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Abstracts

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Keynote Lectures

K.1

0116

The IARC Monographs Program: the increasing use of mechanistic data in cancer hazard identification.

Kurt Straif
International Agency for Research on Cancer, Lyon, France

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K.2

0113

Importance of toxicokinetics in understanding and interpreting biological monitoring results

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Biological monitoring is increasingly used to assess exposure to environmental or occupational contaminants. However, understanding and interpreting biomonitoring data from a health risk perspective remains an issue. Knowledge of the toxicokinetics of contaminants and their metabolites is a key element. In this context, the time courses of biomarkers of exposure to different environmental contaminants, such as polycyclic aromatic hydrocarbons and pyrethroid, organophosphate, carbamate, fungicide pesticides, have been studied in various biological matrices of animals and humans. Relevant toxicokinetic parameters were determined from these profiles, such as absorption and elimination rates or time-to-peak values, following different exposure routes. More complete toxicokinetic analyses were performed using toxicokinetic models that allow relating a biomarker time course measurement in a sampled matrix, such as urine, to the time-profiles in blood and tissues and input rates per unit of time for different exposure routes and temporal scenarios. Information on the time course of the exposure biomarker of interest is essential prior to routine analysis in potentially exposed groups to assess most appropriate sampling strategies and establish the significance of a measurement at a specific time point. It also raises questions whether spot sampling is sufficient for routine follow-up of individuals and highlights limits related to the units of expression of biological measurements (e.g. creatinine-adjusted concentrations). With toxicokinetic models, it further becomes possible to reconstruct exposure or absorbed doses from biomonitoring data. Biological guideline values aiming at preventing adverse effects may also be derived by linking exposure limits with corresponding biomarker values in the sampled matrix.

K.3

0117

State of the art in exposome research.

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The introduction of omics in environmental epidemiology represents a new paradigm for studying the influence of environmental agents on health over a lifetime. The ability to generate efficiently parallel omics datasets and recent advances in personal environmental monitoring provide a strong technological backdrop for exploiting cohort biospecimens to assess personal-level exposures and responses. Several aspects of these studies require methodological development to make best use of such opportunities. What is clear is that the scope of the exposome concept will require the input and collaboration of researchers across many disciplines in order for exposome studies to succeed, and will rely as much upon the design and philosophy that underpin them, as on our ability to generate complex datasets about their participants. I will discuss aspects of the use of omics that will require further development in the near future, including (a) the underlying causal interpretation and models; (b) the "meet-in-the-middle" concept, with examples; (c) the role of life-course epidemiology; (d) the role of "calibration"; (e) the development of adequate biostatistical models.

K.4

0118

Human Biomonitoring in mercury and lead contaminated hot spots in Africa and Asia.

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Artisanal small-scale gold mining is performed in over 70 countries all over the globe. Mercury is used to extract the gold from the ore. The smelting of so-called amalgams is the main source of high human exposures to mercury vapours. Several projects of UNIDO (United Nations Industrial Development Organization) and WHO (World Health Organization) have been performed to medically examine miners and community members, including children.

Human specimens were taken, such as urine, blood, hair and breast milk. These specimens were analysed for total mercury and a sub-set were analysed for methyl-mercury. The results of these projects will be shown, indicating a very high mercury exposure especially for the miners. Moreover a focus of the presentation will be on the opportunities and restrictions for human biomonitoring sampling in remote hot spot areas (the Philippines, Indonesia, Zimbabwe, Tanzania and Mongolia) e.g. a mobile mercury analyser was used to measure inorganic mercury in urine. This is a useful instrument to get immediate results and to communicate these results with the affected population.

Finally a case report from Medecins sans Frontieres (MSF) will be presented, where lead was the main contaminant in a mining area in Nigeria. Mobile equipment was used to assess the lead levels of intoxicated children, and to monitor the detoxification with chelating agents.

Human biomonitoring in hot spot areas is possible. Results showed very high exposure of the population to mercury or lead. These results are mainly useful for risk estimation. Human biomonitoring is a good tool to assess the quality of interventions.

Session 1: Adduct biomarkers

1.1

0034

Biomarkers of Polycyclic Aromatic Hydrocarbon Exposure in Coke Oven Workers: relationship between PAH internal dose markers and target organ DNA adduct levels

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Aims: Coke oven workers have increased risk of urinary bladder cancer, but etiological agents are unknown. PAH are common carcinogens in coke oven emissions, but aromatic amines are also present. The purpose of this work was to determine whether there was a relationship between PAH biomarkers of internal and effective dose.

Methods: Pre-exposure urine samples were collected from 32 coke oven workers. Samples were filtered to collect the exfoliated urothelial cells for carcinogen-DNA adduct analysis using 32P-postlabelling. The filtrate was used to determine 1hydroxypyrene levels using solid phase extraction and HPLC with fluorescence detection.

Results: Urinary 1HP levels were highest in workers of top, then side ovens then those working both top and side ovens as opposed to area workers and supervisors. 1HP levels were not affected by smoking status, but were negatively affected by seniority. There was no significant difference in total DNA adduct levels between top oven, side, top and side oven and side area workers, but all were significantly greater than the levels seen in supervisors. 1HP levels were correlated with a single DNA adduct measured in exfoliated urothelial cells (r= 0.362, p= 0.05). In side oven workers the correlation was much stronger (r=0.804, p=0.01). This adduct was not related to smoking status, but was negatively correlated with seniority (r=-0.71, p= 0.05).

Conclusions: The data indicate that a single adduct in the urinary bladder of coke oven workers is related to their PAH exposure. This adduct represents about 50% of the total DNA damage seen in this organ.

1.2

0082

Amino acid adducts in urine as a new type of biomarkers of alkylating agents

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Aims

Covalent adducts with blood protein globin are used as biomarkers of cumulative exposure to alkylating agents or other reactive compounds. We hypothesize that following physiological removal of erythrocytes from the circulation, the adducted globin undergoes proteolysis to free amino acids and amino acid adducts, the latter being excreted in urine. Our intended studies include follow-up of urinary adducts in rats dosed with alkylating agents or given intravenously the chemically modified erythrocytes. In the first stage, in vivo fate of model amino acid adducts with methylisocyanate and ethylene oxide has been investigated.

Methods

N-(Methylcarbamoyl)valine (MVU), N_{ε}-(methylcarbamoyl)lysine (MLU), N-(2-hydroxyethyl)valine (HEV) and S-(2-hydroxyethyl)cysteine (HEC), were synthesised and injected intraperitoneally to rats, 10 mg/kg b.w. Urine collected over 2 days was analysed by HPLC/ESI-MSMS for parent compounds and/or metabolic products.

Results

The dominant compounds identified in urine following administration of MVU, MLU, HEV and HEC were MVU, N_{α}-acetyl-MLU, HEV, and S-(2-hydroxyethyl)- and S-carboxymethylmercapturic acids, respectively. More than 90 % of the total products were excreted during 24 h.

Conclusions

All administered adducts were rapidly excreted unchanged or in the form of dominant metabolic products. Identical compounds might be formed also by proteolytical cleavage of adducted globin and might therefore represent a new type of biomarkers, combining specificity, a potential for monitoring of long-term cumulative exposure, and accessibility by non-invasive sampling. Experiments addressing this hypothesis are in progress.

Acknowledgement: The study was supported by the grant NT13401-4/2012 from Internal Grant Agency of the Czech Ministry of Health.

1.3

0026

Suitability of N,N-dimethylformamide derived haemoglobin adduct as long-term biomarker

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Apart from the metabolite N-acetyl-S-(methylcarbamoyl)-cysteine (AMCC), N,N-dimethylformamide (DMF) forms an adduct at N-terminal valine of haemoglobin. For quantitative analysis the haemoglobin adduct is transferred into 3-methyl-5-isoproylhydantoin (MIH). The aim of the study was to clarify whether the MIH level may serve as a reliable long-term biomarker of occupational DMF exposure.

We investigated 152 individuals occupationally exposed to DMF during polyacrylonitrile fibres production. The current exposure was determined by ambient DMF monitoring and biological monitoring. Blood samples were taken during the work shift and urine samples were collected at the end of shift. For 69 employees urine samples were additionally collected several times during a period of three weeks prior to blood sampling. MIH levels in blood were determined in isolated globin by GC-MS. AMCC levels in urine were determined by LC-MS/MS. Additionally, MIH and AMCC levels were determined in 32 individuals without occupational exposure to DMF (controls).

The ambient DMF exposure of the employees ranged between <0.5-21.4 ppm. The median AMCC level for exposed workers and controls was 4.4 mg/g creatinine (range: 0.01-78.8 mg/g) and 0.17 mg/g (0.05-1.16 mg/g), respectively. The median MIH level for exposed workers and controls was 49 nmol/g globin (0.5-414 nmol/g) and 1.3 nmol/g (<0.5-16.3 nmol/g), respectively. A significant association was found between current AMCC excretion and MIH levels. However, statistical reliability increased distinctly using the average AMCC excretion determined during a period of three weeks prior to blood sampling.

The results clearly confirm the suitability of MIH as a long-term biomarker of DMF exposure.

1.4

0031

Biomonitoring of 4,4'-methylenediphenyl diisocyanate (MDI) with new specific biomarker MDA-Val-Hyd

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Biomonitoring MDI means either measuring MDA (methylendianiline) in urine or haemoglobin adduct in blood. With both methods only the sum of MDI (isocyanate) and MDA (aromatic amine) body burden is measured. In rats 5-Isopropyl-3[4-(4-aminobenzyl)phenyl]hydantoin (MDA-Val-Hyd) turned out to be a specific marker for 4,4-MDI. Our aim was to test the validity of this marker for the first time in humans.

A new sensitive analytical method was developed for determining MDA-Val-Hyd in human blood. Secondly, this method was applied in several subjects. MDI biomonitoring was performed in 18 workers of a MDI-producing plant. Then the marker was measured in 40 subjects not knowingly exposed to MDI. Moreover, MDI exposure was investigated in 4 persons who sprayed polyurethane foam containing 10% free MDI on a board for 20 min. Finally, 2 subjects were exposed to MDI for medical reason (verification of an isocyanate asthma) in an exposure chamber.

In the analytical method developed globin was isolated from EDTA-blood. Then, the deuterated internal standard was added and the sample was hydrolysed with hydrochloric acid. The hydantoin formed was extracted with chloroform at pH 9 and subsequently derivated with HFBA. Separation and detection was done by GC-HRMS-NCI. A limit of quantification of 10 ng/L blood was achieved. In 15 out of 18 workers MDA-Val-Hyd was found in concentrations between 10 and 850 ng/l blood. No background level was found in 40 subjects. In 4 persons spraying foam no marker was found eighter. In 2 patients provocated with MDI MDA-Val-Hyd was found.

Session 2: New and emerging hazards

2.1

0053

Testing for new emerging contaminants in biomonitoring studies: How confident are we?

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Testing for new emerging contaminants has proven to be a challenge in the analytical toxicology laboratory not necessarily in the design and development of the analytical methods but in the accuracy of the results that are being generated. A number of accuracy issues have risen in results of past national studies that only show how vulnerable laboratories can be when faced with chemicals or metabolites that very few analytical standard suppliers carry in their catalogue.

The issue lies in the quality and accuracy of those analytical standards. Part of the problem however is a direct consequence of the lack of appropriate biological reference materials and external quality assessment schemes.

Many of these new chemicals are even found in their conjugated form (glucuronide, sulphate, etc) when excreted in urine. This complicates matters even more if we consider that preferably analytical standards to be used should also be obtained conjugated.

This presentation wants to address these issues and provide specific examples for urine triclosan, serum PCB congeners, urine phthalate metabolites and urine trace metal speciation.

2.2

0069

Background levels of metals in urine samples to assist with exposure assessments.

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Aims

The aim of this project was to establish current background levels of elements in urine both for commonly monitored elements and for rarer elements being increasingly utilised in new technologies. These results will be compared with published data and data from routine BM measurements undertaken at HSL.

Methods

Background levels of 61 elements in urine from a UK population are presented here from 137 people. The samples were analysed by ICP-MS in different diluents and matrices depending on the elements.

Results

Mixed effect analysis was carried out on the elements and it has been possible to establish 95th percentile background levels for 45 of the elements. However, based on the high percentage of results < LOQ, the analysis was not carried out for the following elements: Zr, Bi, Nb, Ag, Os, Y, In, Pr, Nd, Sm, Eu, Tb, Dy, Tm, Lu, and Au. The mixed effect analysis showed that, for all of the remaining elements, creatinine correcting the data in all cases gave a reduction in variability or no significant difference in variability. It was also shown that smokers have elevated cadmium and lower boron and selenium levels than non-smokers.

Conclusions

Reference levels based on 95th percentiles for many elements have been established for a UK population. Overall the results compare well with published European and American results, however there are differences for some elements.

The results show that there have been no major changes in the unexposed levels of ‘routine' metals used in everyday biological monitoring at HSL.

2.3

0109

Perfluorinated compounds: advantages and disadvantages of biomarker versus dose in epidemiological research.

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Aims: While internal biomarkers of exposure have the appeal of being closer to a biologically significant exposure than external estimates, there may be drawbacks in some circumstances, where their use may introduce bias. Perfluorooctanoic acid (PFOA) and perfluorooctane sulphonic acid (PFOS) have stable serum biomarker levels with a half-life in humans of 3-5 years. We identify factors that can affect serum levels and bias epidemiological associations, and recommend strategies to control bias.

