adults who participated in the 1999-2006 National Health and Nutrition Examination Survey (n=14,778). Models were adjusted for survey year; sociodemographic and CKD risk factors; and the other metal as a continuous variable. The geometric means of blood cadmium and lead were 0.41 μg/L and 1.58 μg/dL, respectively. The adjusted odds ratios (95% confidence interval) for albuminuria, reduced eGFR, and both albuminuria and reduced eGFR were 1.92 (1.53, 2.43), 1.32 (1.04, 1.68) and 2.91 (1.76, 4.81), respectively, comparing the highest to the lowest blood cadmium quartiles, and 1.19 (0.96, 1.47), 1.56 (1.17, 2.08) and 2.39 (1.31, 4.37), respectively, comparing the highest to the lowest blood lead quartiles. The odds ratios comparing participants in the highest quartile of both metals to those in the lowest quartile of both metals were 2.36 (1.49, 3.73) for albuminuria, 1.88 (1.24, 2.84) for reduced eGFR and 7.80 (3.04, 19.98) for both outcomes. These findings provide strong support for consideration of lead and cadmium as CKD risk factors in the general population and novel evidence of increased risk with exposure to both metals, which is common.

## PS 1566 MICROARRAY ANALYSIS OF THE PULMONARY EFFECTS OF STAINLESS AND MILD STEEL WELDING FUMES IN A/J AND C57BL/6J MICE.

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Our earlier studies found supportive evidence for a tumorigenic effect of carcinogenic metal-containing welding fume in A/J mice. A/J mice are genetically predisposed to spontaneous and/or chemically-induced lung tumors while C57BL/6J (B6) mice are resistant. This genetic disparity provides a unique scenario to identify molecular mechanisms associated with the lung response to welding fume at the transcriptome level. Mice were exposed four times by pharyngeal aspiration to 5mg/kg mild steel (MS) fume, stainless steel (SS) fume, or saline vehicle. Mice were necropsied 28 days after the last exposure and whole lung microarray using Illumina Mouse Ref-8 expression beadchips was done. Ingenuity pathway analysis (cutoffs: $p<0.05$; fold change >1.3) of the microarray data revealed the top global molecular network involved in the A/J response to MS fume was behavior, nervous system development and function, and gene expression. In contrast, the connective tissue disorders, immunological disease, inflammatory disease network was most significant in the B6 strain. In the A/J, 75% of the focus molecules that met the cutoff were up-regulated as compared to 40% in the B6. Six genes were common between the strains such as KLF2, KLF4 and MARCO. SS fume exposure in the A/J induced genes primarily involved in connective tissue disorders, immunological disease, and inflammatory disease. Genes regulating cellular movement, hematological system development and function, and immune response were most involved in the B6 response. Of the significant focus molecules, 88% were up-regulated in the A/J compared to 45% in the B6. Only five common genes were found between the strains such as HSPH1, MMP12 and CTSK. Overall, these data confirm our previous observation that strain-dependent differences in response to welding fume occur in the A/J and B6 lung. Also, in contrast to the B6, the A/J strain exhibited a persistent up-regulation of welding fume-induced gene transcription suggesting that chronic lung cell activation may play a role in the tumorigenic effects of welding fume.

## PS 1567 EXPOSURE TO ARSENIC COMBINED WITH HIGH FAT DIET PROMOTES THE IMPAIRMENT OF GLUCOSE TOLERANCE IN C57BL/6 MICE.

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Obesity is the single most important risk factor for the development of insulin resistance and type 2 diabetes. However, chronic exposures to inorganic arsenic (iAs) have also been associated with an increased prevalence of type 2 diabetes mellitus. The current study examines diabetogenic effects of exposures to iAs combined with consumption of a high fat diet (HFD). Here, weanling, male, C57BL/6 mice were divided into 6 groups which drank deionized water containing arsenite ($iAs^{III}$) (25 or 50 ppm) or water without $iAs^{III}$, *ad libitum*, for 20 weeks while consuming either a HFD (58% fat) or a low fat diet (LFD) (11% fat), also *ad libitum*. Body weight, adiposity, food and water consumption were monitored throughout the study. At 20 weeks fasting blood samples were collected and oral glucose tolerance tests were administered to all mice. In general, the 25 and 50 ppm groups consumed less water than control mice. $iAs^{III}$ intake was estimated at 57 μg/d for 25 ppm groups and 81 μg/d for 50 ppm groups. In general, HFD groups gained significantly more fat mass and had higher fasting blood glucose and serum insulin levels than did their respective LFD groups. However, these measures decreased with $iAs^{III}$ intake in a dose dependent manner. Oral glucose tolerance tests showed an impairment of glucose tolerance for HFD groups compared to their respective LFD groups. The degree of glucose intolerance increased with $iAs^{III}$ intake in a dose dependent manner in spite of the observed decrease in adiposity, fasting glucose and fasting insulin levels. These data suggest that the diabetogenic effects of $iAs^{III}$ are independent of the mechanisms traditionally associated with consumption of high fat diets and/or obesity in mice.

