was to develop a system that allows for the generation of primary combustion particles followed by controlled dilution and conditioning, and subsequent whole-animal inhalation exposure. In these pilot studies a heavy oil # 5 was burned in a residual oil combustor previously shown to produce approximately 150 mg/m3 of PM. The particles were then passed through a 2.2 μM cyclone and diluted with clean ambient air. The resulting PM was then directed to a Hinners animal exposure chamber equipped for continuous monitoring of O_2, Co., CO_2, NO_x, SO_2, as well as total particle concentrations. Mean PM 2.5 concentrations ranged between 2 and 3 mg/m-3 with 40-50 ppm SO_2 and 20-30 ppm NO_x. Balb/C and CD1 mice were exposed to the combustion atmosphere for 4 hrs and immediately and 24 hr later assessed for acute lung injury (both strains) and susceptibility to Streptococcus zooepidemicus infection (CD1 strain). Exposure to the emission atmosphere caused a significant increase in neutrophils and lactate dehydrogenase (LDH) in bronchoalveolar lavage (BAL) of both strains of mice but did not affect levels of protein. Mortality to infection was low in all animals and was not affected by the emission exposure. We conclude that this acute exposure caused mild pulmonary injury and inflammation in a similar fashion to other oxidant pollutants but did not affect host defenses to streptococcal infection. Future studies will determine the relative contribution of gases *versus* particles on these inflammatory responses, and will test whether animals with other forms of cardio-pulmonary disease are further compromised by such exposures. This abstract does not necessarily reflect EPA policy.

1733 COMPARISON OF SINGLE AND MULTIPLE EXPOSURES OF CONCENTRATED AIR PARTICLE (CAPS)ON PATHOPHYSIOLOGIC RESPONSES IN HEALTHY RATS.

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Several studies have reported that exposure to CAPS from various cities causes pulmonary inflammation in rats. The purpose of this study was to determine whether CAPS from the Research Triangle Park area could cause similar effects, and to compare responses between single and multiple CAPS exposures. Using a 4 stage Harvard concentrator system which concentrated particles 80-fold, male Sprague-Dawley rats were exposed to CAPS for 4 hours, 3 times a week for 5 weeks. During the last 2 exposures (chamber concentrations of 0.57 and 1.7 mg/m3 respectively), additional groups of animals were exposed to CAPS or clean air and their acute pulmonary inflammatory responses (18 hr post-exposure)were compared to animals which had been exposed for the entire 5 week period. After 2 and 4 weeks of exposure, animals monitored with a Buxco plethysmograph system showed a small exposure-related decline in enhanced pause values, suggesting an alteration in ventilatory function. At necropsy, no changes were apparent in bronchoalveolar lavage levels of protein and LDH. The higher CAPS concentration however, caused an increase in pulmonary alveolar macrophage and neutrophils. This effect seemed to be driven by the last exposure as animals exposed 14 times to CAPS prior to this exposure did not have significantly greater responses. Further, exposure to the lower concentration had no effect indicating either; a Dose-Response effect, or changes in the physico-chemical makeup of the PM over the last 2 exposures. Other significant differences included a decrease in lung ascorbate levels following acute exposure to the higher CAPS concentration, and an acute, transient increase in plasma fibrinogen levels. The data show that acute CAPS exposure causes a dose-dependent pulmonary infiltration of cells, depletion of anti-oxidants, and increased potential for systemic coagulation. These effects did not appear to be worsened with multiple exposures. This abstract does not reflect EPA policy

1734 PARTICULATE 1->3-β-GLUCAN IS THE MORE POTENT FORM FOR INDUCING PULMONARY INFLAMMATION IN RATS.

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1->3-β-Glucans, derived from the inner cell wall of yeasts and fungi, are commonly found in indoor air dust samples and have been implicated in organic dust toxic syndrome. In a previous study, we reported that 1->3-β-glucan (zymosan A) induced acute pulmonary inflammation in rats. The present study investigates which form of 1->3-β-glucans, particulate or soluble, is more potent in inducing pulmonary inflammation. Zymosan A was suspended with 0.25 N NaOH for 30 min, neutralized, dialyzed for 2 days against deionized water, and particulate and soluble fractions collected. Male Sprague-Dawley rats were exposed *via* intratracheal instillation to NaOH-soluble or NaOH-insoluble zymosan A (1.8 mg/ml, 0.26 ml). At 18 hrs post-exposure, various indicators of pulmonary response were monitored, including indicators of lung damage, such as serum albumin concentration and lactate dehydrogenase activity in acellular bronchoalveolar lavage fluid. Inflammation was characterized by an increase in lavageable polymorphonuclear leukocytes (PMN), pulmonary irritation (breathing frequency increase) and oxidant production (nitric oxide and chemiluminescence (CL)). Exposure to the particulate fraction of NaOH-treated zymosan caused a significant increase in all these indicators. In contrast, rats exposed to the NaOH-soluble fraction did not show significant increase for most of these indicators except for albumin, PMN and CL. However, these increases were significantly smaller than with exposure to NaOH-insoluble zymosan. Therefore, the results demonstrate that particulate zymosan A is more potent in inducing pulmonary inflammation and damage in rats than the soluble form of this β-glucan.