Methods: We use serum PFOA and PFOS and biomarkers in a population of 67000 in the Mid-Ohio Valley, US population. The long half-life reflects active reabsorption via kidney and gut, and we investigate factors affecting individual variation in retention through these pathways. Associations between PFOA/S serum levels are assessed in relation to kidney function (as glomerular filtration rate, GFR) and genetic polymorphisms in some transporter proteins. Among women, serum levels are investigated in relation to pregnancy and lactation.

Results: Reduced GFR was significantly associated with increased serum PFOA – measured but not estimated from external dose. Significant associations were found with polymorphisms for PFOA and OAT3 and PFOS and OAT1 transporter proteins. Both pregnancy and lactation were associated with reduced serum levels of both PFOA and PFOS.

Conclusion: Several individual determinants of serum PFOA and PFOS have been found which could bias epidemiological associations up or down. For example kidney function cans affect a number of clinical markers and breastfeeding is associated with positive health. Distinguishing estimates of internal dose and exposure can identify these biases.

2.4

0009

Blood and exhaled air can be used for biomonitoring of hydrofluorocarbons in humans.

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Aims: Various hydrofluorocarbons (HFCs) have replaced the ozone-depleting chlorofluorocarbons and hydrochlorofluorocarbons. The main objective of this study was to investigate the possibility to use blood and exhaled air for exposure biomonitoring of HFCs.

Methods: We compared data on blood and exhaled air from a series of experiments where healthy volunteers were exposed to vapours of four commonly used HFCs; 1,1-difluoroethane (HFC152a), 1,1,1-trifluoroethane (HFC143a), 1,1,1,2-tetraflouroethane (HFC134a) and 1,1,1,3,3-pentafluoropropane (HFC245fa). The inhalation exposures were performed for 2 h during light physical exercise (50 W) in an exposure chamber. Capillary blood, urine and exhaled air were sampled until the next day and analysed for the parent substance.

Results: All HFCs had similar toxicokinetic profiles in blood with a rapid initial increase of HFC and an apparent steady-state reached within a few minutes. For all four HFCs, the inhalation uptake was low (less than 6%), no metabolism could be detected and only minor amounts were excreted unchanged in exhaled air and urine after exposure. The observed time courses in blood and exhaled air were well described by physiologically-based pharmacokinetic modelling. Considering biomonitoring, the experimental data as well as PBPK simulations suggest that sampling should be carried out 30 min after shift, as the levels in exhaled air and blood drop rapidly during the first minutes post-exposure.

Conclusion: Blood and exhaled air can be used for monitoring of HFC exposure, however, the sampling time has to be carefully considered.

Session 3: Effect Biomarkers

3.1

0105

GENOTOXIC EFFECTS OF OCCUPATIONAL AND ENVIRONMENTAL EXPOSURE TO LOW CONCENTRATIONS OF BENZENE

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Aims: To study the influence of exposure to low concentrations of benzene on the frequency of chromosomal aberrations (CA) and micronuclei (MN) in the peripheral lymphocytes of workers with occupational exposure to automobile fuels, and of control subjects with only environmental exposure to benzene.

Methods: The study included 43 male workers with occupational exposure to benzene, 19 fuel tanker drivers and 24 filling-station attendants, and 31 male subjects with no occupational exposure to this toxic substance (controls). Exposure to airborne benzene was assessed using Radiello® personal samplers. CA and MN frequencies were determined according to standard procedures.

Results: Benzene exposure was found to be significantly lower when comparing fuel tanker drivers (median 246.6 µg/m^3) with filling-station attendants (median 19.9 µg/m^3), and then with controls (median 4.3 µg/m^3). The cytogenetic biomarkers did not show significant differences among the three groups and no influence of cigarette smoking was found. Multiple regression analysis demonstrated a dependency of the frequency of MN on age in all the subjects considered as a single group (R^2=0.11), while only in the fuel tanker drivers there was a dependency on age and benzene exposure (R^2=0.53).

Conclusions: CA and MN do not seem to be able to distinguish among workers with different levels of exposure to benzene and controls, although in the fuel tanker drivers the frequency of MN depends on exposure to benzene. Instead, in the filling-station attendants and the controls, benzene does not seem to have a genotoxic effect, suggesting the possible existence of a threshold value.

3.2

0072

Influence of genetic polymorphism on t,t-MA/SPMA ratio in 301 benzene exposed subjects

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Aims

The benzene metabolism is widely studied, but nevertheless it is not completely understood yet. We examined the influence of several polymorphic genes on the concentration ratio of the main benzene metabolites, trans, trans muconic acid (t,t-MA) and S-phenyl mercapturic acid (SPMA) ratio in subjects working in an oil refinery.

Methods

The concentration of t,t-MA and SPMA was determined in the end shift urine samples of 301 workers by HPLC tandem mass spectrometry, and mean and median R (t,t-MA/SPMA) were calculated. GSTT1, GSTM1, GSTA1, GSTP1, mEHex4, mEHex3, NQO1, CYP2E1, CYP1A and MPO genotypes were determined in blood samples. Each subject filled in a questionnaire and the status of smoker or non-smoker was registered.

Results

The mean value of R was 171,28 and the median R 74.96. Subjects carrying GSTT1 null (70), GSTM1 null (157) and GSTA1 mutant (67) genotypes show increased values of R (mean 281.59; mean 173,32 – median 82.87; mean 188.89 respectively). All other genotypes do not influence the value of R. The smokers (164) have instead a reduced mean R (141.64).

Conclusions

Subjects carrying the null genotypes of GSTT1, GSTM1 and GSTA1 show a reduced conjugation of benzene epoxide with GSH with lower production of SPMA. The other polymorphisms examined do not influence the metabolite production, including GSTP1. Smokers show an increased production of SPMA, probably because of an increased level of GSH. These data should be taken in consideration when benzene exposure at low doses is assessed by means of biological monitoring.

3.3

0077

Clara cell protein in serum or urine as biomarker for airway effects -aspects on variability

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Clara cell protein (CC16) is produced in different tissues, especially in non-ciliated Clara-cells in the lungs, and eliminated by glomerular filtration. It is almost completely reabsorbed by proximal tubules. CC16 has an anti-inflammatory effect and it also modulates the innate immune system. A small "leakage" usually occurs through lung epithelium to serum. Serum CC16 is therefore used as a biomarker for airway damage and CC16 in urine is a potential marker for airway damage and renal tubular dysfunction. Men have a post-renal secretion from the prostate, complicating urinary CC16 as a biomarker. Knowledge about variability of serum and urine CC16 for healthy persons is limited.

The aim was to study the variability of CC16 in serum and urine between and within women. The study includes 23 non-smoking females 21-62 years. They donated blood and urine twice with a one week interval. Urine was collected at six fixed times during 24 hours.

CC16-excretion was higher during the day compared with the night. The range of CC16 in 24-h urine was large (0.36-20 ng/mL) and the within-individual-variation was high (>60% expressed as CV between days).

Serum CC16 had less variability between (means 10.5-54.5 ng/ml) and within individuals (CV<10% between days).The relative clearance of CC16 (compared with creatinine clearance) was (0.13%). There was no significant correlation between CC16 in serum and 24-h urine.

The results suggest that urine CC16 is not a useful biomarker for airway damage or tubular dysfunction due to high variability during the day and within -individuals in 24-h urine.

3.4

0003

Association of Past Diseases with Levels of Cadmium and Tubular Dysfunction Markers

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Objectives: The present study was initiated to examine possible association of previous diseases with Cd exposure parameters.

Methods: Data were cited from previous publications of this study group on Cd, α_1-MG, β_2-MG, NAG and urine density makers in urine of more than 17,000 adult women. Information on previous disease history was obtained by self-administered questionnaires. 13,031 never-smoking women were selected. Control cases were randomly selected after stratification by 5 years of age at a ratio of one case to three controls from those with no disease history; summation for all age strata made up the control groups. The random sampling to set up control groups was repeated three times in total. The difference between the disease group and control groups was considered valid in cases the difference was statistically significant ($p \leqq 0.05$) in all three cases after correction (or non-correction) for urine density.

Results: In the anaemia group, Cd-U was higher over corresponding three control groups. In the diabetes mellitus group, NAG-U was higher than controls, whereas the elevation in α_1-MG-U was not reproducible. In case of the hypertension group, the elevations in Cd-U, α_1-MG-U, and β_2-MG-U were observed. In the analysis of dose-response relationship, the diabetes mellitus group showed a steeper slope for β_2-MG-U and a greater intercept for NAG than control groups.

Conclusions: Care should be taken in evaluating Cd-related health examination results for those with history of such diseases as hypertension, anaemia and diabetes mellitus in particular.

Session 4: Occupational exposures 1

4.1

0012

Occupational exposure to cytotoxic drugs. French survey from 13 hospitals and about 300 health-care workers.

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Aims

Cytotoxic drugs, whose uses are increasing in cancer chemotherapy, are classified as potentially mutagenic, teratogenic and carcinogenic. A survey on professional risks carried out in 2003 has estimated that 8.2% of healthcare workers (approximately 49,000 people) are exposed to these compounds in France. But occupational exposure data remained incomplete. A study was then set up by the French Occupational Safety and Health Institute (INRS) between 2008 and 2012 to assess occupational exposure to cytotoxic drugs.

Methods

Urinary cyclophosphamide, ifosfamide, methotrexate and α-fluoro-β-alanine (5-fluorouracil metabolite) were monitored from pharmacy technicians, nurses, auxiliary nurses and cleaning agents. About 300 health-care workers were followed in 13 hospitals. Wipe surface samplings were also conducted in hospital pharmacies and oncological departments in order to make workers aware of potential sources of contamination.

Results

Positive urine samples for one or more biomarkers were quantified in all 13 hospitals. More than 50 % of the overall workers were concerned by exposure to cytotoxic drugs, with some differences between hospitals. Moreover wipe samples have revealed contamination on various surfaces in pharmacies and oncological wards.

Conclusions

These exposures to cytotoxic drugs, highlighted by biomonitoring, showed that improvements of preventive measures are still needed. They should cover both information about health risks and potential sources of contamination and adequate training about the use of protective equipment. An evaluation of the effectiveness of these preventive measures should finally be carried out regularly.

4.2

0025

Results and implications of a longitudinal biomonitoring study on mercury exposure

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Mercury is used as a flow-cathode in the chloralkali process, e.g., for the synthesis of sodium hydroxide, chlorine and alcoholates. During maintenance and repair works, exposures are likely to be higher than under regular working conditions. Apart from ambient monitoring, biological monitoring is usually applied for individual exposure analysis and assessment. Recently, limit values for mercury in urine were significantly reduced due to the neurotoxic effects of the element.

Frequent biomonitoring in urine samples by cold-vapour AAS has been carried out since several years in an electrolysis plant in order to assess the mercury exposure, and as a pro-active surveillance program to implement and control adequate safety measures. About 200 employees were divided in subgroups with different job categorisation: maintenance and repair workers, shift workers in two different cell rooms in the plant, and others. The maintenance and repair workers were monitored monthly, while the others were monitored on a quarterly or annual basis.

Under regular working conditions, limit value excursions were observed only in isolated cases while most results were in the range of the general population. In contrast, higher mercury concentrations were more frequently observed among the maintenance and repair workers. In all cases, however, the mean results of repeated measurements were below the current limit values. Occupational hygiene measures were implemented and a general reduction of the mercury exposure was achieved.

The study shows that frequent biological monitoring is an adequate and practicable tool for exposure analysis and assessment, with significant advantages over ambient monitoring.

4.3

0106

Results of a large Italian survey of biomonitoring of carcinogenic risk factors in secondary metallurgical plants.

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Aims. We performed a cross-sectional study that was aimed at evaluating the current exposure levels to some carcinogenic compounds, including metallic elements [arsenic (As), beryllium (Be), cadmium (Cd), chromium (Cr), nickel (Ni)] and aromatic polynuclear hydrocarbons (PAH) in a large sample (n=779) of male foundry workers by a biomonitoring approach, using validated biomarkers of exposure.

Methods. Workers were recruited from a sample of 15 secondary foundries that can be considered representative of the local metallurgical production in the Lombardia region of Italy. Plants included aluminium (n=3), copper alloy (n=3), electric steel (n=5) and cast iron (n=4) factories. Each worker provided an end-of-shift urine sample to determine concentrations of As, Be, Cd, Cr, Ni, creatinine and 1-hydroxypyrene (1-OHP) and received a structured questionnaire investigating lifestyle habits. Metallic elements were determined either by inductively coupled plasma mass spectrometry (Be, Cd and Cr) or by atomic absorption spectrometry (As, Ni), whereas 1-OHP was determined by high pressure liquid chromatography with fluorimetric detection. Statistical analysis included non-parametric univariate as well as multivariate linear and logistic regression analyses.

Results. Most of the determinations were within the laboratory's reference values showing that biomarkers fell below the current occupational biological limits. Age and lifestyle habits (smoking, alcohol, diet) played a significant interfering role on biomarkers' values.

Conclusion. Results demonstrate that current occupational exposure to some carcinogenic compounds in Italian secondary foundries is controlled by adopted preventive measures.

