

(BAL cells) is increased by exposure to O<sub>3</sub> in rats. The present study designed to investigate concentration dependencies of the effect of O<sub>3</sub> on the expression of cell-surface molecules associated with antigen presentation and on accessory activity of BAL cells. Male Wistar rats were exposed to 0.3, 0.56, 1 ppm O<sub>3</sub> or filtered air for 3 days. Expression of cell-surface molecules (Ia, B7.1, B7.2, and CD11b/c) was measured by flow cytometry. Accessory activity of BAL cells was assessed by the allogeneic mixed lymphocyte reaction (MLR) and ovalbumin (OVA)-specific antigen-presenting activity. The numbers of Ia<sup>+</sup>, B7.2<sup>+</sup>, CD11b/c<sup>+</sup>, Ia<sup>+</sup>/B7.2<sup>+</sup>, and Ia<sup>+</sup>/CD11b/c<sup>+</sup> BAL cells were increased by O<sub>3</sub> exposure concentration dependently. The accessory activity of BAL cells measured by MLR and OVA-specific antigen-presenting activity was also enhanced by O<sub>3</sub> exposure concentration dependent manner. These results suggest that the enhancement of antigen-presenting activity of BAL cells is caused by the increasing of expression of cell-surface molecules associated with antigen presentation by O<sub>3</sub> exposure. This enhancement may trigger the subsequent immune response that could make worse allergic asthma and rhinitis.

#### 948 ULTRASTRUCTURAL CHANGES IN THE AIRWAYS OF RATS INHALING BUTTER FLAVORING VAPORS.

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A cluster of eight cases of fixed airway obstruction occurred in former workers in a microwave popcorn plant. As part of a request to NIOSH to find the cause, extensive medical and environmental measurements were made at the plant. High levels of organic gases and decreased pulmonary function among workers were associated with butter flavoring in use at the plant but other exposures existed. To assess the biological effects of the flavoring, we exposed rats by inhalation for 6 hours to butter flavoring vapors. Qualitative GC-MS analysis yielded a variety of organic gases including diacetyl and acetoin. Average diacetyl concentration in the exposure chamber was about 350 ppm. By transmission electron microscopy (TEM), the principal finding in the mainstem bronchus of exposed rats was airway epithelial necrosis. Unusual features of the epithelial alterations included rarefaction of basilar cytoplasm and relative preservation of cilia. Denuded basement membrane was frequently observed although a thin fragment of basilar cytoplasm of respiratory epithelium remained attached in some foci. Damage in the mainstem bronchus extended beneath the basement membrane into the lamina propria where edematous changes were characterized by disorganization and separation of collagen fibers and fibrils. Necrotizing changes were less frequent in smaller airways. By scanning electron microscopy (SEM), ulceration of bronchiolar epithelium tended to be localized at bronchiolar bifurcations. No evidence of alveolar injury was evident in TEM or SEM sections. These findings document that artificial butter flavoring, while considered safe to consume at concentrations present in food, produces vapors capable of inducing severe airway injury in laboratory animals when inhaled at high concentrations similar to peak exposures in the workplace.

#### 949 SPECIES DIFFERENCE IN ACUTE RESPIRATORY RESPONSES TO VAPOR AND AEROSOL IRRITANTS BETWEEN RATS AND MICE.

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This study was to compare acute respiratory responses upon exposure to a vapor (cumene) or an aerosol (vanadium pentoxide, V<sub>2</sub>O<sub>5</sub>) irritant between young male F344 rats and SW mice. Animals (4/species/chemical/dose/timepoint) were exposed to either chemical and their tidal volume (TV), respiratory rate (RR), and minute volume (MV) were measured. For cumene exposure, respiratory function was measured for 10-min preexposure and during 30-min nose-only inhalation exposure to 100 or 300 ppm cumene. For V<sub>2</sub>O<sub>5</sub> exposure, animals were exposed *via* intratracheal instillation (0, 0.63, or 6.3 mg V/kg in saline) and respiratory function was measured 1 and 3 days post dosing. For V<sub>2</sub>O<sub>5</sub>-instilled mice, bronchoalveolar lavage (BAL) was performed, and data were compared with those from V<sub>2</sub>O<sub>5</sub>-instilled rats under the same study design (Lee et al., 2000). Cumene exposure at both concentrations significantly depressed TV and RR of mice, resulting in 39-41% reduction in MV compared to preexposure baseline. In rats, reduced respiratory function was observed only at 300 ppm (38% reduction in MV). For V<sub>2</sub>O<sub>5</sub>-instilled mice, respiration became rapid (RR ↑) and shallow (TV ↓), which was most severe with the high-dose group on day 1 (MV reduced by 37% compared to saline-instilled controls). Signs of pulmonary inflammation (increases in LDH, NAG, protein, and neutrophil count in BAL fluid) were also observed in V<sub>2</sub>O<sub>5</sub>-instilled mice. For V<sub>2</sub>O<sub>5</sub>-instilled rats, rapid and shallow breathing was most severe in high-dose group on day 3 (MV reduced by 43%). Therefore, although acute respiratory responses between rats and mice varied depending on the exposure concentration and time, mice appeared to be more sensitive in terms of modifying respiratory functions or inducing inflammatory responses upon single exposure to these respiratory irritants.