## PS 1568 CADMIUM INDUCES REDUCED PLACENTAL ENOS ACTIVATION, REDUCED UMBILICAL ARTERY BLOOD VELOCITY AND FETAL GROWTH RESTRICTION IN MICE.

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Cadmium is an environmental toxin present in industrial wastes, road and house dust, and food crops grown in cadmium-polluted soil. The most significant route of cadmium exposure is via cigarette smoke. Women who smoke during pregnancy have a higher incidence of placental insufficiency and intrauterine growth retardation (IUGR) than their nonsmoking counterparts. We hypothesized that cadmium could induce fetal growth restriction and placental insufficiency through a reduction of placental blood vessels and reduction of blood flow through the umbilical artery. Methods: Cadmium chloride (40ppm) was administered via drinking water to female C57Bl/6 mice from 2-4 weeks prior to conception. Due to the reduction of successful pregnancies, the treatment was adjusted to 20ppm starting at day 1 until E15 of pregnancy. Umbilical artery blood velocity was assessed on E15 via ultrasound using the Doppler pulse method before euthanasia. Fetuses and placentas were weighed and evaluated by histopathology, TUNEL staining and western blotting. Results: Mice treated with cadmium chloride demonstrated a significant reduction of umbilical artery velocity with control mice having 59.67±14.15 mm/sec versus 35.84±1.89 mm/sec in the cadmium group. Mean weights for fetuses of cadmium-treated mice were reduced 0.119 ±0.007g compared to the controls 1.349 ±0.119. Placental weights were also reduced from 0.164 g ±0.009g in the controls to 0.131±0.008g in the cadmium group. Fewer blood vessels and more TUNEL positive cells were found in the placenta with cadmium treatment. Western blots determined that endothelial nitric oxide synthase, peNOS and heat shock protein 90 (chaperone of eNOS) were decreased in placentas from cadmium exposed mothers. In conclusion, cadmium compromises HSP90 and eNOS pathways leading to reduced placental blood flow with subsequent fetal growth restriction suggesting that this metal may be one of the compounds in cigarette smoke that induces IUGR in pregnant women who smoke.

## PS 1569 HYPOXIA INDUCIBLE FACTOR 1 ALPHA (HIF1α) PROTECTS MICE LUNGS FROM COBALT-INDUCED INJURY.

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Millions of American workers are exposed to cobalt, primarily through inhalation, leading to several disorders including respiratory tract hyperplasia, fibrosis, and asthma. Cobalt is a known hypoxia mimic, attributed to its ability to stabilize hypoxia inducible factor(HIFs). HIFs are oxygen-regulated transcription factors that are critical to the development of the lung and processes such as inflammation. The role of HIFs in cobalt-induced lung injury has not been determined. To address this knowledge gap, a doxycycline-inducible, lung-specific HIF1α knockout mouse model was generated. In this study, wild type(WT) and HIF1α lung-deficient male mice were treated for two weeks (5 days on, 2 days off, 5 days on, 2 days off) with saline, 5 mM CoCl2, or 10 mM CoCl2 via oropharyngeal aspiration. HIF1α-deficient mice were more prone to cobalt-induced toxicity when compared to WT controls and the severity of the lesion correlated with the level of loss of HIF1α. In comparison to WT mice, HIF1α deficient mice had greater numbers of eosinophils and macrophages in bronchoalveolar lavage fluid following cobalt exposure with greater eosinophil infiltration in affected alveolar tissues.In addition, there was greater airway mucous cell metaplasia in the bronchiolar epithelium and greater chitinase-like protein (YM1) expression in the airway epithelium and alveolar macrophages (MBP) in the lungs of HIF1α deficient mice following metal challenge, when compared to similarly treated WT mice. Finally, inflammatory cytokine profiling revealed significant induction of KC and IL-4 only in metal-treated HIF1α deficient mice. These results suggest that HIF1α regulates the cobalt-induced inflammatory response in the lung with asthma-like phenotype.

