

terminations during the exposure phase or recovery phase of the study. However, pathological effects were observed at all concentrations in nVC exposed rats of both sexes. The effects were confined to the upper respiratory tract and consisted of degeneration/necrosis of olfactory epithelium, mucoid depletion of goblet cells, and squamous metaplasia and hyperplasia of respiratory epithelium in the anterior nasal passages and squamous metaplasia of the larynx. At the end of the four-week recovery period, the depletion of goblet cells in noses of female rats was no longer present, and was of decreased severity in the male rats, however, the olfactory epithelial degeneration/necrosis was still present in both sexes. Further work is underway to determine a no-effect level for nVC exposure in rats.

943 DIMETHYL GLUTARATE (DMG), DIMETHYL SUCCINATE (DMS), AND DIMETHYL ADIPATE (DMA): 90-DAY INHALATION TOXICITY STUDY IN RATS.

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Groups of male and female rats were exposed *via* inhalation to 0, 10, 50, or 400 mg/m³ DMG, 400 mg/m³ DMS, or 400 mg/m³ DMA for 6 hrs/day, 5 days/wk over a 90-day period. The exposure period was followed by a 1-month recovery period. Rats were evaluated for clinical signs and growth throughout the study. Samples for hepatic, lung, and nasal cell proliferation (CP) were collected from rats approximately 2 weeks and 90 days after study initiation. Clinical pathology, anatomical pathology, male reproductive endpoints, neurobehavioral assessments, neuropathological evaluation, estrous cycle, and hormonal analyses were conducted during the study. No compound-related effects were observed on mortality, clinical signs, clinical pathology, neurobehavioral endpoints, neuropathology, sperm motility or morphology, or estrous cycle. Male rats exposed to 400 mg/m³ DMG had lower mean body weights and mean body weight gains during the study. Compound-related focal and minimal effects were observed in the noses of rats exposed to 400 mg/m³ of DMG, DMS, or DMA for 90 days. CP in the noses of rats exposed to 400 mg/m³ of DMG, DMS, or DMA was increased compared to controls during the study. In male rats exposed to DMG, serum testosterone concentrations were statistically significantly decreased at concentrations of 50 and 400 mg/m³. Serum luteinizing hormone concentrations were decreased in a dose-dependent manner and were statistically significantly decreased at 400 mg/m³. In female rats, DMS caused a statistically significant decrease in serum estradiol concentrations. There was an increase in epididymal sperm counts following exposure to DMG and the number of sperm per cauda and per gram cauda epididymis was significantly increased at 50 and 400 mg/m³. In male rats exposed to DMS, epididymal sperm counts were significantly increased. In this study, the no-observed-effect level (NOEL) for repeated exposure to DMG was 10 mg/m³. NOELs for DMS and DMA were not established. Sponsored by the Dibasic Esters Group, Washington DC.

944 ROLE OF SENSORY NERVES IN THE AIRWAY AND CARDIAC RESPONSES TO SULFUR DIOXIDE (SO₂) IN A GUINEA PIG MODEL.

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Sulfur Dioxide (SO₂) is a common component of polluted urban air. Exposure to SO₂ has been shown to significantly alter airway compliance and resistance. Recently, high concentrations of SO₂ during air pollution episodes have been associated with heart rate elevation. Using non-invasive methodology, our laboratory has previously shown that exposure to SO₂ produces a concentration dependent increase in airway resistance and a significant decrease in breathing frequency. The purpose of our current study is to: 1) determine if exposure to SO₂ produces simultaneous changes in airway and cardiac function and, 2) ascertain the role of sensory nerves in these responses. To this end, guinea pigs were surgically implanted with radiotelemeters capable of transmitting ECG, heart rate and core body temperature data in 1-minute intervals. Animals were then exposed to either 0 or 100 ppm SO₂ in the head-space of a double-chamber plethysmograph. Airway and cardiac function were monitored continuously for a 10-minute baseline period and the 60-minute exposure period. Exposure to SO₂ produced a significant decrease in heart rate during the second half of the exposure period (p<0.05). To determine the role of sensory nerves in these responses, animals were pretreated with the neurotoxin, capsaicin (total dose 125 mg/kg sc). Pretreatment with capsaicin significantly diminished the SO₂-induced increase in SRAW and decrease in breathing frequency (p<0.05). In addition, capsaicin pretreatment attenuated the SO₂-induced decrease in heart during the second half of the exposure period (p<0.05). In summary, these results suggest that exposure to SO₂ produces simultaneous changes in both airway and cardiac function and that stimulation of sensory nerves play a role in both of these responses. (Funded by the NCSU/EPA Cooperative Training Program CT826512010.) (This abstract does not reflect EPA policy.)

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EFFECTS OF WELDING FUMES ON LUNG INJURY AND INFLAMMATION: THE POSSIBLE ROLE OF FREE RADICAL PRODUCTION.

