

binding 1 hr, 1 day, 3 and 7 days after treatment. Studies on other possible CO targets (such as cGMP) are in progress in order to identify valuable peripheral biomarkers of central effect (Supported by grant QLK4-CT99-01356 from the European Commission).

1391 SENSITIVE EARLY INDICATORS OF HEPATIC AND KIDNEY DAMAGE IN WORKERS EXPOSED TO JET FUEL(JP-8).

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Jet Propellant type 8 (JP-8) is used for all US military operations. Because of the widespread exposure and concern for potential health effects, three hundred twenty-four US Air Force (USAF) active duty personnel participated in a study at six USAF bases between April and September, 2000. Animal & human studies suggest that exposure to fuels and solvents can adversely effect the liver and kidney. Glutathione transferase (GST) isoenzymes possess specific patterns of distribution in organs and are released to biological fluids in response to toxic insult. ELISA techniques can be used to measure those GSTs associated with liver and kidney damage. Pre- and post-shift serum and urine samples were collected from USAF personnel and commercial GST assays were used to measure alpha GST in serum (marker for liver damage) and alpha and pi GST in urine which are associated with proximal and distal tubule damage, respectively. Exposed workers were tank-entry personnel with at least nine months of persistent exposure to jet fuel; the unexposed group were USAF personnel with no significant exposure to fuels or solvents. Levels of serum hepatic alpha-GST, and urinary nephritic alpha- and pi-GST in the study subjects fell within the normal range for healthy subjects. No differences were observed indicative of liver or kidney damage attributable to any of the exposure, lifestyle and other demographic variables examined. Creatinine, used to normalize urinary GSTs was elevated in post-shift samples from the highest exposure category. This study group represents a very healthy segment of the population. Sensitive measures for liver and kidney damage did not detect any adverse effects in this study group. Evidence of elevated creatinine in the mean post-shift samples of the high exposure category was seen. However, while these values are within normal clinical ranges, they are consistent with concentrated urine indicative of mild dehydration.

1392 A BIOLOGICAL LIMIT VALUE (BLV) FOR OCCUPATIONAL EXPOSURE TO PERFLUOROOCTANOATE.

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A biological limit value (BLV) of 5 ppm for perfluorooctanoate (PFOA) in the serum of workers has been established by 3M. Ammonium PFOA (APFO) is a polymerization aid used in fluoropolymer production. The 3M BLV represents the best scientifically-based estimate of a concentration of PFOA in a biological fluid (serum) that, if present, even on a chronic basis, is not expected to correlate with a risk of adverse health effects in workers. Serum levels above the 5 ppm BLV do not necessarily imply a health risk. A significant body of toxicological, epidemiological, and medical surveillance information is available for PFOA and APFO to support a BLV of 5 ppm PFOA in serum. The results of toxicology studies indicate that the major target organ of APFO is the liver. Oral administration of APFO to monkeys at 3 and 10 mg/kg/d for six months resulted in mean serum concentrations of approximately 50 and 70 ppm, respectively, and was associated with increases in both absolute liver weight and liver-to-body weight ratios without gross or histopathological abnormalities or changes in clinical chemistries. Approximately 90 percent of 3M workers exposed to APFO have had serum PFOA levels below 10 ppm. Investigators have not observed any exposure-related clinical hepatic toxicity or hormonal changes in these workers. The repeated analyses, to date, provide reasonable assurance that workers with serum PFOA levels below 10 ppm do not experience exposure-related clinical hepatotoxicity; however, there have been too few employees with serum PFOA concentrations above 10 ppm to draw statistically-significant conclusions regarding a lack of clinical hepatotoxic effects with serum PFOA levels at or above 10 ppm.

1393 DIFFERENT RESPONSES IN THE PATTERN OF EXPRESSION OF P53 CHALLENGED WITH ARSENIC.

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Different pattern of expression of the p53 protein were observed when lymphocyte cultures were challenged with arsenic. To evaluate the reproducibility of this effect we determined the presence of p53 in blood samples from 22 healthy individuals,

using 4 different treatment conditions: (1) non-stimulated lymphocytes (Go); (2) lymphocytes stimulated with phytohemagglutinin during 48h (Control); (3) stimulated lymphocytes treated with arsenic(As); or (4) with actinomycin-D (AcD) during the last 24h. Proteins were obtained at the end of culture, and measured by immunoblot. Data show three different patterns of p53 expression: I) 16 individuals had bands in As and AcD treated cultures but not in Go; II) 4 individuals in addition to the previous pattern, showed a band in Go; III) 2 donors did not show any p53 response. No relation of these expression-pattern differences with cell proliferation could be established. Since we have found a higher frequency of polymorphisms in the intron 1 (Bgl II P53) among breast cancer patients, we analyzed the p53 expression in females with and without polymorphism. No relationship among both parameters was found. The expression of p53 in lymphocyte cultures could be of relevance in the understanding of individual susceptibility to xenobiotics and might have a great potential as a biomarker.