#### 950 INITIAL CONCENTRATIONS AND DISAPPEARANCE OF SELECTED MALODOROUS COMPOUNDS FROM FRESH AND AGED DAIRY MANURES.

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Malodorous compounds from livestock manures are offensive and can cause health hazards to humans and cattle. Changes of manure storage and handling methods may prevent the formation and/or enhance the degradation of odors. This study was to quantify volatile fatty acids (VFAs), phenol, cresols, indoles and NH<sub>3</sub> in and emitted from fresh and 12-day-aged manure. Loss of these compounds was monitored during pilot-scale composting in 205 L vessels either aerated continuously (AC) with high (2.3 kg/hr)/low (0.8 kg/hr) air flow controlled by thermostats or intermittently (AI) on a 5 min high air flow 55 min off cycle. Manures were mixed with sawdust (3:1, w/w). Six replicates were conducted on each treatment combination, with 16 day trials. Emissions from the composting masses were measured. FID/GC was used to analyze VFAs in condensates and pH 2 water extracts of solids. Ether extracts of phenolics and indolics were quantified by GC/MS. Mean NH<sub>3</sub> emissions from fresh and aged manure AI were 50 and 60 g. Fresh and aged manure AC emitted 121 and 110 g NH<sub>3</sub>. NH<sub>3</sub> peaked early and decreased to undetectable by day 17. Aged, compared to fresh manure, contained greater varieties and amounts of VFAs, phenols and indoles with the most offensive odors. Fresh manure contained acetate, propionate, isobutyrate, isovalerate, phenol, p-cresol, and indole (5000, 500, 40, 70, 35, 200 and 5 µg/g). Aged manure contained acetate, propionate, isobutyrate, butyrate, isovalerate, valerate, phenol, p-cresol, indole and skatole (9000, 2700, 200, 2500, 2800, 350, 50, 350, 10 and 30 µg/g). By day 8, trace quantities of acetate remained in fresh manure, while acetate, propionate and butyrate (900, 120 and 130 µg/g) were in aged manure. Acetate, propionate and butyrate co-distilled with water being highest from aged manure. Bioprocesses associated with AC and AI influenced the loss of certain chemicals. Avoiding anaerobic aging of dairy manure was important in reducing concentrations of the chemicals studied.

#### 951 WHOLE BODY EXPOSURE SYSTEM FOR ADMINISTERING NITRIC OXIDE (KINOX®) BY INHALATION TO NEONATE RATS.

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A whole body exposure system has been designed in order to expose neonate rats to controlled concentrations of nitric oxide for inhalation toxicity studies and to prevent levels of the oxidation product NO<sub>2</sub> rising above 1 ppm for an atmosphere containing 100 ppm NO. The exposure chambers comprise a polycarbonate nesting box with a perforated floor and a pyramidal lid incorporating a gas mixing chamber. Each exposure chamber accommodates a dam plus litter. A nitric oxide/nitrogen mixture of known concentration, oxygen and clean air are mixed and pass into the chamber *via* a duct in the chamber lid. The atmosphere is exhausted through the perforated floor. Gas flow rates are set to ensure a minimum residence time in the chamber to prevent NO<sub>2</sub> build up while maintaining temperature and relative humidity in the chamber conducive for exposure of animals. The NO/N<sub>2</sub> mixture, oxygen and airflow rates are controlled, monitored and recorded throughout exposure. An automated sampling and data capture system monitors the chamber concentrations of NO and NO<sub>2</sub> in real time. An inhalation toxicity study was conducted where neonate rats were exposed for 6 hours a day with dams from Days 2-10 *post-partum* and litters alone from Days 11-29 *post-partum*, target levels of NO were 10, 30 and 100 ppm. Mean achieved concentrations of NO were 10.2, 30.3 and 100.2 ppm. Concentrations of NO<sub>2</sub> were 0.0, 0.2 and 1.1 ppm. In conclusion, the study results demonstrate that the system is capable of excellent control of NO concentration and can maintain the required low levels of NO<sub>2</sub>.

#### 952 ALDEHYDE DEHYDROGENASE (ALDH2) POLYMORPHISM AND THE PULMONARY EFFECTS ASSOCIATED WITH EXPOSURE TO ETHANOL VAPORS IN THE RAT.

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Addition of ethanol to gasoline aiming at reducing the greenhouse effect is likely to increase atmospheric emissions of ethanol and acetaldehyde. By converting acetaldehyde to acetate ALDH2 plays a major role in the metabolism and toxicity of EtOH. A significant polymorphism exists in both humans and rats. In the latter, a

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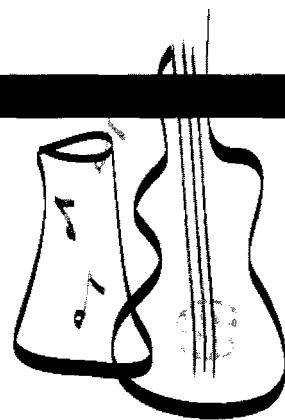


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## *Preface*

**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 41<sup>st</sup> 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.**

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