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The goals of this study were to examine lung damage and inflammation as well as free radical production caused by welding fumes of different composition. Fume was collected during flux-covered manual metal arc welding using a stainless steel consumable electrode (MMA-SS) and gas metal arc welding using a mild steel electrode (GMA-MS) or a stainless steel electrode (GMA-SS). Metal composition analysis by energy dispersive spectroscopy revealed that only MMA-SS was highly soluble, containing both soluble Cr and Mn, while GMA-MS and GMA-SS were relatively insoluble. Using electron spin resonance, hydroxyl radicals were observed in a suspension of MMA-SS fume containing hydrogen peroxide. Both GMA fumes showed no evidence of free radical production. To examine the effects of the fumes on lung damage and inflammation, male Sprague-Dawley rats were intratracheally instilled with either a welding fume suspension at 2 mg/rat or the saline vehicle. On day 3, the right lung was assayed for lipid peroxidation (LPO) products while the left lobes were subjected to bronchoalveolar lavage (BAL). LPO products were elevated in the lungs following MMA-SS treatment only, implicating possible oxidative damage. All fumes caused increases in BAL cell number, including elevated macrophage and neutrophil recovery. However, only MMA-SS led to an increased recovery of eosinophils, indicating a possible immune reaction. MMA-SS treatment caused an elevation of albumin in the first BAL fraction, indicating damage to the alveolar-capillary barrier, while all fumes produced an increase in lactate dehydrogenase activity in that fraction. Total protein in the first BAL fraction was most elevated following MMA-SS treatment. These findings indicate that different welding fumes caused varied responses in the lungs of rats, and that these responses may be correlated to the soluble metal composition of the fume and the ability of the fume to produce free radicals.

946 TEMPORAL CHANGES IN BAL ELECTROLYTE LEVELS IN MICE AFTER EXPOSURE TO AN IDEMAGENIC GAS.

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Detection of acute lung injury is important if therapeutic medical countermeasures are to be used to reduce toxicity in a timely manner. Indicators of injury may aid in the eventual treatment course and enhance the odds of a positive outcome following a toxic exposure. This study was designed to investigate the effects of a toxic exposure to the industrial irritant gas phosgene on the electrolyte levels in bronchoalveolar lavage (BAL) fluid. Phosgene (CG) is a well-known chemical intermediate capable of producing life-threatening pulmonary edema within hours after exposure. Four groups of 40 each CD-1 male mice were exposed whole-body to either air (A) or a concentration x time (c x t) amount of 32 mg/m³ (8 ppm) CG for 20 min (640 mgxmin/m³). BAL from A- or CG-exposed mice was taken at 1, 4, 8, 12, 24, 48, and 72 h postexposure. After euthanasia, the trachea was excised, and 800 ul of saline was instilled into the lungs. The lungs were washed 5x. Eighty ul of BAL was placed in a cartridge and inserted into a clinical I-STAT analyzer. Na⁺, K⁺, Cl⁻, and ionized Ca⁺⁺ were analyzed within 2 minutes of insertion. The left lung was removed to determine wet weight (WW), an indicator of pulmonary edema. Temporal changes in BAL Na⁺ and Cl⁻ in CG mice were not statistically different from those in the A mice. Both Ca⁺⁺ and K⁺ were significantly higher than in the A mice over 72 h, p<.03 and p<.001, respectively. Significant changes in BAL Ca⁺⁺ and K⁺ occurred as early as 4 h postexposure in CG, p<.05, versus A mice. CG caused a time dependent significant increase in WW from 4-12 h, p<.05, compared with A mice. BAL Ca⁺⁺ at 1 hr in CG-exposed was 60% higher than in the time-point matched A mice. These data indicate that measuring BAL electrolyte levels may serve as an alternate indicator of lung injury since both Ca⁺⁺ and K⁺ follow temporal increases in tissue damage. In addition, knowledge of these levels may indicate how rational therapeutic intervention could be most beneficial.

947 OZONE EXPOSURE ENHANCES ANTIGEN-PRESENTING ACTIVITY ON BRONCHOALVEOLAR LAVAGE CELLS CONCENTRATION DEPENDENTLY IN RATS.

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Previous studies have shown that O₃ exposure aggravates allergy like diseases such as asthma and rhinitis. Our previous studies have shown that expression of cell-surface molecules associated with antigen presentation on bronchoalveolar lavage cells

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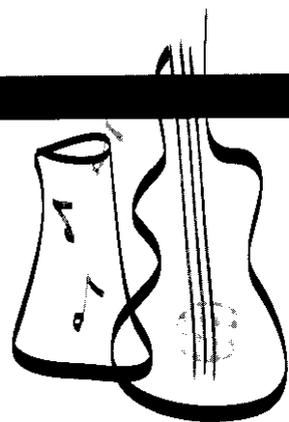


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An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 385.

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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