Results There were 5437 cancer cases among agricultural workers. Among men, an increased risk of multiple myeloma was observed (HR: 1.38, 1.04–1.83), as well as oral cancer (HR: 1.28, 1.09–1.51), specifically lip cancer (HR: 2.94, 2.26–3.83), but had decreased risks of lung, esophageal, and liver cancers. Female agricultural workers were at increased risk of pancreatic cancer (HR: 1.44, 1.05–1.99), but decreased risk of lung, breast and cervix cancer. Higher risks of rectal cancer were also observed specifically among female farm workers and labourers (HR: 1.44, 1.02–2.04).

Conclusions Exposure to pesticides may have contributed to the increased risks of multiple myeloma in men and pancreatic cancer in women. Increased risks of lip cancer in men could be attributed to sun exposure in agricultural workers while the array of decreased risks suggests reduced smoking and alcohol consumption in agricultural workers compared to the general population.

| 394 | 2,4-D USE AND CANCER INCIDENCE IN PESTICIDE APPLICATORS IN THE AGRICULTURAL HEALTH STUDY |

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Objectives 2,4-dichlorophenoxyacetic acid (2,4-D) is one of the most widely used herbicides in the world. It has been associated with increased risk of non-Hodgkin lymphoma (NHL) in multiple epidemiologic studies, with some evidence for association with cancer at other sites. Findings from experimental studies, however, have been largely negative with respect to NHL. Within the Agricultural Health Study (AHS), a prospective cohort of licensed pesticide applicators in the United States, we evaluated use of this herbicide and multiple cancer sites.

Methods We used Poisson regression to estimate relative risks (RR) and 95% confidence intervals for cancers that occurred from enrollment in the AHS (1993–97) through 2008. Total lifetime days of use of 2,4-D were calculated based on information provided at enrollment and at a follow-up interview conducted 5 years later. In addition, an intensity-weighting algorithm was applied to account for factors that modify exposure.

Results Overall, 78% of the 52,324 applicators who provided information on 2,4-D use and who were cancer free at enrollment reported using 2,4-D. Among this group, there were 5,168 incident cancers. Compared to non-users, there was no association with cancer risk overall (p-trend = 0.68), NHL overall (p-trend = 0.84), or any sub-type of NHL with intensity-weighted lifetime days. Conversely, in the highest quartiles, there was an elevated risk of gastric cancer (RR = 2.3, 95% CI:1.1–5.2, p-trend = 0.03) and a suggestion of elevated risk of brain cancer (RR = 2.3, 95% CI: 0.9–5.7, p-trend = 0.31).

Conclusions The results from this prospective study showed no association between use of 2,4-D and NHL, the cancer most often linked to this herbicide. The increased risk of gastric cancer is noteworthy but supporting data are limited. Some previous studies of brain cancer have suggested a role for pesticides, particularly herbicides; to our knowledge there is no other study specifically suggesting an association with 2,4-D.

Session: 33. Hazard identification and biomarkers

| 395 | SOLVENT-INDUCED DNA METHYLATION CHANGES: A TRANSLATIONAL STUDY |

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Objectives Workers exposed to solvents are at risk for developing cancer and neurobehavioral diseases. Evidence is growing on the role of epigenetic alterations involved in the development of both diseases. In this project, we set up a translational study to investigate the impact of solvents on DNA methylation alterations and neurobehavioral changes.

Methods First, we assessed global DNA methylation changes in human lymphoblastoid (TK6) cells *in vitro* in response to 10 solvents. Next, a cross sectional study was set-up to validate these results in 128 solvent workers. Liquid chromatography-mass spectrometry was used to quantify global DNA methylation profile in TK6 cells and in lymphocytes of the workers. Each participant underwent a series of tests based on the Neurobehavioral Evaluation System.

Results Benzene, hydroquinone, styrene, carbon tetrachloride and trichloroethylene induced global DNA hypomethylation in TK6 cells. DNA methylation in solvent-workers was, after correction for age, negatively associated with total exposure time (r = -0.198, p = 0,025) and the cumulative exposure index (r = -0.244, p = 0,006). Age and smoking were associated with a global DNA hypomethylation, while use of alcohol was associated with hypermethylation. Interestingly, both DNA methylation and exposure were significant predictors for neurobehavioral effects in the multivariate regression models.

Conclusions We report changes in global DNA methylation as an early event in response to solvents. Global unmethylated DNA is known to dysregulate transcription, which has an impact on the gene expression and the function of cells, e.g. loss of control of cell division. These results are suggestive for the possible involvement of epigenetic mechanisms in neurodegenerative diseases and cancer. Lymphocytes are not necessarily the target tissue, but might be a good surrogate because of their accessibility and the high correlation with methylation profiles in somatic tissues.

| 396 | OCCUPATIONAL EXPOSURE TO IRON AMONG STEEL WORKERS INCREASED OXIDATIVE DNA DAMAGE IN PERIPHERAL LEUKOCYTES |

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Objectives The role of iron on Reactive Oxygen Species (ROS) generation by catalysing Fenton reaction have been suggested by many studies as an important factor in increasing oxidative DNA damage. Mitochondria represents an important biological source and target of ROS that induce 8-hydroxy-2'-deoxyguanosine (8-OHdG) formation. Occupational exposure to metal