4.4

0050

Determinants of exposure to chromium, nickel and manganese during gas metal arc welding (GMAW)

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Introduction:

Welding is an industrial process emitting dangerous fumes containing metal oxides. Risk assessment is thus justified to ensure acceptable working conditions. Exposure studies have mainly focused on atmospheric monitoring. The aim of this study was to use biomonitoring in order to assess occupational exposure to chromium (Cr), nickel (Ni) and manganese (Mn) in GMA welders and to determine the factors influencing urinary concentrations for these metals.

Methods:

137 welders performing GMAW were recruited. Urine samples were collected at the end of shift the last day of working week, and a dedicated questionnaire was systematically filled. Analyses were performed by ICP-MS and multiple linear regression analysis was used to identify the determinants of exposure. Occupational exposures were compared with levels measured on 756 controls in French population.

Results:

Low urinary concentrations were measured among welders, with 0.43, 1.69 and 0.27 µg/g creatinine geometric mean concentrations for Cr, Ni and Mn respectively. Cr and Ni concentrations were significantly higher in welders than in controls, whereas Mn concentrations in welders did not differ from controls. The regression model explained 52% / 22% / 38% of the observed Cr/Ni/Mn concentrations variability. Confinement, mechanical ventilation, composition of welding consumables, welding / grinding durations were the main determinants influencing urinary metals concentrations.

Conclusion:

Although GMAW generates less welding fumes than other welding techniques, our results showed occupational exposures higher than controls for Cr/Ni and pointed out the factors influencing urinary concentrations that can be used for implementing risk management measures.

Session 5: Maternal and children's exposures

5.1

0055

Cell Proliferation of umbilical cord blood cells as a biomarker of environmental exposures

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Individual exposure assessment requires sensitive biomarkers easy to perform. An effect of air-pollution on cell physiology involves impairment of cell oxygenation and its proliferation process. We aimed to assess feasibility of using cell proliferation (CP) ratio of lymphocytes in umbilical cord blood as an indicator of a subclinical pathology in foetus.

We enrolled 210 Arab-Bedouin women giving birth in a local hospital. This population is featured by high rates of birth anomalies and multiple environmental exposures, originating from the local industrial park (IP), frequent male smoking and open fire usage. A questionnaire was collected and cord blood samples were tested by MTT Cell Proliferation Assay.

An average CP ratio was 2.4±1.2, (0.3-6.7). Women in the 1st quartile of CP ratio more frequently complained about noisy neighbourhood (14.7% vs. 2.5% in 4th quartile), reported noise and vibration at their husbands' work (88.2% vs. 62.5%; 61.8% vs. 37.5%, respectively). Women in the 4th quartile frequently lived in shacks or tents, used open fire or stove without chimney for heating or cooking (42.5% vs. 29.4% in 1st quartile), complained more about transport (45.0% vs. 20.6%) and smell (20.0% vs. 8.8%). They were more likely to reside in the direction of a prevailing wind from the IP (30.0% vs. 11.8%). CP ratio was higher among new-borns with minor anomalies and lower within new-borns with major anomalies, compared to healthy new-borns, probably reflecting their different pathophysiology.

Cord blood cells proliferation might be considered as a biomarker sensitive to environmental exposures and indicator of subclinical pathology.

5.2

0006

Phthalates metabolites in amniotic fluid and maternal urine samples

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Aims

Phthalates are diffuse pollutants possessing endocrine-disrupting properties, for which foetuses are the most vulnerable population. They are metabolized to monoesters, glucuronidated and excreted in the urine. The aim was to verify the correlation between concentrations of metabolites of four phthalates in amniotic fluids and maternal urines in order to consider maternal urine concentration as a measure of foetal exposure.

Methods

SPE followed by HPLC/MS/MS quantitation with isotopic dilution for 5 urinary phthalate metabolites was applied to 70 pairs of amniotic fluid and maternal urine after enzymatic hydrolysis with glucuronidase. On 25 additional samples pairs these concentrations were determined without enzymatic hydrolysis.

Results

A significant number of mothers has urinary metabolites concentrations higher than the 95% confidence interval of the Reference Values. Mono-n-butyl-phthalate (MnBP) and mono-2-ethylhexyl phthalate (MEHP) are the most abundant metabolites in amniotic fluids. The metabolites concentration in urine samples increases after enzymatic hydrolysis while it did not increase in amniotic fluid. There is no correlation between amniotic fluid and maternal urine concentration after enzymatic hydrolysis, while there is significant correlation for the free (non hydrolysed) forms of MEHP, MEHHP (mono-2-ethyl-5-hydroxyhexyl phthalate) and MEP (Mono-ethyl-phthalate).

Conclusions

Results indicate that phthalates metabolites don't cross the placenta in the conjugated form and that a correlation exists between the concentration of free metabolites in amniotic fluids and maternal urine. Besides, pregnant women show a higher urinary concentration of phthalates metabolites than non-pregnant women of the same age living in the same area.

5.3

0104

Biomonitoring for HCHs, DDTs and PBDEs in breast milk in Shenzhen, China

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HCHs, DDTs and Polybrominated diphenyl ethers (PBDEs) are important environmental Persistent Organic Pollutants (POPs). However, Shenzhen as the emerging immigrant city, accumulative levels of HCHs, DDTs and PBDEs in human breast milk have never been reported.

Objective To first investigate the accumulative levels of HCHs, DDTs and PBDEs in human breast milk of primipara in Shenzhen, analyse influencing factors for the concentration of pollutants in human breast milk and assess exposure risk of breast-fed infants in Shenzhen.

Methods 133 primipara were recruited, and their breast milk samples were collected and questionnaires were filled out simultaneously. The samples were extracted, cleaned up, and quantified by gas chromatography-election capture detection (GC-ECD) and HRGC/HRMS for HCHs, DDTs and PBDEs respectively. Correlations between chemicals and some factors were also examined.

Results The median levels of ∑HCHs, ∑DDTs and PBDEs were 60.77 ng g^{-1} lipid, 251.71 ng g^{-1} lipid and 7.24 ng g^{-1} lipid respectively. The average estimated daily intakes of HCHs, DDTs and PBDEs by infants are 0.37 μg kg^{-1} bw per day、1.21 μg kg^{-1} bw per day and 27.7 ng kg^{-1} bw per day respectively.

Conclusion The average levels of HCHs, DDTs in the breast milk in Shenzhen general population are lower than those of Chinese average levels, which positively correlated with maternal age, and the amount of freshwater and poultry meat dietary intake. However, the levels of PBDEs body burden in Shenzhen were higher than those from other non-exposure areas reported in China previously.

5.4

0054

High levels of manganese exposure and neurobehavioral effects on children

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High levels of waterborne manganese have been associated with problematic behaviours in school-aged children, however to date this has not been reported with respect to airborne manganese. We report here our results on children's exposure to airborne manganese from an alloy plant and its relation with children's behaviour. Seventy children (34 boys) age between 6 and 13 years, living in two communities close to a ferro-manganese alloy plant in Bahia, Brazil were evaluated.

Hair manganese (MnH) and blood lead levels (BLL) were measured by graphite furnace atomic absorption spectrometry. Children's Behaviour Check List (CBCL) Portuguese version validated in Brazil was administered to parents or caregivers, providing indices of internalizing (composed of withdrawn, somatic complaints, and anxious/depressed scales) and externalizing (that combines disruptive and aggressive) behaviours and a separate scale for inattention.

Median and range of MnH and BLL were 11.48 (0.52 – 55.74) µg/g and 1.1 (0.5 – 6.1) µg/dL, respectively. Spearman correlation analyses showed that behavioural indices were correlated with MnH levels: disruptive (rho=0.347, p=0.004), aggressive (rho=0.326, p=0.001) behaviours and inattention (rho=0.364, p=0.002). A linear regression model was fitted with these indices as dependent variables in which log transformed MnH, age, sex and maternal education in years were entered as covariables. Aggressive behaviour and inattention were significantly associated with children's MnH (β coefficients for LogMnH: 5.91 (95%CI 2.03-9.78) and 3.01 (95%CI 0.81-5.28), respectively.

These results provide evidence that children's high exposure to airborne Mn may be having detrimental effects on children's behaviour, especially those related to externalizing anti-social behaviours.

Session 6: New biomarkers

6.1

0089

DNA Methylation Modifies Urine Biomarker Levels in 1,6-Hexamethylene Diisocyanate (HDI) Exposed Workers

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Individual differences in genome-wide DNA methylation may mediate systemic response to HDI exposure. Genetic and epigenetic factors are not currently used as predictors of outcome in exposure assessment. We have developed tools to investigate and identify individual differences in DNA methylation associated with HDI biomarker levels.

Exposure (respiratory and skin) to HDI, along with urine biomarker levels, was repeatedly measured in 20 automotive spray-painters. DNA methylation was analysed using peripheral blood mononuclear cells and the Illumina HumanMethylation450 BeadChip. Variation in 5methyl-CpG associated with urine HDA level was determined using linear mixed models that accounted for mediating effects between personal HDI exposure, ethnicity, age, and smoking.

We identified significant DNA methylation marks ($P<1.5\times10^{-06}$) associated with individual differences in urine HDA levels. Effects of HDI induced DNA methylation on homeostasis was inferred through network analysis (Ingenuity Pathway Analysis and Metacore) and functional gene (GO terms) enrichment (DAVID). Bioinformatics analysis revealed two significant predicted networks ($P=1\times10^{-26}$ and 1×10^{-08}) associated with this phenotype in HDI exposed workers. Functional pathways identified genes involved in (1) antigen processing and presentation and (2) immune responses (asthma, graft vs. host disease).

Results indicate that this innovative approach can determine the contribution of individual DNA methylation differences following HDI exposure, along with other personal predictors, to HDA levels in urine. This research provides critical new information on intrinsic factors affecting individual differences in HDI biomarker levels that may allow identification of susceptible subpopulations in future studies and novel input to aid setting HDI exposure limits.

6.2

0005

Quantification of the mercapturic acids of acrylonitrile and its genotoxic metabolite cyanoethylene-epoxide in a pilot human biomonitoring study

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Background: Acrylonitrile is one of the most important monomers in plastic production worldwide with an enormous production volume. It is a known animal carcinogen and also a major constituent of tobacco smoke, which is the main source of exposure for the general population.

Aims: The metabolic conversion of acrylonitrile to its genotoxic metabolite cyanoethylene-epoxide in humans by liver cytochromes is mainly responsible for the carcinogenic properties of acrylonitrile. Therefore, our research was aimed to elucidate this metabolic pathway in humans.

Methods: We have developed a specific LC/MS/MS-method to simultaneously quantify the mercapturic acids of acrylonitrile (N-acetyl-S-(2-cyanoethyl)cysteine, CEMA) and its oxidative metabolite cyanoethylene-epoxide (N-acetyl-S-(1-cyano-2-hydroxyethyl)cysteine, CHEMA) in human urine. The LOQ for both metabolites was 1 µg/L urine. In a pilot study we applied this method to spot urine samples of 47 non-smoking and 36 smoking persons of the general population.

Results: Median levels for CEMA and CHEMA in urine samples of non-smokers were 1.9 and < 1 µg/L urine. CHEMA was quantified only in 4 of the 47 samples. In contrast, both metabolites were quantifiable in more than 94 % of the smokers' urine samples. CEMA-excretion was highly correlated to our anamnestic information about daily smoked cigarettes. Median levels of CEMA and CHEMA were 184 and 29 µg/L urine, respectively. The mean relationship between CHEMA and CEMA in these samples was 13 %, but showed considerable variability.

Conclusions: Our method is highly suitable for human biomonitoring of exposures to acrylonitrile and the future derivation of risk-based biological guidance values.

6.3

0049

Identification and quantification of tebuconazole urinary metabolites in agriculture workers

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Aims. Tebuconazole (TEB) is a fungicide widely used in vineyards. Objective of this work was the identification of urinary metabolites for biological monitoring of occupational exposure.

Methods. Urine samples from vineyard workers exposed to TEB during the application were analysed by LC/MS/MS to obtain a profile of candidate metabolites. Based on the presence of the triazole moiety in the full scan mass spectra five major candidates were found. From their mass spectra t-butylhydroxy and t-butylcarboxy-tebuconazole (TEB-OH and TEB-COOH), both as free molecules and as glucoronide conjugates, were identified together with a minor amount of unmetabolized TEB. Urine was submitted to hydrolysis with glucoronidase to obtain the free chemicals, that were quantified using a suitable calibration curve.

Results. TEB-OH was the most abundant metabolite, with mean concentration 3.5-fold higher (from 0.3 to 12.9) than TEB-COOH and a wide inter-subject variability. In seven investigated subjects mean levels in 24 h post-exposure urine samples were 401 nmol/L TEB-OH (range 25-1198) and 104 nmol/L TEB-COOH(range 17-305). Excretion of TEB and its metabolites peaked within 24 h from the end of exposure. Urinary metabolites were correlated with the potential and actual dermal exposures assessed measuring TEB on the coverall and on the skin, respectively, with Pearson' r of 0.86 and 0.46.

Conclusion. Our results suggest that TEB-OH and TEB-COOH in 24 h post-exposure urine samples are promising candidates for biomonitoring TEB exposure in agriculture workers.

