provide an up to date overview of the iAs problem in Mexico. To achieve this objective, we conducted an exhaustive literature mining focused in geological data and its relevance to human health. Arsenic concentrations exceeding the drinking water Mexican norm (0.025 mg/L) have been reported in 17 states, and up to now there are 5 towns with arsenicism reports. iAs chronically exposed populations have shown skin lesions, peripheral vascular diseases, hepatotoxicity, immunotoxicity, diabetes mellitus and genotoxicity. In addition, children living close to smelting areas showed neurological disorders. Therefore biomarkers associated with health effects by chronic exposure to iAs have been actively investigated. For example, some biomarkers like frequencies and types of chromosomal aberrations in lymphocytes, urinary COPRO/URO and COPROIII/COPROI ratios, TGF-alpha level in bladder urothelial cells, as well as micronuclei in buccal and urothelial cells have been investigated. In summary, due to the abundant presence of iAs in soil and water in Mexico, and its reported effects on human health, it is necessary to carry out systematic evaluations of the drinking water sources to identify all the high iAs areas and to develop surveillance program to detect early human effects.

PS 1586 COMPARATIVE TOXICITY AND TISSUE DISTRIBUTION AFTER REPEATED ADMINISTRATION ORALLY WITH VARIOUS TYPES OF ARSENIC INTO THE MONKEY.

J. Park[1], C. Kim[2], S. Choi[1], D. Kim[1], M. Huang[1], B. Choi[1], K. Park[3], Y. Yum[4], E. Han[4] and T. Kang[4]. *[1]Chung-Ang University, Seoul, Korea, South, [2]Korea Institute of Toxicology, Daejeon, Korea, South, [3]Korea Institute of Science and Technology, Seoul, Korea, South and [4]National Institute of Toxicological Research and Technology, Seoul, Korea, South.*

Arsenic (As) is an ubiquitous element in several forms in food and environment. The main route of As in general population is an oral exposure. However, the toxicity of As varies much by chemical forms. In this study, we compared the toxicity and tissue distribution of the various types of As after repeated administration orally into the animal. The cynomolgus monkey was used in this study. The dosage of repeated administration orally into the monkey was determined based on the previous single administration study. We prepared arsenics, such as sodium arsenite (low: 1.0 mg As/kg/day, high: 5.0 mg/kg/day), arsenocholine (low: 1.5 mg/kg/day, high: 15 mg/kg/day) and dimethyl arsenic acid (DMA, 15 mg/kg/day). Animals were administered with chemical in each group for 4 weeks except the sodium arsenite high-dosed group. We terminated the administration of As on day 6th, because observed died or abnormal positioned animals in the high dose sodium arsenite group. Where, the lethality was 60% (3/5). In DMA (15 mg As/kg/day) group, one animal showed abnormal position on day 23rd. No significant change was not observed in the low-dose sodium arsenite and in the low- or high-dose arsenocholine administered animals during experimental period. The total As in the liver and kidney were increased with dose-dependent pattern. The level of As was higher in the liver than in the kidney in sodium arsenite or arsenocholine administered animals, while was higher in the kidney than in the liver in DMA group. These results from monkey support the previous studies that inorganic As is much more toxic than DMA and organic As, and As is accumulated in the tissue.

PS 1587 EFFECTS OF ARSENITE IN DRINKING WATER ON MOUSE LUNG IN A 30 DAY EXPOSURE.

J. Chilakapati[1, 2], K. Wallace[2], D. Thomas[2], T. Moore[2], H. Ren[2], W. Ward[2] and K. Kitchin[2]. *[1]Curriculum in Toxicology, UNC, Chapel Hill, NC and [2]ECD, NHEERL, U.S. EPA, RTP, NC.*

Humans in Taiwan, Chile and Argentina exposed to inorganic arsenic in their drinking water have demonstrated elevated risks of lung cancer deaths. Since, the carcinogenic mode of action of arsenicals is unknown; we investigated the effects of inorganic arsenic (iAsIII) in female C3H mice, exposed to 0, 0.05, 0.25, 1, 10 and 85 ppm arsenite in drinking water for 30 days. As traditional rodent diets contain arsenic, both inorganic and seafood derived arsenicals, we reduced food arsenical exposure by using a purified diet (AIN-93M). Arsenite-treated mice drank less water at all doses (significantly lower at 85, 10 and 1 ppm (66, 49 and 42 % respectively). Only mice in the 85 ppm group weighed considerably lower (12 %) than the control group. Mouse lungs were analyzed for inorganic arsenic, monomethylated and dimethylated arsenicals by hydride generation atomic absorption spectroscopy. The total lung mean arsenical levels were 2.4, 22.5, 30.1, 50.9, 105.3 and 316.4 ng/g lung tissue after 0, 0.05, 0.25, 1, 10 and 85 ppm, respectively. At 85 ppm, the total mean lung arsenical levels increased 14-fold and 131-fold when compared to either the lowest non-control dose (0.05 ppm) or the control dose, respectively. Gene expression analysis was conducted using Affymetrix Mouse Genome 430A 2.0 GeneChips®. Differentially expressed genes (DEG) were determined using a one-way ANOVA ($p<0.05$) by Rosetta Resolver®, a Benjamini-Hochberg FDR multiple testing correction (<0.05) and a + 1.5 fold change cut-off. Surprisingly, we found that arsenic exposure caused minimal numbers of DEGs (57, 9, 3, 22, and 17 DEGs after 0.05, 0.25, 1, 10 and 85 ppm respectively). Thus, from 0.05 to 85 ppm arsenite, we observed monotonic increases in mouse lung arsenical concentrations but no clear dose- related increases in DEGS. Increasing the dose above the current doses might show more significant biological changes in the lungs. (This research was supported by UNC/EPA Cooperative Agreement EPA CR 833237. This abstract does not necessarily reflect EPA policy.

