the observed variability suggest it appropriate to ignore such factors when evaluating ΔpH data. The next step in our project is to correlate the ΔpH values with those from the more commonly used colorimetric Ellman test. Supported by DOD (DAMD17-01-1-0772), NIOSH (#CDC U07/CCU906162-06) and NIEHS (#ESO5707).

864 IDENTIFICATION OF INTER-INDIVIDUAL VARIATION IN AFLATOXIN METABOLIZING ENZYMES USING HUMAN URINARY DNA.

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Aflatoxin B_1(AFB_1) is a factor in the etiology of hepatocellular carcinoma (HCC). Xenobiotic metabolizing enzymes (XMEs) such as mixed-function oxidases, microsomal epoxide hydrolases (mEH) and glutathione S-transferases (GSTs) are involved in the metabolism of AFB_1. It has been shown that AFB_1-albumin adduct levels may be modified by *mEH* and *GST* genotypes. Moreover, it has been hypothesized that inherited differences in DNA sequence of *mEH* and *GST* genes influence an individual's risk of HCC in response to AFB_1. In order to study genetic differences in these XMEs, a simple and non-invasive DNA extraction procedure was followed. Quantifiable amounts of DNA (9.5-573 ng ml^{-1} urine) were extracted from ≤4.5 ml of urine from AFB_1-exposed individuals and amplicons of 162 bp and 357 bp were generated for single nucleotide polymorphism (SNP) analysis of *mEH* exon 3 (*Y113H*) and exon 4 (*H139R*), respectively, by PCR-RFLP. In a single run, 49 (55%) and 71 (79%) of 89 samples were genotyped for *mEH* exon 3 and exon 4 polymorphisms, respectively. For *mEH* exon 3 SNP typed, there were 37 wild types (*113YY*), 11 heterozygotes (*113YH*) and 1 homozygote (*113HH*). All individuals SNP typed for *mEH* exon 4 were heterozygotes (*139HR*). Urinary DNA was also analyzed by multiplex-PCR to identify deletion polymorphisms in *GSTM1* and *GSTT1* genes using a fragment of the albumin gene as an internal control. Presence or absence of amplicons of 215 bp (*GSTM1*) and 450 bp (*GSTT1*) were indicative of gene polymorphisms. A total of 62 of 89 individuals were genotyped for *GSTM1* and *GSTT1* polymorphisms. Twenty-one and 48 individuals were found to be *GSTM1* and *GSTT1* null respectively, while 20 individuals were doubly null. These results suggest that exfoliated nucleated cells in urine can be a significant source of DNA and may be useful as a non-invasive method for assessing the genetic susceptibility of AFB_1 exposed populations to HCC (Supported by USAID LAG-G-00-96-90013-00, NIEHS P42-ES04917, and NIEHS Center Grant ES09106).

865 NEW APPROACH FOR MONITORING EXPOSURE TO ENVIRONMENTAL TOXIC AGENTS.

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One of the major limitations of the current methods of biological detection of exposure to hazardous environmental agents is their inability to detect long-term exposures, and exposures that occurred in the past without immediate clinical effects. In the current study we examined the potential of a new bioassay that is based on the hypothesis that serum of exposed individuals contains a toxic factor or factors produced by an affected cell or tissue in response to an exposure. In the present study PC12 cell cultures were exposed to serum samples of rats treated with the organophosphate chlorpyrifos. We observed a decrease of up to 31.8% and 40% in cell *via*bility and nerve growth factor-induced neurite outgrowth, respectively, in PC12 cells treated with serum of chlorpyrifos-exposed rats, in comparison to cells treated with serum of control rats. Maximal effect was observed for both parameters 4 weeks after exposure whereas motor activity and cholinesterase activity returned to normal levels within one week after the exposure; thereafter the rats showed no signs of toxicity, including 4 weeks post-exposure. These results demonstrate the potential of the proposed method to detect environmental exposures long after they have occurred.

866 EVALUATION OF TWO COMMERCIALLY AVAILABLE CARDIAC TROPONIN IMMUNOASSAYS FOR THE DETECTION OF DRUG-INDUCED CARDIOTOXICITY IN RATS.

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Cardiac troponin I (cTnI) and T (cTnT) are established tissue-specific biomarkers of acute myocardial injury in humans. To determine the relative value of cTnI (DPC Immulite) or cTnT (Roche Elecsys) for detection of drug-induced cardiotoxicity in rats, serum concentrations of these analytes were measured in male rats given doxorubicin using both acute and chronic dosing protocols. These levels were compared with concentrations of standard serum chemical markers of tissue injury (e.g., LDH, CPK), light microscopic findings and immunohistochemical staining of cTnI and cTnT in the myocardium. Results demonstrated good correlation between measurable serum TnT levels and doxorubicin-induced myocardial degeneration in rats. Correlations were less robust between histologically observed cardiac lesions and serum TnI levels, or the other serum markers evaluated. Immunohistochemistry of heart sections for either TnI or TnT demonstrated diffuse staining of the myocardium with attenuated, or absent staining of the degenerate myofibers indicating that cTnI and cTnT immunostaining of the myocardium can complement light microscopy in delineating foci of injury. In summary, evaluation of serum cardiac troponin T appears to be valuable for detection of some types of drug-induced cardiotoxicity in rats.