6.4

0033

Determination of Bis(2-propylheptyl)phthalate (DPHP) exposure in the general population

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We developed a GC-HRMS method to analyse three postulated main DPHP-metabolites Mono-2-(propyl-6-hydroxy-heptyl)-phthalat (OH-MPHP), Mono-2-(propyl-6-oxoheptyl)-phthalat (oxo-MPHP) and Mono-2-(propyl-6-carboxy-hexyl)-phthalat (cx-MPHxP) in urine. The limits of quantification were 0.15 µg/l to 0.3 µg/L. In a human volunteer study 5 subjects received ca. 50 mg D4-DPHP orally. Urine was continuously collected for 48 hours and DPHP elimination kinetics were determined in these samples. The study was approved by the ethical committee of Ruhr University Bochum (No. 4022-11). We also applied the method in 40 urine samples of occupationally non-exposed subjects.

The human kinetic study showed that the major share of above D4-DPHP metabolites were eliminated within the first 24 hours. On average 22.50 % of the oral dose was recovered in urine as these three metabolites with oxo-MPHP-D4 representing 12.41 %, followed by OH-MPHP-D4 (9.66%) and cx-MPHxP-D4 (0.43 %).

Present LC-MS/MS methods can only be used as a screening method for the sum of DPHP and diisodecylphthalate (DiDP) exposures. It was shown that only by GC-HRMS DPHP-metabolites can be separated from the isomeric metabolites of (DiDP). Only this way the DPHP body burden can be distinguished from the DiDP body burden. GC-HRMS measurements unambiguously identified DPHP related oxo-MPHP in 15 out of 40 urine samples above the limit of quantification in concentrations up to 0.93 µg/l. OH-MPHP was detected in 3 samples, cx-MPHxP in none.

With this study we validated urinary DPHP biomarkers and proved to be able to specifically determine DPHP exposures (separate from DiDP) in the general population.

Session 7: Interpretation of population surveys

7.1

0010

Interpreting Population Level Biomonitoring Data in a Risk-Based Context: A Canadian Perspective

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Aims

Since 2007, the Canadian Health Measures Survey (CHMS) has been collecting biomonitoring data from the general Canadian population for various age groups. To date, the survey has provided nationally representative baseline concentrations for approximately 141 environmental chemicals in blood or urine (e.g. phthalates, bisphenol A, pyrethroids). Biomonitoring Equivalents (BE) and other biomarker-based screening values can be useful tools for interpreting biomonitoring data in a risk-based context.

Methods

Geometric mean and 95th percentile population concentrations (in blood and urine) for selected CHMS analytes, from cycles 1 (2007-2009) and 2 (2009-2011), were tabulated and compared to available biomarker-based screening values to generate chemical-specific hazard quotients (HQ). HQ values greater than 1 provide an indication that exposure levels may be of concern and require further investigation.

Results

HQ values generated from CHMS data identified two metals and one persistent organic pollutant as chemicals exhibiting HQ values greater than 1 for some portion of the population. For the majority of chemicals, the HQ values were less than 1 suggesting that most environmental chemicals measured were below existing levels of concern.

Conclusions

This approach represents a novel assessment of Canadian biomonitoring data in a risk-based context. It has potential to be used by researchers, risk assessors and risk managers in screening and prioritization efforts.

7.2

0047

Trends of chemical exposure in Finland in recent years based on biomonitoring results

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Background: The Finnish Institute of Occupational Health has a database for the test results of biomonitoring. Over the last ten years, this data has been analysed to determine the main exposures and working areas mostly at risk. The aim of the analyses is to further reduce workers' exposure to hazardous chemicals by finding the most dangerous jobs and greatest exposures.

Results: Quantitatively, the most significant biomonitoring analyses have been those of urinary chromium and nickel, blood lead, urinary inorganic arsenic and aluminium, and urinary mandelic and phenyl-glyoxylic acids. The amounts of chromium and nickel measured in workers' urine exceeded target levels the most often. A clear upward trend in exposure levels was observed in blood and urine cadmium levels in casting, hazardous waste treatment and hard soldering. Exceptionally high urinary cobalt levels, over 2000 nmol/l, were also observed in the grinding and manufacturing of cobalt chemicals. In the mining and metal production industry, inorganic arsenic in urine often exceeds the biomonitoring action limit (BAL). The amount of measurements exceeding the BAL was greatest in styrene exposure - still in 2011 this was over 20% of all measurements. In contrast, urinary aluminium levels have decreased in the last decade, due to improvements in the working habits of welders.

Conclusions: These results prove that the need for biomonitoring remains indisputable. Biomonitoring is often the only way to reliably estimate the exposure to chemicals which are absorbed through the skin.

7.3

0096

Interpreting biomarker data from the COPHES-DEMOCOPHES twin projects: Using lifestyle and environmental data to understand biomarker differences among countries

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In 2011 and 2012, the COPHES/DEMOCOPHES twin projects performed a first ever harmonized human biomonitoring survey in 17 European countries. In more than 1800 mother-child pairs, cadmium, cotinine and certain phthalate metabolites were measured in urine, and total mercury in hair samples. The presentation provides an overview of the analyses that studied whether it was feasible to interpret the observed differences in biomarker values among different countries, using external databases on environmental quality and lifestyle.

Despite the fact that harmonised biomonitoring data was available from 17 different European countries, the assessment was hampered by a lack of consistent data on lifestyle and environmental quality. This implied that most analyses could only be performed for about half to two thirds of the participating countries. Nonetheless, it was feasible to relate aggregated fish consumption data to mercury in hair, to relate the strength of anti-smoking legislation to urinary cotinine levels, and to find a borderline significant relationship between cadmium levels in air or food and urinary cadmium levels across DEMOCOPHES countries. However, the challenge to integrate environmental exposure and lifestyle data with biomarker data is to have data available on a similar geographical resolution and therefore remains a pitfall for human biomonitoring to achieve its true potential for evidence-based policy making.

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7.4

0002

Benchmark Dose for cadmium (Cd) among general Japanese populations

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Background: BMD has been gaining popularity in epidemiological studies including Cd studies. However, reproducibility of BMD values has seldom been examined.

Objectives: This study was initiated to determine whether consistent BMDs are obtained for similar non-exposed populations.

Methods: Cd (an exposure marker), α_1-microglobulin (α_1-MG), β_2-microglobulin (β_2-MG) and N-acetyl-β-D-glucosaminidase (NAG) (three effect markers of tubular dysfunction) levels in urine of adult Japanese women were examined. Data on Cd, α_1-MG and β_2-MG were available for 17,375 cases (in 16 prefectures), and on NAG for 6,409 cases (in ten prefectures). With the hybrid approach, it was possible to calculate BMD for α_1-MG and β_2-MG for all 16 prefectures (17,375 cases), and for NAG for nine prefectures (5843 cases).

Results: The application gave BMD values of 1.92, 2.46 and 2.32 μg Cd/g cr for α_1-MG, β_2-MG and NAG, respectively. There was about 4-fold difference in BMD for α_1-MG and β_2-MG in 16 prefectures, and the variation was even greater (about 7-folds) for NAG in nine prefectures. Multiple regression analyses revealed that BMD was significantly influenced by Cd concentration in cases of α_1-MG and β_2-MG, it was by creatinine for NAG. Analyses for BMDL essentially reproduced the BMD results.

Conclusions: Even when the analysis was conducted in a single nation, BMD for Cd effect markers varied by ca. 4 folds when α_1-MG or β_2-MG were examined and by ca. 7 folds for NAG among Cd non-exposed Japanese populations. The most influential factors include urine density and Cd levels in the urine.

Session 8: Occupational exposures 2

8.1

0067

Towards a biological monitoring guidance value for acrylamide

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This project aimed to improve current exposure assessment and management techniques for acrylamide in the workplace, through the use of biological monitoring.

Twenty-nine workers at an acrylamide production facility provided two blood samples (approximately three months apart) and four urine samples (one whilst off work and three for each of their different shift duties). Personal air samples and hand rinse samples were collected during the same shifts as the urine samples. The mercapturic acid conjugates of acrylamide (AAMA) and glycidamide (GAMA) were measured in urine and acrylamide haemoglobin adducts were measured in blood. A second round of monitoring was conducted the following year.

Good correlations were found between air levels and acrylamide haemoglobin adducts (r=0.65); AAMA (0.65) and GAMA (0.56). All biomarkers were very well correlated; AAMA and GAMA with haemoglobin adduct (r=0.91 and r=0.88, respectively), indicating that multiple urine sampling would be as reliable as using blood samples to assess long-term exposure.

A mixed effects model for urinary AAMA showed that airborne acrylamide exposure, dermal exposure (assessed by hand rinse samples), smoking (cotinine concentration) and creatinine concentration were all statistically significant factors.

Acrylamide mercapturic acid in urine (AAMA) is recommended as the biomarker of choice, based on non-invasive sampling, strength of correlations and reliability of the method. A biological monitoring guidance value for these workers (based on the 90th percentile of outdoor shifts in non-smokers) of 540 µmol AAMA/mol creatinine is recommended. National reference ranges for AAMA may need establishing due to apparent national differences in diet.

8.2

0101

Circulating mitochondrial DNA as an effect-biomarker after exposure to halo-alkane based pesticides

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There is a need for a panel of suitable biomarkers for detection of environmental chemical exposure leading to the initiation or progression of degenerative diseases or potentially cancer. Since the peripheral blood contains increased levels of circulating cell-free DNA in diseased individuals, we aimed to evaluate this DNA as effect biomarker recognizing vulnerability after exposure to environmental chemicals.

We recruited 164 humans presumably exposed to halo-alkane-based-pesticides. Exposure evaluation was based on human biomonitoring analysis, as biomarker of exposure parent halo-methane's/-ethane's/ and metabolites, haemoglobin-adducts methyl valine, hydroxyl ethyl valine in blood were used, complemented by expert evaluation of exposure and clinical intoxication symptoms and questionnaire.

Exposure assessment showed exposures to haloalkanes in the concentration range: higher than non-cancer reference doses but (mostly) lower than the occupational exposure limits. We quantified circulating DNA in serum from 86 individuals with confirmed exposure to off-gassing haloalkane pesticides (in storage facilities or in home environment) and 30 non-exposed controls, and found that exposure was significantly associated with elevated serum levels of circulating mitochondrial DNA (in size of 79 bp, mtDNA-79, $p=0.0001$). The increased integrity of mtDNA (mtDNA-230/mtDNA-79) in exposed individuals implicates apoptotic processes ($p=0.015$). The relative amounts of mtDNA-79 in serum were positively associated with the lag-time after intoxication of these chemicals ($r=0.99$, $p<0.0001$). The specificity for this biomarker increased from 30% to 97% several months post-exposure in patients with intoxication symptoms.

Our findings indicate that mitochondrial DNA has a potential to serve as a biomarker recognizing vulnerable risk groups after exposure to toxic chemicals.

8.3

0040

Human Biomonitoring of N-methyl- and N-ethyl-2-pyrrolidone in automobile industry workers and non-exposed controls

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N-methyl-2-pyrrolidone (NMP) and N-ethyl-2-pyrrolidone (NEP) are important organic solvents in industry. NMP and products containing more than 5 % NMP must be labeled as developmental toxicants. Therefore NMP is increasingly substituted by other organic solvents including NEP. After incorporation, NMP and NEP are hydroxylated to the 5-hydroxy metabolites (5-HNMP, 5-HNEP) and further metabolized to the corresponding 2-hydroxy-N-alkyl-succinimides (2-HMSI, 2-HESI); all are eliminated into urine.

In this field study, we determined the internal exposure of 23 workers (17 male, 6 female) to NMP and NEP in a spraying department of an automobile plant and nine non-exposed controls. The metabolites were extracted from urine using solid phase extraction, derivatised and analysed by GC-MS. Quantification was carried out by isotope dilution. The limits of quantification were between 8 and 30 µg/L depending on the metabolite.

Metabolites of both NMP and NEP were detected in all urine samples of exposed workers. Maximum values were 25.9 mg/L 5-HNMP and 40.0 mg/L 5-HNEP and 4.8 mg/L 2-HMSI and 8.0 mg/L 2-HESI. Significant differences were observed depending on the work tasks. In case of NMP, the Biological Limit Values of the European Union (70 mg/g crea 5-HNMP, 20 mg/g crea 2-HNMP) were not exceeded. No threshold limits are available for NEP metabolites. Three resp. five out of nine controls showed metabolites of NMP resp. NEP in urine. Thus the general population seems to be exposed to both NMP and NEP.

Overall, our data contribute to exposure assessment of the two important industrial organic solvents NMP and NEP.

8.4

0048

Occupational exposure to Polycyclic Aromatic Hydrocarbons (PAHs) during bitumen application

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Introduction: In France, 1,600,000 workers are exposed to PAHs mixtures. Although many data exist for some industries, there are few data on individual PAHs exposure levels during road paving and roofing with bitumen products. The aim of this study was to determine occupational PAHs exposure using airborne and biological monitoring.

Methods: 90 personal air samples were collected at 15 workplaces. Urine samples from 180 workers and 180 controls were collected at different sampling times. Gaseous and particulate PAHs and metabolites were analyzed using HPLC with fluorescence detection. In addition of measuring 1-hydroxypyrene (1OHP) at the end of the shift, we used a recently developed sensitive method quantifying 3-hydroxybenzo(a)pyrene (3OHBaP) 16 hours after the end of shift.

Results: Atmospheric BaP and pyrene concentrations remained below 12 and 154 ng/m^3 respectively, while naphthalene levels reached 300 µg/m^3. BaP and pyrene levels were correlated but there was no correlation with naphthalene. 1OHP urinary concentrations in workers involved in road paving or roofing were higher than those of controls for the whole population (med = 0.10 vs 0.04 µmol/mol) and for non-smokers (med = 0.08 vs 0.03 µmol/mol). 3-OHBaP levels of workers were below the quantitation limit for 86% of non-smokers and 57% of smokers.

