

cubes algorithm. This was followed by application of a novel scale-invariant, multi-material mesh-generation algorithm that produces a quality, nearly orthogonal paving of biological geometries based on the concept of local scale. Finally, we have developed efficient constitutive models for myocardium, papillary muscle, chordae tendinae, cardiac valve tissue and coronary artery. Much work remains to be done. However, we believe that a predictive computational model that links circulation to respiration can become an important tool for predicting regional deposition of ultrafine particulates and site selectivity of atherosclerotic plaque formation. Funded by DOE LDRD DE-AC05-76RL01830

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**IN VITRO 2-METHOXYACETALDEHYDE ADDUCT FORMATION USED FOR PROTEOMIC-BASED GLYCOL ETHER BIOMARKER DEVELOPMENT WITH SURFACE ENHANCED LASER DESORPTION IONIZATION (SELDI) ANALYSIS.**

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The protein adduct formation of 2-Methoxyacetaldehyde (MALD, CAS 10312-83-1) was tested as a potential biomarker of glycol ether exposure. MALD is a reactive intermediate in the metabolism of 2-methoxyethanol (2ME, CAS 109-86-4), a glycol ether known to produce reproductive effects in laboratory animals and is a potential carcinogen. Bioactivation of 2ME is reported to occur via oxidation by alcohol dehydrogenase to MALD and subsequent aldehyde dehydrogenase to methoxyacetic acid (MAA, CAS 625-45-6). Protein and DNA adducts have been reported for 2ME, and MALD has been suggested as the likely source of macromolecular adduct formation. In the current study MALD, along with 2ME and MAA were tested in vitro to evaluate adduct formation using human hemoglobin or albumin. Surface Enhanced Laser Desorption Ionization (SELDI) with Time of Flight mass spectrometry was used to detect adduct formation in 0.1 µg hemoglobin or albumin incubates. The study showed that the reactivity of MALD with albumin was several fold greater than for hemoglobin. The reaction of MALD with the alpha-globin chain was greater than that of the beta-globin portion of hemoglobin. After 3 hours the MALD-adduct levels for albumin > alpha-globin > beta-globin. The MALD adduct levels did not continue to increase further during the 24-hour test period, and no corresponding adduct formation was noted for 2ME or MAA. Tryptic digests of the proteins may be utilized for specific proteomic-based biomarkers of exposure to glycol ethers.

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**(2-METHOXYETHOXY)ACETIC ACID: A URINARY BIOMARKER OF EXPOSURE TO JP-8 JET FUEL.**

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(2-Methoxyethoxy)acetic acid (MEAA), the major urinary metabolite of the deicing agent 2-(2-methoxyethoxy)ethanol (diEGME) added to JP-8 jet fuel, was used to measure exposure to JP-8 in air force personnel at six airbases in the United States. JP-8 is a kerosene based fuel containing over 200 different compounds, including aliphatics, aromatics, benzene, and naphthalene, all of which vary in concentration depending upon the specific batch of JP-8. DiEGME is always present at 0.1 %. Post-shift urine specimens were obtained from personnel who performed fuel tank maintenance and their attendants (high category, n = 98), fuel handlers (moderate category, n = 38) and personnel with no direct JP-8 contact (low category, n = 61). Urine containing a deuterated (2-butoxy)acetic acid internal standard was extracted with ethyl acetate, followed by esterification to the ethyl ester. The ethyl ester was extracted with methylene chloride and concentrated. Quantitation was by a gas chromatograph equipped with a mass spectrometer. The mean urinary MEAA level was significantly greater in the high (6.9, SD = 15.5 µg/ml) category, as compared to the means of the moderate (0.4, SD = 0.9 µg/ml, p = 0.0024) and low (0.1, SD = 0.02 µg/ml, p = 0.0002) categories. The maximum concentrations of urinary MEAA were 110.0 µg/ml, 4.8 µg/ml, and 0.2 µg/ml and the percent of measurements below the limit of detection (0.1 µg/ml) were 6%, 67%, and 97% for the high, moderate, and low categories, respectively. This study demonstrated that urinary MEAA can be used as a biomarker of exposure to JP-8.

