland, March 5-9, 1995.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 327.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 351.

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