Conclusion: Urinary 1OHP remains currently the best biomarker to assess PAHs exposure during bitumen application because 3OHBaP levels are too low to be used. Although naphthalene concentrations are high, the analysis of their metabolites is not useful because this compound is not correlated to BaP or pyrene levels.

Session 9: Derivation of guidance values

9.1

0039

Updated proposal for biological limit value of 1-hydroxypyrene in urine

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Introduction - 1-Hydroxypyrene in urine is routinely used in industry to assess and to control exposure of Polycyclic Aromatic Hydrocarbons (PAH). Due to lacking dose-response data from epidemiological studies, a health risk-based limit of 1-hydroxypyrene in urine cannot be derived.

RESULTS - For the period in between, it is suggested to take the "*lowest observed level without genotoxic effects in the body* = LOL-GEB" as the critical level for setting the limit value. In order to set this level, cross-sectional studies were searched that report on dose - response in workers of early genotoxic effects in white blood cells related to the degree of exposure (expressed as 1-hydroxypyrene in urine). Nine studies were traced that met the requirements. From each study, the concentration of 1-hydroxypyrene in end-of-shift, end working week urine samples was determined, at which no genotoxic effects was found (= study threshold). The study thresholds of the 9 studies ranged from <4.3 to 1.0 umol/mol. The lowest study threshold was 1.0 umol/mol.

CONCLUSION - The LOL-GEB limit for occupational exposure to PAH is 1.0 umol/mol creatinine. This value is recommended as a state-of-the-art biological limit value, valid for coke oven workers with an average pyrene/-benzo(a)pyrene ratio of 2.5. For work environments with deviating pyrene/benz(a)pyrene ratios an adjustment procedure is recommended. The PAH-ratio adjusted biological limit values for work environments with deviating pyrene/benz(a)pyrene ratios, ranging from 1.5 - 4.0, are 0.7 - 1.45 umol/mol creatinine, respectively.

9.2

0059

Occupational exposure limit values for cadmium: the challenge of an integrated approach considering biomarkers and airborne concentrations

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Recommending occupational exposure limit (OEL) values (airborne and biomarkers concentrations) based on critical health effects is a task of the scientific committee of the French Agency for Food, Environmental and Occupational Health and Safety (ANSES OEL committee). This committee recently studied cadmium in order to recommend OELs for this heavy metal.

The committee concluded that despite evidence of cadmium carcinogenicity, literature data are inadequate to derive OELs based on quantitative risk assessment. It consequently retained nephrotoxicity as the critical effect. The lack of relevant studies for identifying a dose-response relationship between cadmium airborne concentrations and nephrotoxicity led the committee to derive its recommended atmospheric value on the biological limit values (BLVs).

Cadmium in urine (CdU) was proposed for the biological monitoring of long-term exposure and cadmium in blood (CdB) for the short-term exposure. For CdU, the BLV was derived from results of field studies reporting dose-response relationship between CdU concentrations and nephrotoxicity biomarkers (beta-2-microglobulin, retinol binding protein). Owing to the long biological half-life of cadmium, a two-tier approach was proposed to prevent irreversible long-term health effects. When CdU exceeds 2µg/g of creatinine, measurement of nephrotoxicity biomarkers is recommend as well as a more frequent follow-up of current exposure. When CdU exceeds 5µg/g of creatinine, the workers should be removed from Cd exposure. The committee also derived a BLV of 4µg/L for cadmium in blood for the monitoring of recent exposure.

The next task is to study several approaches for the derivation of an atmospheric OEL value (correlations, toxicokinetics models).

9.3

0070

A perspective on biological monitoring guidance values

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Biological monitoring (BM) is a useful tool for assessing 'systemic' exposure resulting from inhalation, ingestion and dermal absorption. Critical to the utility of BM is the availability of guidance values to help interpret the results but the number of guidance values is small in comparison to the number of chemicals in the workplace and environment. One of the major obstacles is the availability of good (peer-reviewed) data. Another is the need to derive health-based guidance values (particularly acute for non-threshold carcinogens and sensitisers). We have a simultaneous need for more data but also a need to understand and manage the limitations of the data and guidance values we have.

Different organisations have different approaches and may have different guidance values for the same substance. Sometimes the difference is due to new data e.g. the UK guidance value for mercury 35 µg/g set in 1995 and the ACGIH BEI of 20µg/g proposed in 2012. Sometimes the difference is due to the basis for the value e.g. the ACGIH BEI proposed for toluene diisocyanate of 5 µg/g based on equivalence to the airborne limit and the UK value of 1 µg/g based on the 90th percentile of data from a study of UK workplaces. Particularly challenging from a control of exposure point of view are guidance values based on background levels in the non-occupationally exposed population. There is a clear requirement for occupational hygiene and health professionals to understand the basis of the guidance values and not use them as simple 'limits'.

9.4

0095

A quantitative determination of provisional Biological Exposure Indexes (BEI) for pesticides

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The assessment of risk from pesticides in agriculture is based on the comparison of the absorbed dose to the Acceptable Occupational Exposure Level (AOEL), a health based limit established in the frame of the authorization process. The AOEL is a systemic dose not directly comparable with biological indicators, thus weakening its preventive value. Biological monitoring is the first-line technique to assess personal exposure, for workplace toxicants for which quantitative BEIs have been proposed. Due to lack of corresponding values for pesticides, this approach cannot be adopted in one of the most health-threatening human activities. To fill this gap, we propose a theoretical frame and an experimental approach to easily establish such values for priority pesticides.

Data from combined biological monitoring (pesticide metabolite measurement in 24-hour urine) and from assessment of personal exposure (e.g., by a suitably simplified modification of the OECD procedure for skin contamination measurement) collected in real-life conditions in a group of exposed individuals is elaborated. A log-log plot of urinary excretion of pesticide metabolite vs. personal exposure referred to the AOEL limit unveils a bimodal relationship, which accounts both for ubiquitous exposure of the general population and the relationship of the excreted biomarker to occupational exposure and from which a tentative value for a BEI can be calculated.

Two proof-of-principle results on a herbicide (propanil, BEI=1 mg 3,4-DCA/L 24-h urine) and on a fungicide (mancozeb, BEI=117 microg ETU/L 24-h urine) are discussed.

This method can be, in perspective, embedded into the requisite information at the regulatory level.

Session 10: Dermal exposures

10.1

0060

Skin permeation and metabolism of di(2-ethylhexyl) phthalate (DEHP)

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Aims: Workers manufacturing products containing phthalates are highly exposed to these lipophilic, low volatile substances. Phthalates are suspected to be endocrine disruptures. Di(2-ethylhexyl) phthalate (DEHP) is assumed to have low dermal absorption; however, previous in vitro skin permeation studies have shown large permeation differences. To better estimate workers' DEHP skin exposures, our aims were to determine DEHP permeation parameters and assess extent of skin DEHP metabolism.

Methods: Surgically removed skin from patients undergoing abdominoplasty was collected immediately after removal and dermatomed (800 µm). Flow-through diffusion cells (1.77 cm2) were operated at 32°C, 40 µl/min; and the reservoir liquid was cell culture media (aqueous solution). The cells were dosed either with neat DEHP or emulsified in aqueous solution (166 µg/ml). Samples were analyzed by HPLC-MS/MS.

Results: DEHP permeated human viable skin only as the metabolite MEHP (100%) after 8 hours of exposure. Applying MEHP to the skin, we showed that the human skin was able to further oxidize MEHP to 5-oxo-MEHP. Moreover, the application of neat and aqueous DEHP solutions had an enormous impact on skin permeation rates; neat DEHP hardly permeated skin while the aqueous solution readily permeated skin.

Conclusion: DEHP pass readily through human skin when emulsified in aqueous solution, while far less when applied neat to the skin. Using results from older in vitro skin permeation studies with non-viable skin may underestimate exposures. Our results are in overall agreement with newer phthalate skin permeation studies.

10.2

0112

The association between urinary N-methylformamide and dermal N,N-dimethylformamide assessed by the tape-stripping method

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The aim of this study was to investigate the dermal exposure of DMF (N,N-Dimethylformamide) vapor using tape stripping that is corrected by protein, and to also determine the importance of the contributions of dermal exposure and inhalation exposure of DMF to the total body burden of the urinary NMF(N-methylformamide).

82 male workers working at 12 synthetic leather-manufacturing industries in Korea were selected. The inhalation DMF by ambient monitoring during their shift and the dermal exposure of DMF at the neck through tape-stripping and the amount of urinary NMF in the spot urine at a post-shift time were measured. The geometric mean of the inhalation DMF was 21.1 mg/L and that of urinary NMF and dermal DMF were 59.9 mg/L and 12.0 mg/g protein, respectively. The correlation between the inhalation and dermal DMF is significantly strong (r = 0.602). The regression model for combined effect of dermal DMF and inhalation DMF on urinary NMF was statistically the best-fit model. However the model fitness score of the regression model of sole exposure for dermal DMF on the urinary NMF was relatively lower than that of inhalation DMF. The inhalation DMF founded stronger constitution to urinary NMF than dermal DMF, which showed correlation with inhalation DMF.

Therefore, by means of a proxy parameter of dermal exposure, inhalation DMF should be addressed and monitored in the exposure scenario, where exposure is considered only to be when there is contact with DMF vapor without direct contact during a single shift in synthetic leather manufacturing.

10.3

0024

Biomonitoring of dermal exposure to cyclosiloxanes from consumer products using end-exhaled air

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Consumer exposure to personal care products (PCPs) can be studied by analysis of cyclosiloxanes present in exhaled air. A promising non-invasive approach to also study consumer exposure to PCPs in a residential setting.

Aim

Quantitative determination of the cyclosiloxanes octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) in end-exhaled air to study skin absorption of PCPs.

Methods

End-exhaled air was collected using a breath sampler (Bio-VOC), transferred to carbograph multi-bed ATD tubes and analyzed by thermal desorption gas chromatography mass spectrometry (TD-GC-MS). Reproducibility and sensitivity of the method were satisfactory (see a separate paper for more technical details). We exposed the forearm of healthy volunteers to the pure substance or a crème (commercial product). Inhalation uptake was minimized by keeping the forearm in a fume hood during dermal exposure and by supplying fresh air to the breathing zone of the volunteer during the post-exposure period.

Results

Preliminary results for D5 showed that a topically applied amount of 3.5 mg/cm2 (neat substance) or 3.2 mg/cm2 (crème) for 60 minutes, resulted in a fivefold increase of the baseline excretion of D5 when applying the neat substance and a twofold increase following application of the crème. Absorption from the crème appears to slow down elimination by a factor two. The contribution of inhaled D5 was monitored and gave a minor contribution to the total uptake.

Conclusion

First results for D5 indicate slower kinetics, comparing the results from topically applied neat substance with those from D5 in a product matrix.

10.4

0052

Uptake and elimination of permethrin related to the use of permethrin treated clothing for forestry workers

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Permethrin treated clothes are supposed to protect forestry workers from tick bites. However, their use mostly entails an uptake of permethrin. Aim of our biomonitoring study was to examine uptake and elimination of permethrin caused by a one-time use of respective clothing. Furthermore, factors potentially influencing uptake should be identified.

28 male volunteers (age: 20-34 years, median: 25.0) were equipped with permethrin treated forestry jackets and pants. The clothing was worn for 8h under differing exposure conditions including comfort conditions (c1) as well as conditions of increased temperature and humidity without (c2) and with additional physical workload (c3). Internal permethrin exposure was monitored by GC-MS determination of the permethrin metabolites cis-DCCA, trans-DCCA and 3-PBA in a set of 12 urine samples, covering a period of 504h from the beginning of exposure for each participant and exposure condition

Starting with median concentrations of 0.31 (c1), 0.39 (c2) and 0.48 µg/l (c3) for the sum of the three metabolites before exposure, metabolite excretion increased in the following samples. Excretion peaked 8 to 16h after termination exposure with median concentrations of 5.62 (c1), 10.63 (c2) and 15.95 µg/l (c3), which were differing significantly from each other (Friedmann test: $p<0.01$, $n=22$).

Internal exposure of the majority of the participants exceeded environmental background exposure (German reference value: 5 µg/l). The elimination kinetics would be in line with dermal absorption of permethrin, which seems to be increased by elevated temperature/humidity and additional physical workload. Enhanced skin perfusion could be an explanation for this observation.

Session 11: Toxicokinetics

11.1

0042

Metabolism of N-ethyl-2-pyrrolidone (NEP) - validation of biomarkers in urine for exposure assessment

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N-Ethyl-2-pyrrolidone (NEP) is an industrial solvent increasingly used to substitute N-methyl-2-pyrrolidone (NMP). Toxicological data for NEP are limited, however. Here, we investigated the human metabolism of NEP to identify and describe biomarkers of exposure to be used both in occupational and environmental population studies.