1394 BIOMARKER CHARACTERIZATION OF ASPHALT FUME EXPOSURE.

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Each year more than 60 million tones of asphalt are produced and used worldwide. It has been estimated that approximately two million workers were employed and potentially exposed to asphalt. Health concern from exposure to asphalt is related to its content of hazardous chemicals, such as polycyclic aromatic hydrocarbons (PAHs). The development of a biomarker to provide an assessment of the integrated external exposure following uptake by living system through inhalation is valuable for this kind of complex mixture exposure. Many PAHs are metabolized to hydroxyl-PAHs and excreted in urine; therefore, urinary hydroxyl-PAH was used as a biomarker for asphalt fume exposure in this study. Female Sprague-Dawley rats and B6C3F1 mice were exposed to asphalt fume in a whole body inhalation chamber for 5 or 10 days (3.5 hrs/day, 71-97 mg/m³). Clean air chamber animals were used as controls. The test asphalt was the type used by paving industry throughout the Midwestern United States. The fume was generated under simulated road paving conditions. Urine sample preparation for the analysis of hydroxyl-PAHs metabolites included enzymatic digestion, solid phase extraction, and isotope dilution GC/MS and microflow LC-Q-TOF MS detections. Four priorities PAH metabolites, including, 1-hydroxypyrene, 9-phenanthrenol, 1-chrysenol, and 2-naphthalenol were identified and determined in urine. Isotope-dilution has proved to be useful for quantification of those metabolites. Preliminary results indicated that urinary PAH metabolite could be a sensitive biomarker following asphalt fume exposure. The method developed in this study has potential application to monitor of PAHs from occupational mixture exposure.

1395 BIOMARKERS OF OXIDATIVE STRESS STUDY: ARE OXIDATION PRODUCTS OF LIPIDS MARKERS IN CCL4 POISONING?

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Oxidation products of lipids in plasma and urine of rats were measured as part of a comprehensive, multilaboratory validation study searching for non-invasive biomarkers of oxidative stress. This is the second report of the nationwide Biomarkers of Oxidative Stress Study (BOSS). The time (2, 7, and 16 h) and dose (120 and 1200 mg/kg ip)-dependent effects of CCl₄ on concentrations of lipid hydroperoxides, TBARS, malondialdehyde (MDA) and isoprostanes were investigated with different techniques. Plasma concentrations of MDA and isoprostanes (measured by GC/MS) and urinary concentrations of isoprostanes (measured with an immunoassay) were increased in CCl₄ treated rats in a time- and dose-dependent manner. All other products were not changed by CCl₄ or showed only high-dose and/or single time point effects. It is concluded that measurements of MDA and isoprostanes concentrations in plasma and urinary isoprostanes are promising candidates for general biomarkers of oxidative stress. Acknowledgements: B Ames¹, N Brot², G Fitzgerald³, R Floyd⁴, M George⁵, G Hatch⁶, J Heineke⁷, K Hensley⁸, J Lawson³, L Marnett⁸, J Morrow⁹, D Murray¹⁰, J Plastaras⁸, L J Roberts², M Shigenaga¹, R Sohal¹¹, Jie Sun¹⁰, R Tice¹², D H Van Thiel⁵, D Wellner¹³, P Walter¹⁴. ¹Children's Hospital Oakland Res. Inst., Oakland, CA., ²Hospital for Special Surgery and Department. Microbiol. Immunol., Weill Med., College of Cornell University, NY, NY., ³Center for Exp. Therapeutics., University. Pennsylvania, Philadelphia, PA., ⁴OMRF, Oklahoma City, OK., ⁵Loyola University. Med., Center, Maywood, IL., ⁶USEPA, Research Triangle Park, NC., ⁷Department. Mol. Biol. Pharmacology, Washington University. School of Medicine, St. Louis, MI., ⁸Department. Biochem, School of Medicine, Vanderbilt University., Nashville, TN., ⁹Department. Pharmacol and Medicine, Vanderbilt University., Nashville, TN., ¹⁰Oxis Inc., Portland, OR., ¹¹Department. Biol.

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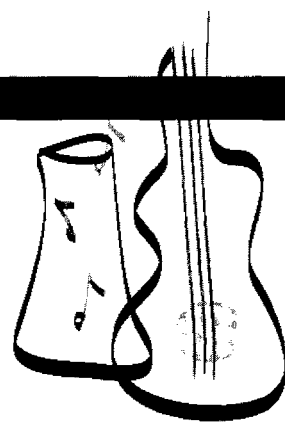


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Preface

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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