867 COMPARISON OF UNCHANGED n-HEXANE IN ALVEOLAR AIR AND 2, 5-HEXANEDIONE IN URINE FOR THE BIOLOGICAL MONITORING OF n-HEXANE EXPOSURE IN HUMAN VOLUNTEERS.

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Biological monitoring of exposure to n-hexane (HEX) is based on the measurement of free urinary 2, 5-hexanedione (2, 5-HD) (no hydrolysis). The current ACGIH biological exposure index (BEI) value (3.5 µmol/L) was derived from 4 field studies involving worker exposures to variable concentrations of HEX and to other solvents. This study was undertaken to characterize, for 5 consecutive days, the relationship between HEX exposure (25 and 50 ppm) and 1) 2, 5-HD urinary excretion and, 2) HEX in alveolar air. Five volunteers (3 women and 2 men) were exposed to HEX in an exposure chamber for 2 non consecutive weeks (7 hours/day). They were exposed to 50 ppm HEX, during the first week, and to 25 ppm during the second week. Unchanged HEX in alveolar air, and urinary 2, 5-HD (with or without acid or enzymatic hydrolysis) were measured. Concentrations of HEX in alveolar air were 18 ppm (25 ppm) and 37 ppm (50 ppm) which shows that 73% of inspired HEX was excreted unchanged. The urinary 2, 5-HD concentrations (mean ± standard de*via*tion) for the last 4 hours of exposure (day 5) following exposure to 50 ppm HEX were 30.4 ± 7.8 µmol/L (acid hydrolysis), 5.8 ± 1.0 µmol/L (enzymatic hydrolysis) and 6.2 ± 0.9 µmol/L (without hydrolysis). Following exposure to 25 ppm HEX, the urinary concentrations were 15.2 ± 1.9 µmol/L, 3.1 ± 0.7 µmol/L and 3.7 ± 0.5 µmol/L, respectively. The 2, 5-HD value measured in this study following exposure to 50 ppm (6.2 µmol/L), which is higher (X1.8) than the average value reported in field studies better reflects the levels of exposure to HEX alone. Inter-ethnic differences caused by genetic polymorphism, and/or metabolic interferences due to co-exposure to other solvents are likely responsible for the lower 2, 5-HD values measured in previous field studies. In conclusion, the current BEI value for HEX is most likely more protective than what has been believed up until now. (Supported by IRSST, Quebec, Canada)

868 URINARY 3-BROMOPROPIONIC ACID: AN EFFECTIVE GAS CHROMATOGRAPHIC TEST METHOD FOR QUANTIFICATION.

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3-Bromopropionic acid is a metabolite and possible biomarker for exposure to 1-bromopropane. 1-Bromopropane is used as an industrial solvent and exposure is a health concern for industrial workers due to its toxicity. Central neurological disorders and peripheral neuropathy has been reported in workers chronically exposed to materials composed of 1-bromopropane in the United States and animal studies have shown reproductive toxicity. Occupational exposure to this widely used industrial solvent is likely, since it is readily absorbed through the skin. A simple and effective general test method for 3-bromopropionic acid in urine samples was developed to monitor any exposed population. Urine specimens were first spiked with 3-chloropropionic acid which was used as a procedural internal standard. The samples were extracted with ethyl acetate, concentrated, and treated with N-methyl-N-[tert-butyldimethylsilyl] trifluoroacetamide (MTBSTFA) to produce the corresponding t-butyldimethylsilane derivatives of 3-bromopropionic acid and the internal standard. Quantification was by means of a gas chromatograph (GC) equipped with a mass selective detector (MSD) using a 50-m X 0.20-mm (id) HP-1 capillary column. A temperature program of 60 to 255oC was used for the gas chromatographic measurement. Ion m/z 211 was monitored for the derivative of 3-bromopropionic acid and ion m/z 165 was monitored for the internal standard. Average recovery of known 3-bromopropionic acid fortified blank urine samples was between 93-98% with relative standard de*via*tions as high as 5.7% using samples at 3-bromopropionic concentrations of 2, 10, 20 and 50 µg/ml . The limit of detection (LOD) for the developed procedure was found to be approximately 0.01 µg/ml in urine.

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Preface

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