We orally dosed three male volunteers with 20 mg NEP and continuously collected urine samples over 4 days. We postulated 5-hydroxy-N-ethyl-2-pyrrolidone (5-HNEP) and 2-hydroxy-N-ethylsuccinimide (2-HESI) as metabolites of NEP based on the well-known human metabolism of NMP. Both, 5-HNEP and 2-HESI were quantified in urine by GC-MS with isotope dilution. 5-HNEP and 2-HESI were found in all urine samples. Both metabolites represented approx. 50.7% (45.9-55.4%) of the applied dose after 4 days; 29.0% (28.6-30.1%) was eliminated as 5-HNEP and 21.5% (17.2-26.8%) as 2-HESI. The majority of 5-HNEP was excreted on day 1 (26.4%), while 2-HESI was predominantly excreted on day 2 (8.2%) due to a later concentration maximum (t_{max} 5-HNEP 2-4hrs, 2-HESI 28-32hrs) and a considerably longer elimination half-time ($t_{1/2}$ 5-HNEP ~7hrs, 2-HESI ~16hrs). Even on day 4, 2.4% of the applied dose was excreted as 2-HESI, while only traces of 5-HNEP could be detected.

With this study we present valuable biomarkers which can be used to determine NEP exposure in both occupationally and environmentally exposed populations. In addition, our data on the excreted amount of NEP metabolites contributes to the calculation of the amount of NEP taken up at the workplace or via the environment. Preliminary biomonitoring data indicate that the general population is exposed to NEP.

11.2

0051

BIOMONITORING SHORT AND LONG TERM TERBUTHYLAZINE EXPOSURE BY HAIR AND URINE SPECIMENS

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Aims. Aim of this work was to evaluate short-term and long-term exposure to the herbicide terbuthylazine (TBA) using urine and hair samples.

Methods. Twelve corn agriculture workers (AW), 13 rural residents (RR), and 17 urban residents (UR) entered the study. Urine samples were collected with two protocols: AW collected a spot urine sample before starting the application season (U_0) and after the application of TBA, at bed time (U_1), and prior to the next shift (U_2); RR and UR collected a spot sample any day during the application season (U_e). For all subjects two hair samples were collected: a pre-application season sample (H_0) and a post-application season sample (H_1). TBA and its metabolite desetylterbutylazine (DET) were measured by LC-MS/MS.

Results. DET was detected only in urine samples while TBA mainly in hair samples. In AW urinary DET was below the quantification limit at U_0, while at U_1 and U_2 was present in all samples with median levels of 1.81 and 2.95 µg/L. In UR and RR urinary DET was always below the quantification limit.

In hair samples at H_0 median TBA was undetected in UR, and 0.010 ng/mg hair in both AW and RR ($p=0.004$). In H_1 median TBA was undetected in UR, 0.017 ng/mg hair in RR, and 0.128 ng/mg hair in AW ($p<0.001$).

Conclusion. Urinary DET and hair TBA are promising candidates for biomonitoring short- and long-term exposure to TBA. The use of this herbicide in agriculture impacts the exposure of rural residents.

11.3

0043

Inter- and intra-individual variability in biomarker values over a continuous six-day sampling period

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Aim

In large-scale human biomonitoring (HBM) surveys, single samples of blood, urine or other matrices are collected from large numbers of individuals recruited from the general population. The single sample analyses capture the variability of internal dose in the population, but do not allow evaluation of inter- vs. intra-individual variation. This may lead to misclassification of individuals with high/low exposures and is of particular concern if the exposure pattern is discontinuous and the compounds have a short half-life in the biological matrix. A biomonitoring study was set up to quantify inter- and intra-individual variation in a number of biomarkers with different half-lives and exposure pathways.

Methods

For a period of 6 days, 8 individuals (4 males and 4 females, age range 32 – 67) collected each individual urine sample. At the same time, food consumption data and use of personal care products was documented at 30-minute intervals. In each urine sample, 4 different metals (arsenic, cadmium, manganese, nickel), and different parabens, triclosan, and triclocarba, were measured.

Results

In total, 352 individual urine samples were collected. Both urine production and number of personal care products varied largely between individuals, as did the amount of personal care products used, and the timing of usage.

Conclusions

While large-scale HBM studies often use first-morning urine voids as a convenient way of collecting specimens, this may not always be the most representative sample. Aspects of exposure frequency and magnitude, biomarker half-life, and other variables need to be taken into account as well.

11.4

0017

Elimination and biological half-time of cadmium in kidney

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Introduction:

Cadmium (Cd) is an occupational and environmental contaminant which can potentially affect human health at relatively low concentrations. Cd accumulates in the kidney where it has a long biological half-time (T1/2). The aim of this study was to investigate the T1/2 of Cd in kidney.

Methods:

152 healthy kidney donors were recruited to the study. A kidney cortex biopsy was available for Cd analysis in 109 donors. A 24h urine sample was also collected and Cd concentrations of the kidney biopsies (K-Cdconc) and the urine samples (U-Cd) were analysed using ICP-MS. The kidney weight for each subject was estimated from body surface area. The estimated kidney weights were multiplied by the K-Cdconc and divided with 1.25 (higher kidney Cd in cortex then in remaining part) to get K-Cdtot. The Cd elimination coefficient (k) and T1/2 were calculated from the association between U-Cd/24h and K-Cdtot using weighted regression. The half-time of Cd in kidney was assessed using the equation T1/2=ln(2)/k.

Results:

The relationship between K-Cd and U-Cd was nonlinear, with slower elimination of Cd at high K-Cd. Estimates of the K-Cd half-time varied between 18 and 44 years. A K-Cd of 25 µg/g corresponds to U-Cd of 0.42 µg/g creatinine in overnight urine (U-Cd/K-Cd ratio: about 1:60). There was a strong association between K-Cd and U-Cd adjusted for creatinine (r_p=0.70, $p<0.001$). Multivariate models showed Cd in blood and urinary albumin as determinants for U-Cd excretion.

Conclusion

Previous estimates of the U-Cd/K-Cd ratio (1:20) may underestimate K-Cd at low U-Cd.

Session 12: Population surveys

12.1

0021

Overview of Biomonitoring Initiatives Under the Government of Canada's Chemicals Management Plan

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Aims

The Chemicals Management Plan (CMP) is part of the Government of Canada's environmental agenda to ensure the safe management of chemicals. Under the CMP, Health Canada performs health-based monitoring activities (including biomonitoring) to inform policy to help Canadians maintain and improve their health. The objective is to establish nationally representative concentrations of chemicals in Canadians, including vulnerable populations. This presentation will present an overview of the Government of Canada's biomonitoring initiatives and highlight some key results.

Methods

In Canada, biomonitoring is performed through four major initiatives: 1) the national Canadian Health Measures Survey, 2) the Maternal-Infant Research on Environmental Chemicals study, 3) the Northern Contaminants Program, and 4) the First Nations Biomonitoring Initiative. Smaller targeted studies include monitoring and surveillance in populations living in geographic areas of concern, research to support biomonitoring, and targeted environmental monitoring.

Results

These studies provide national-level data on exposure to environmental chemicals in Canada. This presentation will highlight data from selected chemical groups (e.g., POPs, metals, phthalates) from some of the major national biomonitoring initiatives.

Conclusions

These data will serve as a baseline for comparison with future surveys, will help to determine trends over time, and help assess the effectiveness of risk management actions. Data will also contribute to the evaluation of chemical exposure and the development of policies to help Canadians maintain and improve their health.

12.2

0092

Bisphenol A and Organophosphate Exposure in the Israeli Population: Sources and Risk Factors

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The Ministry of Health Biomonitoring Study measured internal exposure to bisphenol A (BPA), organophosphate pesticides (OPs), and other contaminants.

From December 2010 to January 2011, 250 individuals ages 20 - 73 were recruited from five regions in Israel. Urine samples and questionnaire data, including 24 hour dietary recall data, were obtained. Regression analyses were performed to identify risk factors for BPA and OP exposures.

Median creatinine adjusted urinary BPA concentrations were higher than those reported for the U.S., Canada, and Germany. Median creatinine adjusted urinary concentrations of the OP metabolites dimethyl phosphate and dimethyl thiophosphate were higher than in the U.S. and Canada, and comparable to those in France. Urinary BPA concentrations were higher in Jews than in Arabs or Druze (2.49, 0.82, and 0.89 mcg/g creatinine respectively; p=0.02). BPA concentrations were higher in smokers, but not significantly (p=0.055). Mushroom consumers had BPA concentrations twice as high as nonconsumers in a multivariate analysis (p=0.03). Canned fish consumers had higher urinary BPA (2.36 mcg/g creatinine) than nonconsumers (1.87 mcg/g creatinine) but the difference was not significant. Females age > 44 y had higher urinary DAP concentrations for several metabolites. Fruit and vegetable intakes > 75th percentile were related to urinary diethyl phosphate metabolites but not to dimethyl forms. In a multivariate model, total molar DAP levels increased with age, by a factor of 1.01 per year (p=0.04), and were higher in subjects with high income compared to subjects with the lowest income by a factor of 1.59 (p=0.02).

12.3

0103

Mercury and cadmium levels in Belgian children and their mothers

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Aims

Within the frame of the EU projects DEMOCOPHES and COPHES, a harmonized European human biomonitoring pilot study was set up involving 17 European countries. The biomonitoring study consisted in measuring in each participating country the level of some environmental pollutant biomarkers in children and their mothers. Here we present the results of cadmium and mercury levels in respectively the urine and hair of the Belgian participants.

Methods

From October 2011 until February 2012, 129 Belgian school children (6-11y) and their mothers (≤ 45y) living in urban and rural areas of Brussels were selected to provide morning urine, hair, and information on their life style, diet and home environment. Cadmium levels were measured in centrifuged and acidified urine by ICP-MS (LOQ=0.01µg/g), while total mercury was analyzed by FIMS on hydrolyzed hairs (LOQ=0.08µg/g).

Results

The geometric mean level for mercury in hair were 0.383µg/g and 0.204µg/g for respectively mothers and children. Cadmium in mother's and children's urine was detected at a geometric mean concentration of respectively 0.21 and 0.04µg/L. Cadmium was detected in 99.2% of mother's urines and 86.4% of children's urines while 95.3 and 80.3% of mother's and children's hair showed mercury levels higher than the LOQ.

Conclusions

The levels of mercury in hair and cadmium in urine were higher in mothers than in children. The cadmium levels were higher in the urban area in both mothers and their children, and boys had increased levels compared to girls. Fish consumption and amalgam fillings in mothers were determinants of hair mercury levels.

12.4

0062

Exposure to PAHs in subjects living in the vicinity of a solid waste incinerator

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Aim: Investigate exposure to polycyclic aromatic hydrocarbon (PAHs) in subjects living in the vicinity of a solid waste incinerator (SWI) in Modena (Italy).

Methods: Sixty-five subjects living and working within 4 km from the incinerator (exposed) and 103 referents living and working outside this area, within a 15 km distance from the incinerator (not exposed), were recruited. Information about personal characteristics, lifestyle, residential history, and health status were collected. Exposure to incinerator particulate matter was estimated using fall-out maps from a quasi-Gaussian dispersion model. Urine spot samples were analyzed for the detection of 10 unmetabolized PAHs (from naphthalene to chrysene).

Results:. Urinary PAHs were above the limit of quantification (LOQ) in 6% (acenaphylene) to 100% (naphthalene and phenanthrene) of samples. Median level of PAHs with more than 50% of values above LOQ were: naphthalene 36.7 ng/L (>LOQ 100%), fluorene 1.46 ng/L (90%), phenanthrene 6.0 ng/L (100%), anthracene <0.5 ng/L (56%), and pyrene 1.1 ng/L (98%). Urinary phenanthrene and anthracene were higher in exposed subjects ($p<0.01$). Multiple regression analysis showed that urinary fluorene, phenanthrene, anthracene, and pyrene were inversely correlated to the distance of residence from the plant, and that phenanthrene and fluorene were positively associated with exposure to incinerator particulate matter.

Conclusions: This study suggests that specific urinary PAHs may provide information about the exposure arising from SWI.

Session 13: Incident exposures

13.1

0007

Biological Monitoring of Industrial Cleaners after a Large Scale Chemical Incident- a Complex (Mixture) Case Study

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Aims

In January 2011 a chemical plant blaze took place in The Netherlands. The authorities set up a co-ordination centre for emergency services. Clean-up activities by specialized industrial cleaning companies started the next day. One such company consulted an occupational health service for performing biological monitoring. The aim of the study was to monitor and control the exposure of the workers.

Method

Based on environmental measurements by the National Institute for Public Health and the Environment, the following lead biomarkers in urine were chosen: 1-Hydroxypyrene, Methylhippuric Acid, Hippuric Acid and S-Phenylmercapturic Acid. Sampling took place by the company itself applying their internal protocol. Contextual information was provided by the HSE manager. In total 36 workers were sampled on different days.

Results

The main activity of the workers was clean-up of contaminated fire water out of ditches using vacuum trucks. During the first two days not all workers were using personal protective equipment. Later on adequate respiratory protective equipment and chemical coveralls were used. Levels of Methylhippuric Acid were very low. For 3 workers on one day the action value for 1-Hydroxypyrene was exceeded. For 6 other workers on other days the action value was exceeded due to non-cleaning activities. The levels of Hippuric Acid were too high for 2 workers due to non-cleaning activities.

Conclusions and discussion

The most striking result was that the internal companies sampling protocol did not take into account the half-life of the substances. Additional control measures were necessary, especially with regard to skin exposure.

