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EPIGENETIC CHANGES IN FIREFIGHTERS

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Introduction Firefighters are exposed to carcinogens and have elevated cancer rates. Cancer may be caused by activation of oncogenes or inhibition of tumour suppressor genes, such as through alterations in microRNA (miRNA) concentrations and DNA methylation. We hypothesised that occupational exposures in firefighters would lead to epigenetic changes associated with activation of cancer pathways and increased cancer risk. We designed this study to compare epigenetic changes in incumbent firefighters and new recruits.

Methods At the time of subject selection, the study population consisted of 119 incumbents and 70 recruits. From this group, 108 subjects were randomly selected for miRNA analysis and 96 for DNA methylation analysis, both evenly divided among incumbents and recruits. Only non-smoker male firefighters were included in the final comparison. MiRNAs and DNA methylation were measured with the nCounter Human v3 miRNA expression assay with over 828 miRNAs and the Illumina MethylationEPIC 850 k chips, respectively.

Result After adjusting for age and BMI, miR-1260a, miR-145-5 p, miR-181c-5p, miR-331-3 p, miR-361-5 p, and miR584-3 p were significantly downregulated in incumbent firefighters. MiR-208b-5p, miR-30e-3p, and miR-486-3 p were significantly overexpressed in incumbents. Controlling the genome-wide false discovery rate at 5%, 22 CpGs were annotated to promoter regions of a gene and were hypermethylated in the incumbents including YIPF6, HELB, SYT5 and DVL2.

Discussion MiR-181c-5p, miR-145-5 p, and miR-584-3 p are involved in tumour suppression. MiR-30e-3p is upregulated in skin cancer and is a poor prognostic factor in lung cancer. Co-amplification of the YIPF6 gene with the androgen receptor may stimulate prostate tumour progression. Aberrant activation of HELB reduces genomic stability, a hallmark of cancer. SYT may have a novel function in breast cancer. DVL2 is a part of the Wnt signalling pathway involved in multiple cancers. These epigenetic biomarkers of carcinogenic exposure in firefighters should be further evaluated in larger studies.

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THE DECREASE OF BIOLOGICAL BLOOD LEAD LEVELS AT A LEAD NITRATE PLANT IN SOUTH AFRICA

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Introduction Following a significant increase in production at a Lead Nitrate plant in South Africa, the blood lead levels in their employees also increased. This was concerning as the average blood Lead results in 2015 increased to 43 ug/dl, well above the legal South African National limit of <20 ug/dl. This prompted the need to introduce more stringent controls/interventions in order to decrease the average blood Lead levels and avoid adverse health effects to the workers.

Methods The controls/interventions used, comprised the following;

- a retrospective analysis of all historical biological monitoring results with direct comparisons to the man-job specifications, as well as the occupational hygiene monitoring results of airborne pollutants;
- an intensive Lead study, which included a visit to a nearby Lead refining facility to obtain comparative data;
- the demarcation and separation of work zones including changing and dining facilities;
- conducting of medical examinations, to include Lead effect monitoring;
- a review of personal protective equipment (PPE) and implementation of controls to ensure correct use thereof;
- introduction of a comprehensive Lead-health training programme; and
- introduction of a three-monthly biological blood Lead monitoring and counselling programme.

Results As a consequence of the above controls/interventions, the average blood Lead level decreased from 43 ug/dl in 2015, to 23 ug/dl for the half year average of 2017, representing a 45% decrease over a period of 18 months. Some employees achieved significant decreases in lead levels, from well above 30 ug/dl to well below 20 ug/dl.

Discussion An increased understanding and awareness of the hazards of Lead, both by the employer and employees, resulted in a significant decrease in the average blood Lead burden of the workforce. The continuous application of control/interventions in the workplace should lead to further decrease in the average blood Lead levels well below the South African legal limit.

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OCCUPATIONAL DIOXIN EXPOSURE OF WORKERS IN MUNICIPAL WASTE INCINERATORS

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Introduction In combustion ashes and dust in the machine hall of two municipal waste incinerators in Flanders, dioxin-like substances were found. The aim of this study was to explore if exposure to these ashes and dust induced an increased uptake of dioxin-like substances.

Methods 50 subjects working in two municipal waste incinerators participated, comprising 32 maintenance workers exposed to dust and ashes, 7 garage workers and 11 administrative workers. The exposed workers were divided according to seniority (≤10 years. and >10 years.). Serum dioxin-like activity was assessed by chemical-activated luciferase gene expression (CALUX) assay. Following non-occupational factors were assessed by questionnaire: BMI, smoking, living near a road with heavy traffic and nutrition intake.

As dioxins accumulate in the body, higher serum dioxin levels could be expected in the exposed maintenance workers. Therefore, the serum dioxin levels of the maintenance workers group were compared with those of the other groups. Additionally, maintenance workers with ≥10 years. seniority were compared with workers with <10 years. seniority. Mann-Whitney U test and Kruskal-Wallis were used where appropriate.

