(CK18) M30 and M65 (hepatocellular apoptosis and necrosis biomarkers) and adipocytokines were measured. Group means were compared by ANOVA with significance set at $p<0.05$. CK18 M65 was increased in ACHS vs. HC, while CK18 M30 was decreased. Both CK18 M65 and M30 were decreased in ACHS vs. NASH. IL-6 and IL-8 were increased in ACHS vs. both HC and NASH. Of these, IL-8 was increased to the greatest extent in ACHS (52 fold vs. HC). TNFα was increased in ACHS vs. NASH. Compared to HC, adiponectin was decreased and leptin increased to similar degrees in both ACHS and NASH. Insulin was increased in NASH vs. both ACHS and HC. Steatohepatitis biomarkers were abnormal in ACHS. Some differences existed between ACHS and unexposed subjects with NASH apparently related to obesity. Liver injury in ACHS was characterized by necrosis with high-level elevation of IL-8. These data further implicate PCB exposures in steatohepatitis and systemic inflammation.

PS 1570 Quantification of Tissue Bisphenol A and Global Methylation Profiles in Kidney, Liver, and Placenta from 1st and 2nd Trimester Human Clinical Samples

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The ubiquitous monomer, bisphenol A (BPA), is an endocrine active compound used in a variety of consumer products. BPA has been associated with adverse health outcomes ranging from reproductive dysfunction to chronic diseases. Studies suggest that BPA operates by altering DNA methylation or other epigenetic markers, especially during critical windows of development. Characterization of BPA levels and epigenetic profiles across multiple tissues are currently limited to animal models or not well defined. Herein, we report tissue concentrations of BPA and global DNA methylation levels in healthy 1st and 2nd trimester human kidney, liver, and placental specimens (matched N=12 per tissue) obtained from the University of Washington Laboratory of Developmental Biology. Total BPA concentrations, measured using liquid chromatography tandem mass spectrometry, significantly differed across matched specimens (p-value: 0.002) with geometric means at 0.81, 9.19, and 1.62 ng/g for kidney, liver, and placenta, respectively. When global methylation was quantified at long interspersed retrotransposons (LINE1) repetitive elements using pyrosequencing and at CCGG sites across the genome using the Luminometric Methylation Assay (LUMA), methylation significantly differed across kidney, liver, and placenta (p-values <0.001). Average LINE1 methylation was 77.9% in kidney, 79.5% in liver, and 58.3% in placenta, while average LUMA methylation was 76.9% in kidney, 66.4% in liver, and 59.1% in placenta. No significant association was observed between total BPA and global methylation in fetal kidney or liver. However, there was a 0.23% increase in LINE1 methylation with 1 ng/g increase in total BPA in placenta (p-value: 0.002). Results suggest that BPA concentrations and methylation profiles are tissue specific in early life, and characterizing these differences will be important for exposure and risk assessment.

PS 1571 Biochemical Parameters and Fluoride Levels in Serum and Urine of Livestock Animals Accidentally Exposed to Hydrofluoric Acid

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This study aimed to evaluate the exposure of hydrofluoric acid and health status in cattle and other livestock animals raised near hydrofluric acid accident place by determining the level of fluoride ion and biochemical parameters in urine and serum. Cattle (n=111), goats (n=25) and chickens (n=5) raised in the farm near accident place were selected. Urine or blood serum samples were taken from 10-20 % of cattle per farm considering population on 17 days later of accident. Concentrations of fluoride ion (F-) in the samples were analyzed by fluoride ion selective electrode method. The concentrations of creatinine, calcium ion and other biochemical parameters in serum and urine were determined using a biochemistry analyzer. The fluoride ion concentration in urine was normalized by divided by creatinine values of urine to normalize concentration of fluoride ion in urine. The mean concentration of fluoride ion in urine of cattle (expressed as F- mg/g creatinine) were 27.8 (100m), 24.4 (500m), 11.1 (800m), 16.3 (900m), 3.02 (1.2km), 9.16 (1.5 km) and 3.58 in control group. The mean levels of fluoride ion in serum of cattle (expressed as mg/L) were 0.23 (100m), 0.15 (500m), 0.23 (800m), 0.11 (900m), 0.07 (1.2km), 0.16 (1.5 km) and 0.10 in control group. The mean concentration of fluoride ion in serum of goat (expressed as mg/L) were 0.39 (100m), 0.31 (600m), 0.02 (900m), and 0.08 in control group. The mean levels of fluoride ion in serum of chicken (expressed as mg/L) were 0.35 (100m) and 0.02 (600m). The mean±SD concentration of calcium ion in serum of cattle exposed to hydrofluoric acid (mg/dL) were 9.72±0.41 (100m), 9.54±0.57 (500m), 8.31±0.44 (800m), 9.06±0.40 (900m), 8.36±0.89 (1.2km), 9.13±0.98 (1.5 km) and 10.48±1.43 in control group. This study showed that the level of fluoride in serum and urine of animals exposed to hydrofluoric acid were decreased depending on the distance from leakage site. However, concentration of fluoride ion in samples was below the reference level of fluoride toxicosis in cattle.