PS 1588 COMPARISON OF THE PERSISTENCE OF DEPOSITED PARTICLES AND THE INFLAMMATORY POTENTIAL OF STAINLESS STEEL *VERSUS* MILD STEEL WELDING FUME IN RAT LUNGS AFTER INHALATION.

J. M. Antonini, D. Schwegler-Berry, S. Stone, T. Chen, P. C. Zeidler-Erdely, D. G. Frazer and J. R. Roberts. *NIOSH, Morgantown, WV.*

Epidemiology studies have been unable to correlate chronic adverse lung effects associated with exposure to specific welding fumes generated from different processes. The objective of this study was to use an animal model to compare the persistence of deposited particles and the inflammatory potential after inhalation of stainless steel welding fume (SS WF) or mild steel welding fume (MS WF), the two most common fumes used in U.S. industry. Male Sprague-Dawley rats were exposed to 40 mg/m^3 of SS WF or MS WF for 3 hr/day for 3 days. Controls were exposed to filtered air. Generated fume was collected in the breathing zone of the animals, and particle size, morphology, and composition were determined. Bronchoalveolar lavage was done on days 1, 4, 8, 11, 22, and 43 after the last exposure to assess lung injury/inflammation and to recover lung phagocytes. SS WF and MS WF were similar in particle morphology and size with mass median aerodynamic diameters of 0.26 and 0.31 μm, respectively. Chemical composition of the fumes was different- SS WF: 57 % Fe, 20 % Cr, 14 % Mn, 9 % Ni; MS WF: 81 % Fe, 15 % Mn. There was no effect of MS WF on lung injury/inflammation at any time point compared to air control. Lung injury was elevated through 11 days after exposure to SS WF, whereas inflammation was delayed and not significantly increased until day 11 compared to control. SS WF also was associated with greater recovery of welding fume-laden cells from the lungs at all time points compared to the MS WF group. Few cells contained MS WF particles at 22 days, whereas 25 % of cells recovered from the SS WF group still contained particles at 43 days. Thus, it appears that clearance of SS WF is impaired compared to MS WF, which may explain the delayed and persistent inflammatory response. These observations could be related to the presence of insoluble carcinogenic metals in SS WF, such as Cr or Ni, which may play a role in the development of chronic lung disease.