Results Mean overall serum dioxin level was: 31.4 pg CALUX TEQ/g fat (mean values for the general Flemish population: 35.0–41.8 pg). Maintenance workers had significantly ($p < 0.05$) lower serum dioxin levels (mean 26.9 pg) than garage workers (38.3 pg) and administrative workers (38.8 pg). Maintenance workers with >10 years seniority had lower serum dioxin levels (24.7 pg) than those with ≤ 10 years seniority (31.5 pg). This difference was not significant. No higher serum dioxin concentrations were found in smokers, high BMI, living near a road with heavy traffic.

Conclusion The results showed no increased dioxin-like serum levels in maintenance workers in the two municipal waste incinerators. These results seem to indicate that there is no additional risk for dioxin exposure in the two considered waste incinerators.

357 OCCUPATIONAL EXPOSURE TO SELENIUM COMPOUNDS, ITS EFFECT ON BIOLOGICAL PARAMETERS AND MARKERS OF DIABETES

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Introduction Selenium (Se) exhibits a very small safety margin between recommended daily intake and harmful dosages (e.g. elevated risk for diabetes). Volunteer exposure studies have indicated different metabolisms for organic and inorganic Se compounds. The objective of this study was to establish a comprehensive biological monitoring approach for elemental/inorganic Se exposure at workplaces and to evaluate its potential effects in men.

Methods In a case-control study we determined total Se in plasma and urine, Se speciation in urine, Glutathione peroxidase activity, prothrombin time, glucose, HbA1c and proinsulin in 18 employees of a Se processing plant and 18 age matched controls without occupational Se exposure. For the Se-exposed group we additionally measured the average shift level of total Se and of water-soluble Se-fraction in air, Se in urine at the beginning and at the end of the shift, and after at least two weeks off-work.

Results Se plasma levels of the exposed individuals ranged between 62 and 123 $\mu\text{g/L}$ and urine levels after shift ranged between 22 and 340 $\mu\text{g/g}$ creatinine. Both were significantly higher than the levels in the controls. The air exposure to total Se ranged between $<\text{LOD}$ and 2394 $\mu\text{g/m}^3$. For glutathione peroxidase activity, prothrombin time, glucose, HbA1c and proinsulin there were no significant differences between the two groups.

Conclusion At workplaces in the selenium processing industry considerably high air concentrations of Se were detected, which exceeded the German exposure limit (MAK 20 $\mu\text{g/m}^3$). In contrast, the biological tolerance limit (BAT 150 μg Se/L plasma) was not exceeded. These diverging results necessitate a differentiated look on Se at workplaces. The workplace conditions including the kind of selenium (elemental, inorganic, water-soluble, organic) should be considered. A revision of selenium threshold values seems advisable.

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URINARY BLADDER CANCER IN A FORMER AREA OF COAL, IRON AND STEEL INDUSTRIES IN GERMANY

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Introduction Urinary bladder cancer risk in coal miners is currently under debate. We report on a recently performed study in 2 departments of urology in Dortmund, a centre of the former underground hard coal mining industry in Germany. In the greater Dortmund area in the 1990s when coal, iron and steel industries were still active, 70% of bladder cancer cases were glutathione S-transferase M1 (GSTM1) negative, compared to 54% in unexposed controls.

Methods A total of 400 bladder cancer cases and 442 controls with benign urological diseases but without a history of malignancies, were assessed by questionnaire from July 2009 to July 2013. Furthermore, all patients were genotyped for polymorphic enzymes relevant for bladder cancer like glutathione S-transferase M1 (GSTM1) and N-acetyltransferase 2 (NAT2).

Results More than ten years after closure of these industries, the frequency of the GSTM1 negative genotype decreased to 52%, which is a normal finding in general population (OR 0.96, 95% CI: 0.73 to 1.26; smokers: OR 0.93, 95% CI: 0.66 to 1.30; non-smokers: OR 1.02, 95% CI: 0.58 to 1.80). However, former hard coal miners had still an elevated bladder cancer risk (hospital A: 20 bladder cancer cases (10%) and 8 controls (3%) (OR 3.22, 95% CI: 1.39 to 7.49); hospital B: 32 cases (16%) and 20 controls (10%) (OR 1.72, 95% CI: 0.95 to 3.12). The slow N-acetyltransferase 2 status, which is associated with an increased bladder cancer risk in persons formerly exposed to aromatic amines, was normal in hard coal miners with bladder cancer in all three studies in the Dortmund area.

Conclusion After closure of the coal, iron and industries in the 1990s, GSTM1 negative genotype is currently no more a relevant bladder cancer risk factor. However, an elevated bladder cancer risk in former hard coal miners is still observable.

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PROGNOSIS OF OCCUPATIONAL BLADDER CANCER AND POLYMORPHIC XENOBIOTIC METABOLISING ENZYMES

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Introduction In recent years, approximately 150 bladder cancer patients per year were acknowledged as an occupational disease in Germany. The question rises whether in genome-wide association studies described bladder risk factors may modulate the prognosis of occupational bladder cancer.