1735 VANADIUM-INDUCED PULMONARY INFLAMMATION AND APOPTOSIS IN MICE.

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Pulmonary exposure to vanadium and vanadium-containing compounds is associated with acute pulmonary inflammation, characterized by a rapid influx of polymorphonuclear neutrophils with a peak response at 6 h and resolution by 3 d. Sodium metavanadate [V (V)] can induce cell apoptosis *in vitro*, but little is known about relationship of V (V) and lung cell apoptosis *in vivo*. We hypothesized that vanadium may induce lung cell apoptosis through reactive oxygen species (ROS) *in vivo* and neutrophil apoptosis is involved in the resolution of vanadium-induced lung inflammation. To test this hypothesis, mice were treated with V (V) or saline control, and the bronchoalveolar lavage (BAL) cells were examined at various times for short-lived free radicals by electron spin resonance (ESR) and for apoptosis using terminal deoxyribonucleotidyl transferase-mediated nick end labeling (TUNEL). Control mouse BAL cells showed no significant free radical activity and only resident alveolar macrophages in the BAL fluids with no evidence of apoptosis. In contrast, V (V) induced a greater level of free radicals and caused apoptosis of BAL cells which are predominantly neutrophils. Catalase blocked both free radical generation and apoptosis induced by V (V). The number of apoptotic cells gradually increased and reached a maximal level by 24 h where it subsequently declined. After 24 h when the vanadium-induced lung inflammation was in the resolution phase, we observed an increased influx of macrophages and their engulfment of apoptotic bodies in the BAL fluid. At 72 h when the total number of neutrophils fell to the baseline level, remnants of apoptotic bodies could still be seen in the cytoplasm of macrophages. We conclude that (1): ROS, like H_2O_2, are one of causes of apoptosis induced by vanadium; (2): apoptosis of neutrophils and clearance by macrophages is an important mechanism in the resolution of vanadium-induced lung inflammation.

1736 SYMPATHETIC NERVOUS SYSTEM PLAYS A MAJOR ROLE IN ACUTE COLD/RESTRAINT STRESS INHIBITION OF HOST RESISTANCE TO *LISTERIA MONOCYTOGENES*.

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Multiple studies have demonstrated that both glucocorticoids and norepinephrine (NE) can modulate immune responses *in vitro* and *in vivo*, and it is well known that the sympathetic nervous system innervates both primary and secondary lymphoid organs. Here, we show that acute cold/restraint stress (ACRS) significantly lowers host resistance to *Listeria monocytogenes* (*LM*) in BALB/c mice, and the involvement of stress hormones corticosterone (CORT) and NE is evaluated. CORT and NE were investigated by pretreating mice with the CORT synthesis inhibitor metyrapone and the chemical sympathectomy drug 6-hydroxydopamine (6-OHDA), respectively. *LM* burdens were determined 3 days post-infection. 6-OHDA significantly decreased the *LM* burden in both control and stressed animals. 6-OHDA also completely blocked the stress effects observed in spleens while only partially affecting the liver. The 6-OHDA-uptake inhibitor desipramine confirmed that peripheral sympathetic adrenergic nerves and NE depletion and not the nonspecific 6-OHDA toxicity were responsible for the enhanced host defense. In contrast, metyrapone-treated animals had further decreased host resistance to *LM* after ACRS. The results suggest that the peripheral sympathetic nervous system (SNS) postganglionic neurotransmitter NE plays a major role in *LM* host resistance, but there are significant tissue-dependent effects after ACRS, while CORT provides a potential protective effect after ACRS. Altogether, stress hormones play important roles in stress-modulated host resistance and NE is a major hormone involved in ACRS-induced suppression of host resistance in the spleen but not the liver. (Supported by NYSDOH and NIEHS ES15-3506A).

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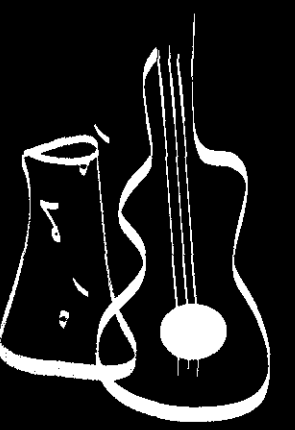

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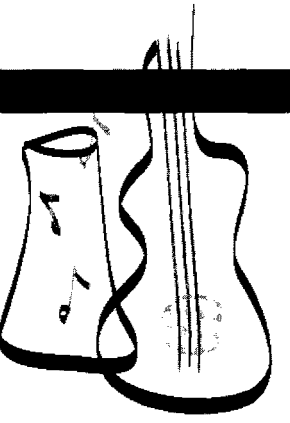

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Preface

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 41st Annual Meeting of the Society of Toxicology, held at the Opryland Hotel and Convention Center, Nashville, Tennessee, March 17–21, 2002.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 385.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 411.

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

Additional Late-Breaking Abstracts are issued in a supplement to this publication and are available at the 41st Annual Meeting and through the Society of Toxicology Headquarters office.

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