## 398 QUANTIFICATION OF WASTE GAS ANESTHETICS IN THE BREATH OF PERIANESTHESIA CARE UNIT (PACU) NURSES.

K. A. Cope[1], W. T. Merritt[2], D. Krenzischek[2], J. A. Schaefer[3], J. A. Bukowski[3] and T. H. Risby[1]. *[1]Johns Hopkins University School of Hygiene and Public Health, Environmental Health Sciences, Division of Toxicology, Baltimore, MD, [2]Johns Hopkins University Medical Institutions, Anesthesiology and Critical Care Medicine, Baltimore, MD and [3]Johns Hopkins University, Department of Health, Safety and Environment, Baltimore, MD.* Sponsor: J. Yager.

Rationale: PACU nurses working in the hospital inpatient post-operative area are chronically exposed to inhalational anesthetic agents that are excreted in the breath by patients. We hypothesized that inspiratory occlusion pressure, a measure of respiratory drive, would decrease as concentrations of anesthetics in exhaled breath increase. To test this hypothesis, we collected samples of exposed breath from nurses before and after an 8 hour shift. During collection the occlusion pressure was measured. Methods: Breath was collected from 13 nurses in the PACU before and after an 8 hour shift. Subjects were asked to breath normally into a sterile filter attached to a Rudolph three-way non-re-breathing valve. During collection tidal volume, 100 ms inspiratory pressure, end-tidal $CO_2$ and steady-state $CO_2$ measurements were recorded continuously. Breath was collected on a mixture composed of graphitized carbon and carbon-molecular sieve for one minute. Samples were analyzed by two-stage thermal desorption and capillary gas chromatography. After obtaining a breath sample an occlusion pressure measurement was recorded. Results: Average exhalation rates for isoflurane were higher at the end of the shift (305 pmol/kg/min) than at the beginning (258 pmol/kg/min). There was a significant correlation between decrease in occlusion pressure and level of isoflurane in breath ($r^2$=0.35, p=0.001). Conclusions: This pilot study demonstrates that nurses may carry gases from a previous shift and that chronic exposure to waste gas anesthetic agents may cause neuro-respiratory depression.

## 399 DEVELOPMENT OF AN IMMMUNOASSAY TO DETECT HEXAMETHYLENE DIISOCYANATE FOR BIOMONITORING OF WORKERS.

R. Lemus[1], L. Lukinskiene[1], M. E. Bier[2] and M. H. Karol[1]. *[1]University of Pittsburgh, Environmental and Occupational Health, Pittsburgh, PA and [2]Carnegie Mellon University, Chemistry, Pittsburgh, PA.*

The chemical 1,6-hexamethylene diisocyanate (HDI) is widely used in the manufacture of polyurethanes for paints and coatings. HDI is an irritant and a chemical asthmagen. Hence, individuals who handle or come into contact with HDI should have medical surveillance. Experimental evidence indicates that isocyanates react with proteins including human serum albumin (HSA) the most abundant protein in blood plasma (approximately 0.60 mM) and hemoglobin. We sought to develop a sensitive and specific immunoassay for use in detecting recent HDI exposure. For this, a highly sensitive and specific rabbit antiserum to HDI-keyhole limpet hemocyanin (HDI-KLH) was used. HDI-HSA conjugates were synthesized and their degree of haptenization was evaluated by MALDI-TOF-MS. The sensitivity and specificity of the anti-HDI antiserum was evaluated by Western blot. The antiserum was found capable of detecting HDI on conjugates comprised of 2 mol HDI per mol HSA. The specificity of the antiserum was apparent from its lack of reaction with toluene diisocyanate or methylenediphenyl diisocyanate-HSA conjugates. The immunoassay consistently detected as little as 6 pmol of HDI. This immunoassay offers significant advantages when compared with current analytical methods for human biomonitoring since it is rapid, inexpensive, capable of screening large numbers of serum samples simultaneously, and has appropriate sensitivity. This bioassay has the potential to impact significantly industrial surveillance programs permitting identification of HDI exposure, and thereby possibly preventing adverse biological consequences. Supported by NIEHS #05651.

## 400 DETECTION OF HEXAMETHYLENE DIISOCYANATE-HEMOGLOBIN ADDUCTS USING AN ELISA ANTIGEN-CAPTURE ASSAY.

L. Lukinskiene[1], R. Lemus[1], A. V. Wisnewski[2], C. A. Redlich[2] and M. H. Karol[1]. *[1]University of Pittsburgh, Pittsburgh, PA and [2]Yale University School of Medicine, New Haven, CT.*

