investigations involves analysis of the shift in cellular metabolism that the bladder epithelia cells (RT4) undergo to sustain the hostile environment generated by B[a]P-induced toxicity.

Methods We applied the two-dimensional blue native SDS-PAGE (2D BN/SDS-PAGE) technique to elucidate the network of protein-protein interactions that regulate cellular metabolism. In order to analyse the effects of B[a]P-induced protein alterations at the metabolite level, untargeted metabolomic profiling of B[a]P-exposed cells was carried out by using gas chromatographic mass spectrometric analysis (GC-MS).

Results It appeared that B[a]P exposure led to a repression of enzymes (fructose-bisphosphate aldolase A, glucose-6-phosphate isomerase, lactate dehydrogenase) involved in glycolysis, and an up-regulation of proteins (glucose-6-phosphate 1-dehydrogenase, 6-phosphogluconolactonase) catalysing the pentose phosphate pathway and one carbon metabolism (10-formyltetrahydrofolate dehydrogenase, bifunctional purine biosynthesis protein). Untargeted metabolomics analysis revealed, lower concentration of glycolytic metabolites, as compared to glutamine, xylulose and fatty acids. The analysis of the glutathione and nucleotide content of the cells revealed a significant increase of these cofactors. Concomitantly, we did not observe any detectable increase in the production of ROS.

Discussion The study provides new insights into a B[a]P-induced shift in cellular metabolism towards processes involved in NADPH generation. B[a]P exposure causes oxidative DNA damage and hence cellular perturbations. To overcome these effects, the cells undergo a metabolic flux change from glycolysis to the pentose phosphate pathway. This shift leads to the generation of the redox cofactor NADPH that is essential for the activity of many antioxidant enzymes and intermediates necessary for the *de novo* generation of nucleotides (purine and pyrimidine) and for the normal functioning of the cells. The study provides preliminary indication of changes in cellular metabolism upon B[a]P exposure.

49 HEALTH EFFECTS FOLLOWING OCCUPATIONAL EXPOSURE TO PAVING ASPHALT FUMES

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10.1136/oemed-2018-ICOHabstracts.1177

Introduction Controversy exists as to the potential of asphalt fumes to induce health effects including respiratory, hepatotoxic, nephrotoxic, or hematotoxic responses. The main purpose of this study was to ascertain whether occupational exposure to asphalt fumes, under normal working conditions, is associated with any respiratory, hepatotoxic, nephrotoxic, or hematotoxic response.

Methods In this cross-sectional study in which 210 subjects (80 exposed and 130 reference subjects) were investigated. Using standard methods, atmospheric concentrations of total particulate and benzene-soluble fractions of asphalt fumes, as well as total particulate were measured. Additionally, urine and blood samples were taken from subjects for complete blood count, white blood cell differential test, urinalysis, and routine biochemical tests of kidney and liver function. For The prevalence of respiratory symptoms among subjects was investigated by a standard questionnaire. Additionally, the parameters of pulmonary function were measured both, prior to exposure and at the end of work-shift.

Results Both groups were similar as far as their demographic variables and smoking habits were concerned. The association between exposure to asphalt fumes and changes in most liver and kidney function tests and complete blood count parameters was statistically significant. Mean values of FEV1, both prior to the exposure (89.58% [SD 18.69%] predicted value) and at the end of shift (85.38% [SD 19.4%]), were significantly ($p<0.05$) smaller than those of the comparison subjects (93.88% [SD 13.93%]). Similarly, pre-shift (87.05 [SD 8.57]) and postexposure (89.95 [SD 6.85]) FEV1/FVC ratio were both significantly ($p<0.01$) lower than those of the unexposed employees (107.56 [SD 9.64]). The pattern of changes in parameters of lung function in asphalt workers was consistent with that of chronic obstructive lung disease.

Conclusion This study showed that exposure to sub-threshold limit value levels of total particulate and benzene-soluble fractions is associated with early liver and kidney dysfunction as well as haematological disorders. Also, significant decrements in the parameters of pulmonary function as well as, a significant increase in the prevalence of respiratory symptoms in asphalt paving workers compared to their unexposed counterparts provided evidence in favour of a significant association between exposure to asphalt fumes and lung function impairments.

515 USE OF URINARY BIOMARKERS AND BIOASSAYS TO EVALUATE CHEMICAL EXPOSURE AND ACTIVATION OF CANCER PATHWAYS IN FIREFIGHTERS

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10.1136/oemed-2018-ICOHabstracts.1178

Introduction Cancer is a leading cause of fire service morbidity and mortality. Measurement of urinary polycyclic aromatic hydrocarbons (PAHs), a group which includes known carcinogens, provides a means of evaluating absorption from all exposure routes. Activation of the aryl hydrocarbon receptor (AhR) and p53 pathways is associated with cancer, and their evaluation through *in vitro* urinary bioassays provides measures of toxicity of the chemical mixtures to which firefighters are exposed.

Methods Urine was collected at baseline and two hours after responding to fires in 80 Tucson firefighters. Urine contaminants were de-conjugated using β-Glucuronidase and extracted using Focus Solid Phase Extraction (SPE) cartridges. Quantification of hydroxylated PAH (PAH-OH) target analytes was conducted with GC-MS/MS. In addition, the urinary extracts were evaluated using AhR and p53 *in vitro* bioassays.

Results Compared to baseline, structural firefighting was associated with an increase in urinary PAH-OH concentrations. Increased concentrations were also found in training fires when self-contained breathing apparatus (SCBA) were used assiduously, suggesting a primary route of dermal exposure in that setting. Contrary to expectations, engineers (vehicle drivers) also demonstrated increased urinary PAH-OH concentrations, which was felt to be due to inhalation exposure as they generally did not wear SCBA. AhR and p53 activation occurred in general with higher concentrations of PAH-OHs