PS 1572 Comparison of the Kinetics of Various Biomarkers of Benzo[a]pyrene Exposure following Different Routes of Entry in Rats

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Exposure to benzo(a)pyrene (BaP), a polycyclic aromatic hydrocarbon (PAH) classified as a known carcinogen in humans (IARC), is of great health concern for both workers and the general population. The project aimed at comparing the kinetics of key biomarkers of BaP exposure in rats following different routes of entry. Blood and excretion time courses of BaP and key biomarkers were assessed in rats exposed to a single intravenous, intratracheal, oral and cutaneous dose of 40μmol/kg BaP. BaP and several metabolites (3-and 7-OHBaP, 4,5-and 7,8-diol-BaP, tetrol, 1,6 -, 3,6- and 7,8-dione-BaP) were measured in blood, urine and feces collected at frequent intervals over 72 h post-treatment, using HPLC/fluorescence. Only 3-OHBaP was detectable in blood at all time points. In urine, total amounts of BaP metabolites excreted over the 0-72h period followed the order: 4,5-diol-BaP≥3-OHBaP>7-OHBaP>7,8-diolBaP following intravenous injection and intratracheal instillation, 3-OHBaP>7-OHBaP>4,5-diolBaP>7,8-diolBaP after cutaneous application and 3-OHBaP>4,5-diolBaP≥7-OHBaP>7,8-diolBaP following oral administration. In feces, total amounts of BaP metabolites recovered over the same period were: 7-OHBaP≥3-OHBaP>>4,5-diolBaP>7,8-diolBaP following all administration routes. Diones were not detectable using the developed method. For all routes of administration, excretion of 4,5-diolBaP was almost complete over the 0-24 h period in contrast with 3- and 7-OHBaP. After intravenous injection, intratracheal instillation and oral treatment, peak excretion of 3- and 7-OHBaP was reached in the 0-24 h period but only after 48 h post-treatment following cutaneous application. This study confirms the interest of measuring multiple metabolites due to the route-to-route differences in relative excretion of the different biomarkers and in time courses of diolBaP versus OHBaP. Concentration ratio of the different metabolites may help indicate time and main route of exposure.

PS 1573 A Cellular Model to Evaluate Salivary Gland Uptake and Clearance of Pesticides: A Novel Non-Invasive Biomonitoring Strategy

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The use of saliva as a biomonitoring matrix has potential to significantly advance quantitative dosimetry as an integral component within epidemiology studies. A major limitation for saliva biomonitoring has been an inability to identify which chemicals are readily cleared in saliva, at levels that can be detected analytically. To address this limitation, immortalized Par C10 cells (parotid gland origin) grown on a Transwell® insert (3 μm pore) were used to quantify the uptake and clearance of trichloropyridinol (TCPy) the metabolite of the insecticide chlorpyrifos. Cells seeded on Transwell inserts were maintained until 7-days post-confluence at which time they displayed expression of parotic acinar cell proteins and localization of tight junction proteins at points of cell-cell contact. For uptake/clearance studies a range of TCPy concentrations (0.2-10 μg/mL) were evaluated. TCPy was added to the basolateral chamber (lower chamber) and sampled from the apical chamber (upper chamber) longitudinally for 4 hours. In the absence of cells, TCPy rapidly diffused across the transwell; whereas, the transport rate was substantially reduced with cells, and apical concentrations of TCPy were proportional to dose. These in vitro results are consistent with in vivo pharmacokinetic model predictions where TCPy salivary gland clearance is described with a 1-compartment model and transfer from blood to saliva is via passive transcellular diffusion. These experiments have established the feasibility of utilizing an in vitro cell based uptake/clearance assay coupled with pharmacokinetic modeling as a novel chemical screening strategy to identify ideal chemical candidates for saliva biomonitoring. This approach will be further evaluated using a broader range of pesticides with varying physical and chemical properties. Once established, this approach can be exploited for biomonitoring without the need to conduct more challenging in vivo saliva clearance studies. Supported by CDC/NIOSH grant R01 OH008173.

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