13.2

0098

Biomonitoring after chemical incidents and during maintenance works: a versatile tool for exposure analysis and assessment in the chemical industry

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Biological monitoring is a well-established tool in occupational medicine and industrial hygiene for the surveillance of workers potentially exposed to hazardous chemical compounds under regular working conditions. Many limit, guidance or assessment values derived for 8-hour work shift exposures are available, and scientific as well as governmental committees review the current knowledge about toxic effects of chemicals on a regular basis. However, biological monitoring may also serve as a quantitative measure for accidental or short-term exposures. While reports on such incidents are rare in the scientific literature, these data may provide significant additional information such as exposure levels for acute toxic effects, distribution and elimination kinetics in humans, effectiveness of technical and personal protective equipment, and also an objective selection criterion for medical aftercare as well as for follow-up studies. In this presentation, the comprehensive approach of a global chemical company to biological monitoring in general as well as to the analysis and assessment of accidental and short-term exposures in particular will be summarised and explained on the basis of several intensively investigated examples. The results are discussed with respect to existing limit and assessment values, background values of the general population and to toxicological considerations such as route of exposure, elimination half-life and, not at least, practical aspects. The experience from more than two decades shows that biological monitoring is a versatile and useful tool not only for adequate exposure analysis and assessment, but also for the communication and appropriate discussion of potential health risks.

13.3

0038

Implementation of a guidance for human biomonitoring following chemical incidents

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In the Netherlands in June 2012 a guidance was published to support early decision-making about the human biomonitoring (HBM) following chemical incidents. For implementation of this guidance a service center was set up to support experts in the field to use HBM following chemical incidents.

Aim

Support the use of HBM in chemical incidents.

Methods

A service center was set up to support the analysis of 215 biomarkers related to 130 chemical substances. The analysis is supported by a network of eight laboratories with EQUAS certificates for 115 biomarkers. Requests for HBM can be submitted by 25 certified public health advisors hazmat to a front office 24/7. Questions concerning the feasibility of HBM in a particular incident setting are discussed with an HBM expert in a back office. Standardized materials for sample collection will be sent to the incident location within 12 hours. Collected samples are pre-treated (if needed) and sent to the laboratory for analysis the same day.

Results

In most cases health complaints and/or clinical signs were the reason to consider HBM. One incident involved mercury exposure in two young children. HBM demonstrated much higher uptake than expected, based on expert judgment of the exposure conditions.

Conclusions

Experience based on the limited number of requests received so far indicates that a feasibility check before introducing HBM in an incident setting was considered useful. The availability of a laboratory infrastructure is promising but many challenges remain regarding adequate collection and transportation of biological materials related to incidents.

13.4

0041

Are aircrews exposed to neurotoxic o-tricresyl phosphate during fume events?

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Cabin air of aircrafts is supplied by bleed-air from the aircrafts` engines. In case of malfunctions engine oil may be released into cabin air resulting in unpleasant odour or even visible smoke. Air crews and passengers experiencing such "fume events" reported symptoms like exhaustion, headache, sight disorders and even incapacity to act. Engine oils contain small amounts of isomeric tricresyl phosphates (TCPs) including the neurotoxic ortho-TCP. Since the latter one has repeatedly been addressed to be responsible for reported symptoms we conducted a study to evaluate to which extent cabin crews are exposed to TCP isomers.

In total, we enrolled 332 flight attendants and pilots who experienced a fume event during flight. In spot urine samples given within less than 12 hours after an assumed fume event we quantified three specific metabolites of isomeric TCPs along with four additional organophosphates after solid phase sample clean-up and derivatisation by means of GC-MS/MS.

None of the 332 urine samples contained metabolites of ortho-TCP. One urine sample contained meta- and para-TCP metabolites close to LOD (0.5 µg/l). Metabolites of tributyl, triphenyl and tri-(2-chloroethyl) phosphates were detected in nearly all samples and found to be significantly higher in aircrews compared to non-exposed persons from the general population.

Specific exposure to TCP isomers and particularly to neurotoxic ortho-TCP was not evident. The reported health effects can hardly be attributed to an ortho-TCP exposure. Elevated levels for the other flame retardants may find an explanation in the flame protected environment in aircrafts.

Session 14: New approaches and new analytical techniques

14.1

0068

Arsenic Speciation in Urine using micro liquid chromatography-ICP-MS for Routine Biological Monitoring

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[1]*Health & Safety Laboratory, Buxton, UK,* [2]*Sheffield Hallam University, Sheffield, UK*

Aims

The aim of this work was to establish levels of individual arsenic species in urine samples from unexposed persons and to compare to those from a semi-conductor workplace.

Methods

Separation of five arsenic species (arsenobetaine (AB), arsenite (As3+), arsenate (As5+), dimethylarsinate (DMA), and monomethylarsonate (MMA)) in urine was achieved using a hyphenated µLC (micro liquid chromatography) system, coupled to an inductively coupled plasma - mass spectrometer (ICP-MS). Samples from 91 workers in the semi-conductor industry and from 75 unexposed volunteers were analysed.

Results

The background equivalent concentration for all five species were less than 0.014 µg/L and limits of quantification were all less than 0.54 µg/L. Overall, the arsenic exposure in semi-conductor workers was low. Both arsenite and arsenate were present at very low levels, with a 95th percentile value less than 0.31 µg/L.

In the workers statistical analysis showed there was no significant difference between the pre and post working week samples for any of the five species. In addition to no significant difference between smokers and non-smokers for arsenite and arsenate.

Conclusions

Using a routine method to measure five species of arsenic in urine by µLC-ICP-MS background levels in urine samples from unexposed persons have been established. Comparison with the data from semiconductor workers showed that exposure is very low in this workplace.

14.2

0080

Benefits of ICP-qqq-MS in MS/MS mode for challenging clinical trace element applications

Raimund Wahlen, Glenn Woods
Agilent Technologies, Cheadle, UK

The presentation will highlight the benefits of a novel ICP-qqq-MS (Agilent Technologies 8800)capable of true MS/MS operation for challenging clinical trace element applications.

Data will be presented on how this new technology can address a variety of common interferences in clinical matrices including polyatomic, doubly-charged and isobaric interferences on commonly interfered elements including Ti, Cr, Co, Mn, V, Cu, As and Se.

Performance characteristics for the method will be presented including data for elements such as S and P which have traditionally been challenging with single-quadrupole ICP-MS, including the use of LC-ICP-MS/MS for studies of P and S containing proteins and peptides.

14.3

0030

A simple and cost-effective benzene biomonitoring test kit.

Lathan Ball[1], John Cocker[2], Kate Jones[2]
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Human exposure to occupational and environmental chemicals can be determined by the measurement of urinary metabolites. Exposure to benzene, a common industrial chemical and ubiquitous pollutant, can be determined by the measurement of urinary S-PMA. The measurement of S-PMA is non-invasive and its use in occupational biomonitoring is recommended by regulatory authorities (HSL, DFG, ACGIH).

A test kit for the measurement of urinary S-PMA has been developed and validated. The test kit employs a competitive ELISA and eliminates the need for sample preparation, providing simplicity, high sensitivity and good specificity. The test kit allows low cost analysis meeting the needs of occupational, environmental and epidemiological monitoring.

The ELISA employs a sheep antiserum raised to an S-PMA-KLH conjugate. The conjugate was prepared by coupling S-phenylcysteine with the homobifunctional cross-linker bis(sulfosuccinimidyl) suberate. Microtitre plate wells were coated with BGG-S-PMA. Coating conjugate was prepared by the diazotisation of m-aminobenzoyloxy-S-phenyl-L-cysteine. Employing a second chemistry increased the assay's sensitivity.

The ELISA has a measuring range of 1-2000µg/l of S-PMA - meeting the DFG recommended limit of detection (1µg/l). The assay is both robust and reproducible and cross-reactivity studies confirm the specificity of the test.

Benzene biomonitoring kits manufactured, stored and transported under Quality Management Systems ISO 9001:2008 and ISO 13485:2003 have been employed in both the USA and SE Asia - confirming the "transportability" of the test. The successful development of a benzene biomonitoring test kit should facilitate the introduction of routine screening programmes by occupational and environmental laboratories and health professionals.

14.4

0074

Biological Monitoring of Exposure to Carbamate Fungicides: determination of ethylene- and propylenethiourea by UHPLC-ESI-MS/MS

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Aims Dithiocarbamates (DTC), one of the mostly used category of fungicides, gained important market share in Europe between 1992 and 2003. These products are still largely used because of their broad spectrum of activity and low price. France, Italy and Spain account for 64% of the total use of fungicides due to the predominance of these three countries in grape production. This study is aimed at determining urinary ethylenethiourea (ETU) and propylenethiourea (PTU), as the main metabolites of DTCs.

Methods Due to the high instability of ETU and PTU in acidic conditions, the effect of chromatographic parameters on the MS detection has been studied. Thus, the analytical challenging related to the retention and ionization efficiency of these small molecules has been worked out using a pentafluorophenyl ligand of a PFP column with new and optimized pH conditions. The developed method doesn't need any derivatization and time-consuming procedures. The use of ETU-D4, as isotope-labeled internal standard, compensated a strong matrix effect observed from the mostly used sources of the matrix.

Results Good accuracy and precision were demonstrated by determining spiked quality control samples prepared in urine. The assay was linear from 0.1 to 40 ng/mL. The validation procedure assessed the limit of detection at 50 ng/L.

Conclusions This method has been successfully applied for evaluating low occupational exposure levels to DTCs and to the biological monitoring of subjects from the general population. Preliminary data suggests that this assay may be further applied to a multi-center study from different European countries.

Short Oral Session A: Public health

A.1

0110

Measuring community exposures to solvent vapours from groundwater solvent plumes

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Petroleum retailers generally use underground storage tanks (UST) to maintain suitable supplies of fuels. In Australia, approximately 1 in 3 UST leak fuel into the surrounding soil. In addition, dumping waste fuel and lubricating oils on site may have contributed further to soil contamination. Volatile organic compounds (VOC) dissolve in groundwater and equilibrate with the surrounding soils as they migrate offsite. Depending upon the porosity and characteristics of the soil, VOC may percolate to the surface and be entrained in structural spaces including homes. Identifying the contribution to indoor VOC exposures from soil rather than from airborne sources such as outdoor traffic and industry emissions or indoor sources such as heating and cooking fuels, furnishings, paints and adhesives is an important step in the management of environmental chemical exposures.

We have examined 6 homes surrounding 2 disused petrol retailers with confirmed contamination. Indoor and outdoor airborne VOC concentrations were collected using Radiello® diffusion tubes that were analysed for multiple VOC using gas chromatography-mass spectrometry. Indoor benzene concentrations ranged from 0.2-1.0 ug/m^3 in test homes with up to 0.2 ug/m^3 in control homes. Outdoor concentrations were generally lower than indoor for benzene, and toluene but were approximately equivalent for other VOC. Urinary concentrations of t,t-muconic acid were measured to indicate personal exposure and uptake of benzene.

These data will be used to establish individual risk estimates for residents. This project will provide baseline data to help assess homes of residents who express concern about potential harmful effects of environmental chemicals.

A.2

0018

Phthalate, bisphenol A, triclosan and parabene exposure of general population in Slovenia

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Aim of this study was to assess exposure of general population to the most relevant toxic substances, including phthalate metabolites (MEP, MEHP, DEHP=5oxoMEHP+5OH-MEHP, MBzP and MnBP), bisphenol A (BPA), triclosane (TCL) and parabene metabolites (MeP, EtP, PrP and BuP).

Urine samples were collected from 156 mothers (<45 years), 172 children (6-11 years) and 69 fathers living in Slovenia. Families were recruited through schools from urban and rural area. Sampling was performed according to Cophes/Democophes protocols (http://www.eu-hbm.info/).

In all biomarkers, significant differences between population groups were obtained. TCL and parabene metabolites were significantly higher in mothers. Children had the highest BPA and phthalate levels. Phthalate metabolite MnBP, TCL and parabens were observed to be significantly higher in urban than in rural area, the opposite was observed for MEHP and DEHP. Phthalate metabolite levels were significantly positively associated with hazelnut spread consumption (MEP, MnBP), ice cream (MEP), chewing gum (MEP, DEHP), and convenience food consumption (MEHP). Negative significant association was observed between MnBP and meat consumption. Presence of PVC floor or walls in family's house influenced MBzP significantly. MBzP was observed to be associated with use of personal care products in children. Among parabene and TCL metabolites, only EtP was significantly associated with the use of personal care products in general, and MeP with body lotion and crème usage. Prominent source of BPA exposure was not observed, however mothers taking contraception pills had higher BPA levels in urine, and when adjusted for pills, significant positive association between BPA and consumption of canned food was observed.

A.3

0065

Urinary nicotine metabolites: usefulness as biomarkers of smoking status

Ilse Van Overmeire[1], Anca Elena Gurzau[2], Fátima Reis Reis[3], Gudrun Koppen[4], Milena Horvat[6], Ioana-Rodica Lupsa[2], Sónia Namorado[3], Dominique Aerts[5], Darja Mazej[6], Pedro Aguiar[3], Janja Snoj Tratnik[6], Joris Van Loco[1], Koen De Cremer[1]
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Aims

Nicotine is metabolised to cotinine (COT) and further to trans-3'-hydroxycotinine (HCOT) by the cytochrome P450 CYP2A6 enzyme. It has been demonstrated that the ratio of HCOT to COT is an index of CYP2A6 activity, thus a marker of nicotine metabolism, with higher ratios indicating faster metabolism. Evidence shows that the ratio, in urine, saliva or plasma, could predict responses to smoking cessation medication and guide pharmacotherapy. Since the literature about the association between this ratio and the cigarettes smoked per day (cpd) is not uniform, our aim was to investigate this relationship using urine samples from smoking females living in Romania, Portugal, Belgium and Slovenia.

