PS 2441 EXPOSURE TO ORGANOPHOSPHATE INSECTICIDES AMONG CHILDREN LIVING ALONG THE US-MEXICO BORDER.

K. Holm[1], R. Tornero-Velez[1], R. Goldsmith[1], D. Chang[1], C. Grulke[1], C. Dary[2] and Y. Tan[1]. *[1]US EPA, Research Triangle Park, NC and [2]US EPA, Las Vegas, NV.*

An important tool for evaluating pesticide exposure is biomonitoring, since biomarkers reflect the dose that actually entered the body and represent an aggregate exposure received by all routes. In several exposure studies, spot urinary concentrations of metabolites of several organophosphate (OPs) insecticides (including chlorpyrifos) were measured from children (ages 1 to 9) who lived in the U.S.-Mexico Border Region. The distributions of chlorpyrifos-specific metabolite, 3,5,6-trichloro-2-pyridinol (TCPY), measured in two exposure studies were comparable to the U.S. population as indicated by the National Health Nutrition Examination Survey (NHANES), except at the higher percentiles (> 95th percentile) these children had higher-than-NHANES urinary concentrations. On the other hand, the distributions of non-specific metabolites, dialkylphosphates (DAPs), measured in two exposure studies were much higher than the NHANES distribution. To further investigate the sources of exposures for children with high urinary metabolite concentrations, pharmacokinetic (PK) and physiologically based pharmacokinetic (PBPK) models were used to simulate the pharmacokinetics of OPs. For model inputs, questionnaire, environmental measurement data, and study protocols were used to generate possible exposure scenarios (e.g., routes of exposure) and specify biomarker measurements (e.g., time when urine samples were taken). Environmental (indoor air) concentrations were measured in one study. Some studies had time-activity diaries, and another one had questionnaire data such as parental occupation information. Using these data and model simulations, our analyses identified several potential sources of exposures that may lead to these higher urinary metabolite concentrations. Examples of these sources included higher exposures from multiple routes, aggregate exposures to multiple OPs, and co-exposure to both parent and degradates. [This abstract has been cleared by the US-EPA but solely expresses the view of the authors]

PS 2442 EXPOSURE TO TRI-O-CRESYL PHOSPHATE AS A POSSIBLE EXPLANATION OF "AEROTOXIC SYNDROME"

M. Liyasova[1, 2], B. Li[2], L. M. Schopfer[2], F. Nachon[3, 2], C. E. Furlong[4] and O. Lockridge[2, 1]. *[1]Environmental, Agricultural & Occupational Health, University of Nebraska Medical Center, Omaha, NE, [2]Eppley Institute, University of Nebraska Medical Center, Omaha, NE, [3]Département de Toxicologie, Institut de Recherche Biomédicale des Armées, La Tronche, France and [4]Department of Medicine and Genome Sciences, University of Washington, Seattle, WA.*

The aircraft cabin ventilation is supplied from unfiltered bleed air directly from the engine. Defective engine seals can result in the release of engine oil into the cabin air supply. Aircrew and passengers have complained of illness following such "fume events". Adverse health effects are hypothesized to result from exposure to tricresyl phosphate, mixed esters added to jet engine oil. Our goal was to develop a laboratory test for exposure to tricresyl phosphate. The assay was based on the fact that the active-site serine of butyrylcholinesterase reacts with the active metabolite of tri-o-cresyl phosphate, cresyl saligenin phosphate, to make a stable phosphorylated adduct with an added mass of 80 Da. No other organophosphorus agent makes this adduct in vivo on butyrylcholinesterase. Blood samples from jet airplane passengers were obtained 24-48 hours after completing a flight. Butyrylcholinesterase was partially purified from 25 ml serum or plasma, digested with pepsin, enriched for phosphorylated peptides by binding to titanium oxide, and analyzed by mass spectrometry. Of 12 jet airplane passengers tested, 6 were positive for exposure to tri-o-cresyl phosphate that is, they had detectable amounts of the phosphorylated peptide FGEpSAGAAS. No more than 0.05 to 3% of plasma butyrylcholinesterase was modified. None of the subjects had toxic symptoms. Four of the positive subjects were retested 3 to 7 months following their last airplane trip and were found to be negative for phosphorylated butyrylcholinesterase. In conclusion, this is the first report of an assay that detects exposure to tri-o-cresyl phosphate in jet airplane travelers.

PS 2443 OXIDATIVE STRESS, INFLAMMATORY, AND IMMUNE RESPONSE AFTER INHALATION EXPOSURE TO BIODIESEL EXHAUST.

