

Discussion GEQUAS enables proficiency testing for the most biomonitoring parameters which are used for the exposure assessment at workplaces (metals, solvents, pesticides, new emerging chemicals). Levels and specification are carefully adjusted to the practice.

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MIXIE, A TOOL TO IMPROVE ASSESSMENT OF CHEMICAL RISK IN CASE OF MULTIPLE EXPOSURE

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Introduction Multiple exposure to chemicals is a common situation in workplaces. However, most methods used to evaluate chemical risk do not consider the potential effects of mixtures. The aim is to present a tool helping to evaluate chemical risk in case of multiple exposure.

Methods MiXie is a web tool (<http://www.inrs-mixie.fr/http://www.inrs-mixie.fr/>) developed in Quebec in 1997 and adapted to the French context by the French National Research and Safety Institute for the prevention of occupational accidents and diseases (INRS). It helps industrial hygienists to assess the potential risk of multi-exposure. Additivity of effects is the basic assumption.

Results Whenever measurements of atmospheric concentrations are provided, MiXie calculates the exposure index of the mixture (i.e. the sum of the ratios between each concentration measured and its occupational exposure limit value x 100). If this index exceeds 100%, MiXie signals that there is a potential risk for certain organs, even though each limit value is respected.

When measurements of atmospheric concentrations are not provided, MiXie highlights the common effects classes of the substances present and warns about a potential risk of additive effects.

If the mixture contains a substance belonging to the 'cancer' or 'sensitizer' effect class, additivity does not apply and MiXie warns the industrial hygienist regardless of the concentration measured.

Conclusion The MiXie database helps to identify potential risk situations related to multi-exposure to chemicals. Such situations may go unnoticed with a monosubstance approach. But MiXie users should be aware of its limits: additivity does not apply to all situations, the number of substances is restricted (130), etc. Experts are working to improve the tool by increasing the number of substances, making it more user-friendly, etc.

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EFFECTS OF METAL-RICH PARTICULATE MATTER EXPOSURE ON EPSTEIN-BARR VIRUS AND HUMAN ENDOGENOUS RETROVIRUS W (HERV-W) METHYLATION HEALTHY STEEL-WORKERS

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Introduction Inhaled particulate pollutants have been shown to produce systemic changes in DNA methylation. Global hypomethylation has been associated to viral sequence reactivation, possibly linked to the activation of pro-inflammatory pathways occurring after exposure. We aimed at evaluating the effects of PM exposure on DNA methylation of the Wp promoter of the Epstein-Barr Virus (EBV-Wp) and the promoter of the human-endogenous-retrovirus w (HERV-w), chosen as a paradigm of an exogenous virus and an endogenous retroviral sequence, in workers in an electric furnace steel plant with well-characterised exposure to metal-rich particulate matter.

Methods We measured EBV-Wp and HERV-w DNA methylation through bisulfite PCR Pyrosequencing on peripheral blood leukocytes DNA obtained from 63 male healthy workers, on the first day of a work week (baseline, after 2 days off work) and after 3 days of work (post-exposure). We determined individual exposure to inhalable particles and metals for all subjects. Paired t-test was used to compare baseline and post-exposure samples. Linear mixed models were fitted to evaluate the association between metal-rich particle exposure and DNA methylation.

Results Comparing samples obtained at baseline and after 3 days of work, the mean methylation of EBV-Wp was significantly higher at baseline compared to post-exposure (baseline=56.7; postexposure=47.9; p-value=0.009), whereas the mean methylation of HERV-w did not significantly differ. In a regression model adjusted for age, body mass index and smoking, nickel, arsenic and lead had a positive association with EBV-Wp methylation (nickel: $\beta=16.16$, p-value<0.001; arsenic: $\beta=13.0$, p-value=0.02; lead: $\beta=16.53$, p-value<0.001).

Conclusions The difference observed comparing baseline and postexposure samples may be suggestive of a rapid change in EBV methylation induced by air particles, while correlation between EBV methylation and metal exposure may represent an adaptive mechanism that should be further characterised in future investigations.

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STEROID HORMONES, MELATONIN AND VITAMIN D IN FEMALE HOSPITAL NURSES WORKING WITH '1-1-1' RAPID CYCLE SHIFT

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Introduction Shiftwork that disrupts circadian rhythms has been classified as probable carcinogenic to humans by IARC (2007). Among possible mechanisms of this effect, the modification of hormone homeostasis has been advocated. Aim of the present study was to evaluate the influence of night-shift work on the levels of steroid hormones, melatonin, and serum vitamin D in hospital female nurses.

Methods Ninety-five female hospital nurses were recruited: 45 performing '1-1-1' fast rotating shift schedule on 5 day cycle (morning – afternoon – night – rest – rest) and 50 working only on dayshift, as controls. Specimens were collected to measure 13 serum steroid hormones, salivary cortisol, cortisone and melatonin in morning and evening samples, and serum vitamin D. All markers were assayed by liquid chromatography coupled with triple quadrupole mass spectrometry.