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**URINARY 2-BUTOXYACETIC ACID: DEVELOPMENT OF AN EFFECTIVE GAS CHROMATOGRAPHIC TEST METHOD FOR QUANTIFICATION.**

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A simple and effective general test method for 2-butoxyacetic acid (2-BAA) in urine samples was developed. 2-Butoxyacetic acid is a metabolite and biomarker for exposure to 2-butoxyethanol (2-BE), a glycol ether and is of concern because of the general toxicity of this class of compounds. Glycol ethers have been frequently reported to damage the male reproductive system, hematopoietic system, and fetal/embryonic development. Occupational exposure by these widely used glycol ethers is likely, since they are readily absorbed through the skin. Specifically, 2-BE is used as a component in paints, inks and common household cleaning products, and is of interest to this laboratory for exposed populations. For the use of this test on urine, specimens were first spiked with deuterated 2-BAA; the deuterated analog was used as a procedural internal standard. The samples were extracted with ethyl acetate, concentrated, and treated by acid catalyzed esterification to produce the corresponding ethyl esters of 2-BAA. Subsequently, the ethyl ester derivatives were extracted using methylene chloride and concentrated to produce the final solution for gas chromatographic analysis. A mass selective detector (MSD) using a 50-m X 0.20-mm (id) HP-1 capillary column and a temperature program of 60 to 150°C was used for the gas chromatographic measurement. Ion m/z 57 was monitored for the ethyl ester of 2-BAA and ion m/z 66 was monitored for the internal standard. A series of recovery studies using 1, 5, 10 and 20 µg/ml 2-BAA spiked urine samples demonstrated good accuracy and precision; recovery varied between 100-102% of theory. The limit of detection (LOD) was found to range from 0.005 to 0.015 µg/ml for this analysis method.

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**EXCRETION OF URINARY BIUREA IN WORKERS EXPOSED AZODICARBONAMIDE.**

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Azodicarbonamide (ADCA), a causative agent of occupational asthma in plastics and rubber industry workers, is an organic low molecular weight agent used as a blowing agent in the manufacture of expanded foam plastics. ADCA is rapidly converted to biurea and that biurea is then eliminated rapidly from all tissues through urine. The urinary biurea has been used as biomarker of ADCA exposure, yet limited studies have been done. Accordingly, we measured airborne ADCA in workplace, urinary biurea, and total IgE in serum, and analyzed the relationship among indices. The study population contained 14 exposed and 14 non-exposed workers in a ADCA manufacturing plant. Urine samples were obtained at prior to shift (PS) and the end of shift (EOS) on the survey day and blood samples collected on the survey day. Analysis for biurea was achieved by oxidation of biurea to ADCA prior to derivation with triphenylphosphine. The derivative was extracted with dichloromethane, and then evaporated. The dried sample was reconstituted in acetonitrile, and quantified using HPLC. Total IgE in serum was analyzed via immunoassay. The mean of environmental ADCA was 1.553±1.930 TWA mg/m<sup>3</sup>, and 80 percent among the collected samples were higher than 1 mg/m<sup>3</sup>, recommend level of Health and Safety Executive. The mean of PS biurea, EOS biurea, and total IgE were 0.19±4.68 mg/g creatinine, 0.18±4.02 mg/g creatinine, and 163.78±4.09 IU/mL, respectively. There was significant correlation between the urinary EOS biurea and the airborne ADCA (r=0.733, p<0.05) and PS biurea (r=0.574, p<0.05) in the exposure group. From the results of simple regression analysis about the urinary concentration of EOS biurea and that of ADCA in the exposed group, coefficient of determination was 0.34 (p<0.05). There was significant correlation between the urinary EOS biurea and the airborne ADCA. The urinary biurea was an effective index as a biomarker of airborne ADCA in workplace, despite the limitation of sample size and variables.

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**GENOTOXIC EFFECTS IN WORKERS EXPOSED TO FUMES AND AEROSOLS OF BITUMEN (FAB).**

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Recently, DNA damage in form of increased strand break frequencies could be determined in white blood cells (WBC) of 66 workers exposed to FAB (Marczyński et al., *Cancer Epidemiol. Biomarker & Prev.* 15: 645; 2006). Meanwhile, 202 exposed

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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, and poster sessions of the 46<sup>th</sup> Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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