E. K. Kisin[1], A. R. Murray[1, 2], A. V. Tkach[1], S. H. Gavett[3], M. I. Gilmour[3] and A. A. Shvedova[1, 2]. *[1]NIOSH, Morgantown, WV, [2]West Virginia University, Morgantown, WV and [3]US EPA, Research Triangle Park, NC.*

Biodiesel (BD) is an advanced fuel produced from renewable domestic sources. The broad uses of BD in different industries including mining may lead to potential health effects. We hypothesized that the toxicity of biodiesel exhaust (BDE) is dependent at least on three major mechanisms: direct reactivity of BDE PM electrophiles towards critical biomolecules, induction of robust inflammatory response associated with the nano-sized components of BD PM, and triggering of oxidative stress via depletion of essential antioxidants and activation of oxidative burst in inflammatory cells. In the current study, we evaluated these pathways in BALB/cJ mice 24 hr after 4 weeks of inhalation exposure to BD (0, 50, 150 and 500 μg/m^3; 4 hr/day, 5 d/wk, 4 wk). Biomarkers of pulmonary damage (LDH) and inflammation (myeloperoxidase, MPO) were significantly elevated in the lungsfrom mice exposed to BDE. Additionally, we observed that inhalation exposure caused a significant accumulation of oxidatively modified proteins (carbonyls), increase in 4-hydroxynonenal (4-HNE), reduction of protein thiols, and depletion of antioxidant - gluthatione (GSH). To assess the effects of BDE on pulmonary antigen presenting cells (APC), expression of CD80, CD86, CD40 and MHCII class molecules on lung dendritic cells (DC) was evaluated. BDE altered the phenotype of APC in the lung and facilitated the recruitment of immature DC into the lung tissues. The proliferative response of spleen T cells upon BDE exposure (*ex vivo*) was increased while no changes were observed in regulatory T cell numbers. Overall, the results show that exposure to BDE induces inflammation and oxidative damage in the lungs and stimulates local and systemic immune responses. Further investigations will compare the relative potency of different blends of BDE against petroleum diesel. (This abstract does not represent US EPA policy.)

PS 2444 SERUM PROTEOMIC ANALYSIS OF CHRONIC ARSENIC EXPOSURE USING 2-D DIGE TECHNOLOGY.

L. Zhao[1], D. Sun[1], Y. Gao[1] and Y. Wei[2]. *[1]Center for Endemic Disease Control, Harbin Medical University, Harbin, Heilongjiang, China and [2]Department of Community Medicine, Mercer University School of Medicine, Macon, GA.*

Environmental arsenic exposure has been a major public health concern in the world. Changes in serum proteins could be potential biomarkers of effect for arsenic exposure. This study was to investigate the changes of serum proteome among human subjects exposed to different levels of arsenic in drinking water, and in the subjects with and without arsenic-related skin lesions. Individuals living in endemic arsenicosis villages of Shanxi Province, China were selected and divided into arsenicosis group with skin lesions and non-arsenicosis group without skin lesions. The non-arsenicosis group was further divided into low, medium, and high arsenic exposure groups based on the arsenic levels in drinking water, < 10 μg/L, 10-50 μg/L, and > 50 μg/L, respectively. Since 2003, five years before the survey, an improved water supply with arsenic < 10 μg/L has been provided to individuals in the arsenicosis group who had used the water containing high levels of arsenic (> 50 μg/L). An equal amount of serum from thirty subjects in each group were pooled and analyzed by two-dimensional differential gel electrophoresis (2-D DIGE) coupled with mass spectrometry (MS). Twelve spots were found to be differentially expressed among low, medium, and high arsenic exposure groups, with a positive or negative correlation with water arsenic levels. Twenty nine spots were found to be related to arsenicosis. Finally, twenty five spots with high abundance and fold changes were selected for MS analysis, and 13 proteins were identified, including plasma retinal binding protein (RBP4), α1-microglobulin, keratin 1 (K1), pigment epithelial-differentiating factor (PEDF), beta-2-glycoprotein 1 (B2GP1), hemopexin, and others. This study identified the serum proteins that may be candidate biomarkers of effect for arsenic exposure and arsenicosis. However, further validation studies are required to prove these observations.

PS 2445 EXPRESSION OF ALDO-KETO REDUCTASE mRNA IN HUMAN LYMPHOCYTES OF SMOKERS.

B. S. Barrón-Vivanco[1, 3], S. J. Rothenberg[1, 4], I. M. Medina-Diaz[3], L. Robledo-Marenco[3], A. E. Rojas-García[3], G. Elizondo[2] and A. Medina[1]. *[1]Toxicología, Cinvestav, México, DF, Mexico, [2]Biología Celular, Cinvestav, México, DF, Mexico, [3]Laboratorio de Contaminación y Toxicología Ambiental, Universidad Autónoma de Nayarit, Tepic, Nayarit, Mexico and [4]Salud Ambiental, Instituto Nacional de Salud Pública, Cuernavaca, Morelos, Mexico.*

Aldo-keto reductases (AKRs) are a group of oxidoreductases that metabolize a wide range of substrates, including polycyclic aromatic hydrocarbons (PAHs), generating metabolites (o-quinones) capable of initiating and promoting carcinogenesis.

The Toxicologist

Supplement to *Toxicological Sciences*

51st Annual Meeting and ToxExpo™

March 11–15, 2012 • San Francisco, California

SOT 2012 San Francisco California

An Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science of Toxicology

www.toxicology.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 126, Issue 1
March 2012

www.toxsci.oxfordjournals.org