Results Comparing fast rotating and day shift nurses, significant differences were found in the levels of steroid hormones. Multiple linear regression analysis, considering hormones or vitamin D as dependent variable and work-shift type as independent variable, showed no differences between the two groups as concerns the levels of stress hormones, whereas a significant increase of corticosterone and a marginal decrease of vitamin D were observed in fast rotating shift nurses, after adjusting for age, body mass index, tobacco smoking, and sampling time.

Conclusion This work shows that the a rapid rotating shift-work schedule '1–1–1' does not modify the global steroid hormone homeostasis; however, further work is needed to investigate the meaning of the observed increase of corticosterone levels.

1281 **MIRNAS IN EXTRACELLULAR VESICLES MEDIATE THE EFFECT OF PARTICULATE MATTER EXPOSURE ON COAGULATION IN A LARGE SAMPLE OF OVERWEIGHT/OBESE ADULTS**

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Introduction In Italy about 45% of people aged ≥ 18 years are overweight/obese and might thus be more susceptible to the adverse health effects of air pollution exposure. Particulate matter $\leq 10 \mu\text{m}$ (PM10) represents a common pollutant of living and working environments and has been associated with increased risk of cardiovascular diseases (CVD) and hypercoagulability. Extracellular vesicles (EV) might play an important role in PM-related CVD, as they can travel in body fluids and transfer miRNAs between cells. We investigated whether PM10 exposure is associated with changes in fibrinogen levels, EV release, and EV-miRNA content in a large sample of overweight/obese adults.

Methods EV concentrations were quantified by nanoparticle tracking analysis and flow cytometry. To identify altered levels of EV-miRNAs, we profiled miRNAs of 883 subjects by the QuantStudio 12K Flex Real Time PCR System. The top 40 EV-miRNAs were validated through custom miRNA plates. Statistical analyses included multiple linear regressions, mediation analysis and bioinformatics analysis.

Results In a sample of 1630 overweight/obese subjects from the SPHERE (Susceptibility to Particulate Health Effects, miRNAs and Exosomes) study, short-term exposure to PM10 was associated with increased release of EVs, especially those from monocyte/macrophage components (CD14+) and platelets (CD61+). Nine EV-miRNAs (let-7c-5p; miR-106a-5p; miR-143-3 p; miR-185-5 p; miR-218-5 p; miR-331-3 p; miR-642-5 p; miR-652-3 p; miR-99b-5p) were downregulated in response to PM10 exposure and exhibited putative roles in CVD. Five of these nine EV-miRNAs were mediators in the positive association between PM10 exposure and fibrinogen levels.

Conclusions Our study sheds some light on the potential mechanisms underlying the adverse cardiovascular health effects of air pollution exposure. Our results were obtained in a hypersusceptible population and thus strengthen the relevance of health promotion interventions for both the general

public and the working population, as they might be particularly feasible in the workplace.

1282 **URINARY 8-OXO-7,8-DIHYDRO-2'-DEOXYGUANOSINE IN TUNISIAN ELECTRIC STEEL FOUNDRY WORKERS EXPOSED TO POLYCYCLIC AROMATIC HYDROCARBONS AND METALS**

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Background Electric steel foundry workers are potentially exposed to several toxic chemicals including polycyclic aromatic hydrocarbons (PAHs) and metals. This study was aimed to assess PAHs and metals exposure in foundry workers and its association with the oxidative DNA damage evaluated as urinary 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG).

Methods Ninety-four male workers from an electric steel foundry entered the study. Sixteen unmetabolized PAHs (U-PAHs), 8 hydroxylated PAH metabolites (OHPAHs), 12 metals and 8-oxodG were investigated in urine samples.

Results Among U-PAHs, urinary naphthalene was the most abundant compound, followed by phenanthrene; benzo[a]pyrene level was $< 0.30 \text{ ng/L}$. Median 1-hydroxypyrene (1-OHPYR) was $0.52 \mu\text{g/L}$. Job title was a significant determinant for almost all U-PAHs and metals: employees in the steel smelter workshop had higher levels of high-boiling U-PAHs, maintenance workers and workers from the galvanization and rolling workshop were the most exposed to metals. Median 8-oxodG level was $3.20 \mu\text{g/L}$. No correlation between 8-oxodG and 1-OHPYR or any OHPAH was found. Significant correlations between 8-oxodG and some U-PAHs and metals were found, particularly acenaphthylene, phenanthrene, anthracene, fluoranthene, pyrene, chromium, manganese, cobalt, zinc, arsenic, barium, thallium, and lead.

Conclusions The oxidative DNA damage was moderate and in the range reported in other occupational fields and in the general population. These results indicate that the investigated biomarkers were only minor contributors to urinary 8-oxodG.

1286 **CLOSING THE GAPS BETWEEN OCCUPATIONAL AND ENVIRONMENTAL EXPOSURES AND HUMAN HEALTH**

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