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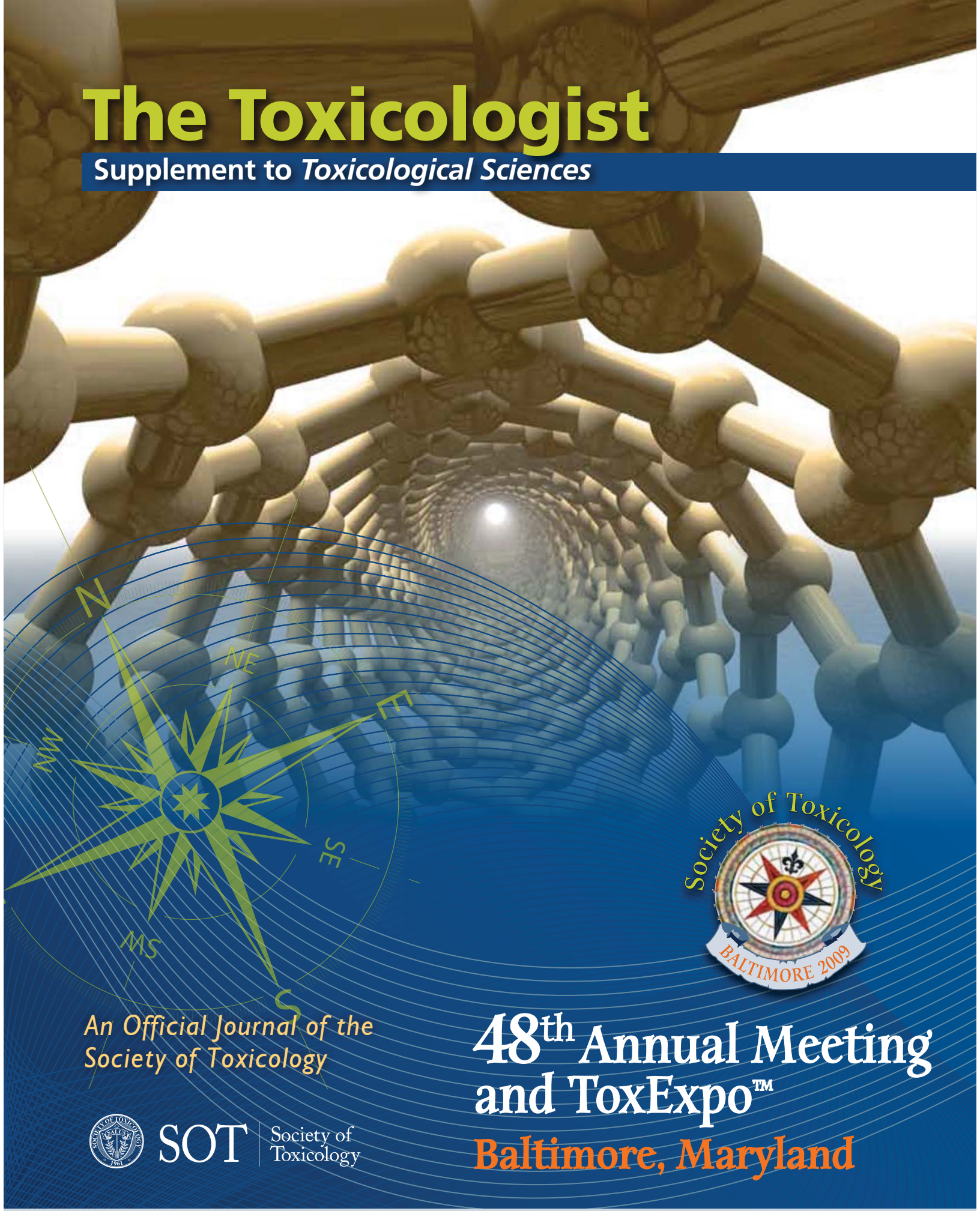


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