Isocyanates including 1,6-hexamethylene diisocyanate (HDI), are a prominent cause of occupational asthma. HDI is used as a polymerizing agent in paint formulations employed in the automobile industry. There is a need to monitor occupational exposure in workers to prevent the onset of disease. HDI has been reported to form stable adducts with N-terminal valine of globin. Since the lifetime of such adducts is 3 or more months, these adducts can be a useful biomarker of exposure over a period of time. The aim of this study was to develop and apply an assay for HDI exposure of auto paint sprayers in local garages. A sensitive and specific rabbit anti-HDI antiserum was used, and an HDI-Hb conjugate was synthesized as a positive control for the immunoassay. A sham-exposed Hb was used as a negative control. To develop the assay, the immunoglobulin G (IgG) fraction from the antiserum was purified by a caprylic acid/ammonium sulfate precipitation. Hemoglobin was purified from human blood samples by gel filtration. Microtiter plates were coated with the rabbit IgG antibodies and detection of the Hb adducts was accomplished using stepwise: Hb samples from workers, goat anti-human Hb, peroxidase labeled anti-goat IgG, followed by substrate. The assay was found to be capable of detecting as few as 6 pmoles of HDI when adducted to protein. This is the first report of a sensitive immunoasay for biomonitoring of workplace HDI exposure. Erythrocytes were obtained from workers who had tested positive for HDI-specific IgG antibodies, as well as workers with recent exposure to HDI. The immunoassay indicated that none of the workers (n=26) had detectable HDI adducted to Hb. Further studies are needed to investigate possible HDI adducts with other proteins (serum albumin) and with sputum specimens, to indicate their potential role as biomarkers in detecting occupational exposure to isocyanates. Supported by NIEHS 05651 and OH03457.

## 401 THE BINDING SPECIFICITY OF SINGLE CHAIN VARIABLE FRAGMENTS (SCFV) ENGINEERED TO DEGRADE A POLYURETHANE BOND.

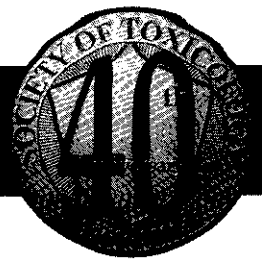
G. Choy and W. E. Brown. *Carnegie Mellon University, Biological Sciences, Pittburgh, PA.*

ScFvs are composed of the VH and VL chains of antibodies covalently linked together by a 15 amino acid chain. They are engineered using recombinant phage antibody technology to recognize any specific antigen. In the current study, the binding specificity of ScFvs engineered to recognize a diphenylmethane diisocyanate (MDI)-based polyurethane was examined. This would allow the usage of these proteins as biological probes to identify diisocyanate modified proteins in individuals exposed to toulene diisocyanate (TDI) or MDI. Enzyme linked immunosorbent assays (ELISA) were carried out to determine the antigen that these ScFvs recognize with highest affinity. The initial ScFv screen identified a particular ScFv, #12, that binds TDI modified human serum albumin (HSA) with the highest affinity. It was found that ScFv #12 has differential binding for TDI-HSA conjugates made at varying pH with the highest binding affinity for conjugates made at pH > 9 or < 8. This result implies that ScFv #12 is recognizing the single phenyl ring of TDI and a urea bond contrary to what was expected. In addition, titration of HSA with TDI indicates a saturation of ScFv #12 binding at molar ratios of TDI:HSA > 50. However, ScFv #12 is also able to recognize conjugates made at molar ratios as low as 10:1. Further confirmation was obtained by determining the binding affinity of ScFv #12 for tolyl monoisocyanate or butyl isocyanate modified HSA, poly-Lysine or poly-Serine. The high affinity of the ScFvs to TDI-HSA conjugates would enable us to develop effective tools for immunohistochemistry and dermal assays to characterize TDI conjugates found in lung and nasal passages of species exposed and sensitized to TDI. This would further our understanding of the mechanism by which occupational asthma is induced by diisocyanates. (Partially supported by a reaseach award from AE-SOT)

## 402 EFFECT OF CO-EXPOSURE TO CATECHIN ON THE DETERMINATION OF EXPOSURE BIOMARKER OF SAFROLE.

M. J. Chang, C. Y. Ko and R. F. Lin. *Chang Gung University, Public Health, Tao-Yuan, Taiwan.*

Co-exposure of safrole, a weak animal hepatocarcinogen and catechin, a plant flavonoid occurs in the chewing of betel quid in Taiwan. Recently, the presence of detectable stable safrole-DNA adducts in human oral tissues was suggested as a contributor to the initiation of oral cancer in betel quid chewing. Catechin, as many other polyphenols, has been thought to have cancer preventive effect. It was the purpose of this study to investigate the effect of co-exposure to catechin on the exposure biomarker (EB) of safrole. Male Wistar rats, 4 per dose group, were gavaged consecutively with a dose of safrole 5 mg/kg and catechin (0, 5, and 25 mg/kg). Urine samples were collected from each rat for day-1 and -2. Both of the acid- and



# Society of Toxicology

## 40th Annual Meeting

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# Preface

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**An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 451.**

**The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 479.**

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