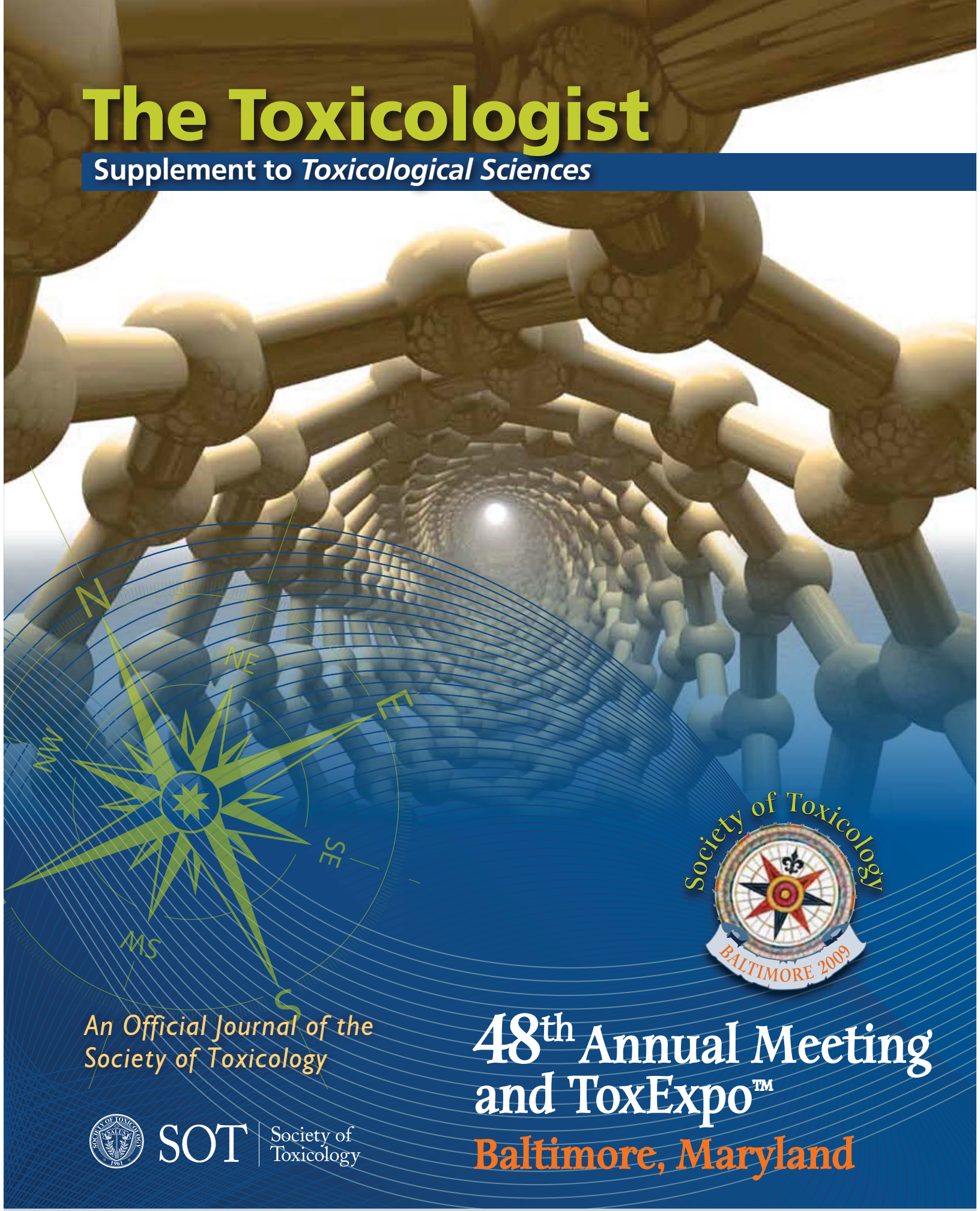
PS 1589 WELL WATER HIGH IN TUNGSTEN, ARSENIC AND POLONIUM 210 FROM CHURCHILL COUNTY, NEVADA INDUCES OXIDATIVE STRESS IN MICE.

C. A. Pritsos[1, 2], K. L. Pritsos[1], R. Seiler[4] and L. Welniak[3]. *[1]Nutrition, University of Nevada, Reno, NV, [2]Environmental Sciences Program, University of Nevada, Reno, NV, [3]Microbiology, University of Nevada, Reno, NV and [4]U.S. Geological Survey, Carson City, NV.*

Between 1997 and 2001, 15 children were diagnosed with acute lymphocytic leukemia (ALL), in Churchill County, Nevada. A CDC investigation of the cancer cluster demonstrated elevated levels of arsenic and tungsten in the urine of study participants and tap water samples. Extremely high levels of alpha radioactivity in numerous domestic wells used for drinking water in the Fallon area were also found which could not be accounted for by naturally occurring uranium activity in the area and were subsequently determined to come from polonium-210 contamination. This study was designed to determine if consumption of drinking water from one or more sources high in one or more of these chemical from Churchill county Nevada induces oxidative stress in mice. C57BL/6 female mice were provided drinking water for up to 10 weeks from selected sources in Churchill County. Several sources of water samples were selected to provide representative ranges of naturally occurring levels of arsenic, tungsten and polonium-210. An in-depth chemical analysis of these water samples was conducted to confirm the concentration and diversity of the contaminants in these tests. The treated mice were assessed for changes in biomarkers of oxidative stress including superoxide dismutase (SOD), glutathione peroxidase (GPOX), total antioxidant capacity(TOAX), lipid peroxidation (LPO) and total DNA damage. Mice provided water high in all three chemicals showed statistically significant increases in SOD, GPOX, TOAX, LPO and DNA damage. Mice provided water high in tungsten but lower levels of polonium 210 and arsenic showed some increases in oxidative stress but not as significant as those high in all three. High tungsten levels are a common feature in the water samples which induce oxidative stress in this mouse model. This study was supported in part by a grant from the U.S. EPA, EM-96963201.

The Toxicologist

Supplement to *Toxicological Sciences*



An Official Journal of the Society of Toxicology

SOT | Society of Toxicology

48th Annual Meeting and ToxExpo™

Baltimore, Maryland

www.toxsci.oxfordjournals.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 108, Number 1, March 2009