Methods

Urine samples from mothers (aged up to 45 years) who participated in the EU project DEMOCOPHES(LIFE09/ENV/BE/00410) were used. The concentrations of COT and HCOT were determined by online-SPE UPLC MS/MS and subsequently normalised to creatinine content. The amount of cpd was available from the questionnaires.

Results and conclusions

As expected, a strong positive correlation between COT and HCOT levels was found.

Regarding the association between HCOT/COT ratio and cpd, no correlation was observed when the data were globally considered.

We confirmed that the correlation between cpd and cotinine differed according to the HCOT/COT ratio: higher correlations for slow metabolizers (low ratio) and almost no correlation for fast metabolizers (high ratio).

A new analytical strategy is in progress to fully explore the usefulness of this ratio as biomarker of cigarette consumption.

Short Oral Session B: New biomarkers

B.1

0066

Fire Fighters' multiple exposure to perfluoroalkyl acids and 2-butoxyethanol present in AFFFs

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The aim of this study was to assess fire fighters' multiple exposure to substances present in aqueous film forming foams (AFFF). We measured perfluoroalkyl acids in order to determine the signs of accumulation during three monthly training sessions. In addition, we evaluated eight commercially available AFFFs from the occupational hygienic perspective and gave recommendations for the best AFFFs to use in the future.

Sthamex 3% AFFF was used as extinguishing foam for jet fuel fires. Fire fighters' exposure to 12 perfluoroalkyl acids was analyzed by LC-MS/MS from serum samples taken before and after three consecutive monthly training sessions. Exposure to 2-butoxy ethanol was assessed by urinalysis of 2-butoxyacetic acid before and after the training sessions.

The range of PFOS, PFOA, PFHxS, and PFNA in the serum samples was measurable. Their average concentrations increased slightly during the three training sessions, but remained the same in concentrations measured among the Finnish population in general. The average concentrations of 2-butoxyacetic acid exceeded the reference limit of the general population in two training sessions.

Fire fighters appear to be exposed to fire fighting foam chemicals despite using standard protective equipment and clothing. The perfluoroalkyl acids measured in the fire fighters' serum followed the same profile as those measured in the liquid of Sthamex 3% AFFF. Exposure can be decreased by introducing small changes to the training sessions and to the maintenance of equipment and clothing. In the selection of AFFFs, non-fluorine based products should be favoured in the future.

B.2

0091

Internal exposure to perfluoroalkyl compounds in a French population of fish consumers

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Context

Due to their properties, perfluoroalkyl compounds are widely spread in the environment and particularly in aquatic systems. Among the 800 congeners gathered in this chemical family, the human toxicity of carboxylates (e.g. PFOA) and sulfonates (e.g. PFOS) compounds is of particular concern. This is mostly due to their protein affinity. However few data are available in the literature concerning the actual human exposure to these compounds.

Objective

This study aims to provide descriptive French data concerning the Human internal exposure to 14 perfluoroalkyl compounds. The included population consisted in 478 freshwater fishermen living in the vicinity of 6 watersheds: Garonne, Loire, Rhone, Somme, Rhin-Moselle, Seine and Rhone. This population was selected as it was thought to be particularly exposed through its diet, due to the potential high level of freshwater fish consumption. The substances were measured in the blood of the studied population and fish consumption was estimated through a dietary questionnaire. In parallel, the chemicals concentrations were also estimated in different species fished in the 6 watersheds.

Results

The presentation will focus on the six (PFHxS, PFHpS, PFOS, PFOA, and PFDA) of the 14 compounds that were quantified in more than 99% of the blood samples. Data concerning the statistical descriptors of the internal exposure, the inter-regional comparison of these exposures and links between fish consumption and contamination will be synthesized.

Authors wish to thank Laberc-Oniris for perfluoroalkyl compounds analyses in biological matrix and InVS for its implication in the design of the survey.

B.3

0037

Mercapturic Acids Derived from 2- and 3-Nitrobenzanthrone

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Aims

Both 2- and 3-nitrobenzanthrone (NBAs) are strongly mutagenic environmental pollutants emitted from diesel engines. They are metabolised to reactive N-acetoxy-aminobenzanthrones (AcO-ABAs), which dissociate to nitrenium ions and are likely to react with endogenous SH groups. The aim of this work was to study in vitro model reactions of AcO-ABAs with N-acetylcysteine (NAC) as well as in vivo formation of mercapturic acids from 2- and 3-NBA.

Methods

NBAs were converted by a two-step synthesis to corresponding AcO-ABAs. Products were allowed to react with NAC. Mercapturic acids, 2-aminobenzanthron-3-yl- and 3-aminobenzanthron-2-ylmercapturic acid (2- and 3-ABA-MA) were isolated, identified and used as standards for the LC/ESI-MSMS analysis of urine samples obtained from rats dosed with 2- and 3-NBA, respectively.

Results

Signifi
cant difference in the metabolism was found between 2- and 3-NBA. A new mercapturic acid, 3-ABA-MA, was identified in the urine of rats dosed with 3-NBA, metabolic yield being about 0.5 %, whereas no 2-ABA-MA was detected after dosing rats with 2-NBA. On the other hand, both AcO-ABAs were found to be direct precursors to the electrophilic nitrenium ions in vitro as their reactions with NAC in aqueous THF gave respective mercapturic acids. These results indicate significant metabolic activation of 3-NBA but not of 2-NBA.

Conclusions

Urinary 3-ABA-MA is a promising biological indicator of exposure to 3-NBA and its effective dose.

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Poster sessions

Biological Effect Monitoring

P.16

0036

Relationship between exposure to low level VOCs and oxidative stress

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People spend large part of the day indoors, where the exposure to VOCs can be significant if the building is new or recently refurbished. It is established that exposure to VOCs and PAHs can directly lead to oxidative stress or to inflammation, that will eventually cause DNA damage arising from oxidative stress. One of the most widely studied biomarkers of oxidative stress is 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG), which can be measured in urine samples. The aim of FIXAT (Fingerprints of eXposure to Air Toxics) project is to find biomarkers of exposure and early health indicators to low-level VOCs arising from building materials and consumer products, using both analytical and metabolomic approaches. The project focuses especially on the exposure level of general population.

The levels of urinary unmetabolized VOCs measured using Headspace GC-MS were correlated with the levels of urinary 8-oxodG, measured with LC-MS/MS in subjects belonging to general population from an on-going study (FIXAT), and selected MATCH (1) subjects exposed to high levels arising generally from environmental tobacco smoke exposure. Other methods such as ELISA and GC-MS were also tested for analysis of oxidative stress biomarkers.

The results showed a significant statistical correlation (P=0.475 for total VOC/8-oxodG) between the levels of the unmetabolized urinary VOCs and the levels of urinary 8-oxodG, suggesting a relationship between the exposure to low level VOC concentrations and the induction of oxidative stress in the general population.

The authors thank CEFIC and Wellcome Trust for financial support.

1. Delgado-Saborit, JM et al. (2009), Environ Sci Technol, 43(12):4582-4588.

P.19

0056

Effect biomarkers in a UK study of workers exposed to silica.

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Aims

A longitudinal study of UK workers exposed to silica is being undertaken by the Health and Safety Laboratory. The initial time point investigation is currently being completed and thus available for analysis as a cross-sectional study. This poster focusses on the relationships between the measured biomarkers of effect and both other health outcome measures and exposure estimates

Methods

Individual exposure estimates for those workers who have volunteered for the study are being calculated from atmospheric measurements and job histories. Health outcome measures include respiratory and general health questionnaires, lung function tests and chest x-rays, as well as a panel of effect biomarkers related to silica exposure, particularly lung and renal damage, measured in blood and/or urine. These biomarkers of effect include the lung markers, Clara cell protein (CC16), lung surfactant proteins (A&D) and a panel of renal markers that includes kidney injury molecule-1 (KIM-1), neutrophil gelatinase -associated lipocalin (NGAL) and cystatin C. Biomarkers reflecting inflammatory response and protein oxidation/nitrosylation are also being measured.

Results

Initial comparisons of the urinary and blood effect biomarkers with the other health measures and exposure estimates will be presented, based on a cross-sectional analysis of the data collected from the initial time point.

Conclusions

The outcomes will be discussed in the context of other studies of silica exposed workers involving biomarkers of effect.

P.31

0079

MicroRNAs as biomarkers in arsenic exposure

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Aims Exposure to inorganic Arsenic (iAs) is a major public health problem in most Countries. Although numerous studies have shown the related adverse effects of iAs, sensitive appropriate biomarkers are still required for studies of environmental epidemiology. The aim focuses on the role of microRNAs, negative regulators of gene expression which play a key role in many physiological and in pathological cellular processes, in iAs exposure. MicroRNA changes trigged by iAs exposure were investigated in Jurkat cell line.

Methods We performed microarray technology to profile the expression of microRNAs following 2 µmol/L sodium arsenite treatment at different time points (24h and 144h), microRNA and mRNA validation by Real Time PCR (RT-PCR) and cell phenotypic analysis. Bioinformatics techniques were applied, including knowledgebase analysis of molecular interactions, functional annotations and network visualization tools, to reconstruct iAs-relevant molecular pathways and microRNA regulatory networks from expression data.

Results Changes in microRNA profiles after iAs treatment were highlighted. In particular, 36 microRNAs exhibited consistent dysregulation, we focused our attention on a panel of 12 microRNAs further validated by RT-PCR (e.g. miR-663, miR-222, miR-638). Predicted target genes of 12 microRNAs involved in arsenic-response pathways were validated by RT-PCR (e.g. TGFβ1, RNF4). Furthermore, iAs exposure is associated with an induction of cell cycle progression supporting the idea of its carcinogenic action.

Conclusions Our study highlights the importance to proceed in the investigation of microRNA expression profiles aimed to the possibility of the use of some microRNAs as potential biomarkers of iAs effect with useful diagnostic value.

P.32

0081

GENETIC BIOMARKERS IN THE DETOXIFICATION OF STYRENE OXIDE. APPLICATION TO BIOLOGICAL MONITORING OF OCCUPATIONAL EXPOSURE TO STYRENE.

María José Prieto Castelló[1,4], Antonio Cardona Llorens[1,4], Dolores Marhuenda Amorós[1,4], José María Roel Valdés[2,1], Andrés Corno Caparros[3,1]
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The aim of this study was to evaluate the usefulness of genotyping of detoxification enzymes styrene oxide (SO), the intermediary genotoxic metabolite of styrene, as biomarkers of susceptibility for the risk assessment of occupational exposure to styrene, correlating genotyping data with other biomarkers of exposure and of cytogenetic effect.

We studied genes encoding enzymes involved in the pathway of styrene detoxification in humans: The glutathione-S-transferase (GSTM1) and microsomal epoxide hydrolase (EPHX1) involved in the transformation of SO in specific mercapturic acids (PHEMAs) and phenylglyoxylic and mandelic acids (PGA+MA), respectively. We collected samples of urine, blood and buccal swab from 49 non-exposed workers and 255 workers exposed to styrene in companies in the marble, plastic and building boats industry, for chromatographic determination of biological indicators in urine, for genotyping by RFLP-PCR and for determining the possible cytogenetic effect using micronucleus (MN) test.

In exposed group the mean concentrations of styrene in the environment and PGA+MA in urine samples were 54 mg/m3 and 213 mg / g creatinine respectively (lower that respective TLV and BEI proposed by ACGIH (86 mg/m3 and 400 mg / g creatinine, respectively), but significantly higher in the building boat and plastic workers, with respect to the marble workers. We found a decrease in the PHEMAs excretion in individuals carrying the null GSTM1 genotype. The exposed workers showed a significantly higher frequency of MN (8.42±2.67) compared to controls (6.48±2.16).

Our data suggest that EPHX1 polymorphisms and smoking habit can influence the induction of cytogenetic damage in exposed workers.

P.37

0087

METHODOLOGICAL SAMPLING APPROACH TO THE USE OF GENETIC BIOMARKERS IN THE RISK ASSESSMENT OF OCCUPATIONAL EXPOSURE TO SOLVENTS

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The aim of this paper is to propose an effective sampling methodology for using genetic markers in the assessment of the occupational exposure risks to organic solvents. Using this methodology is intended to further the study of risk factors for toxic solvents, evaluating if genotyping and phenotyping of solvent metabolizing enzymes can be useful in the biological monitoring and correlating with biological indicators commonly used in surveillance programs of Occupational Health. We will study the genotypes and phenotypes of the most important genes encoding enzymes involved in metabolic pathways of organic solvents in humans, depending on the particular exposure in the industrial sector under study.

Under the support of the Prevention Services will select workers and jobs at risk of exposure to solvents. All these workers will be submitted to: 1. A questionnaire which collects occupational-hygienic and medical-clinical data related to the study. 2. Environmental monitoring of exposure to solvents present in the workplace. 3. Biological monitoring by determining the biological indicators proposed by ACGIH for each solvent. 4. Study metabolising enzymes involved in the biotransformation pathway of solvent (genotypes and / or phenotypes using PCR techniques) 5. Evaluation of the possible biological effect by a useful test. To carry out all these methods is needed to collect samples of urine, blood and buccal mucosa from workers which is often very difficult to achieve.

The proposed strategy takes advantage of the annual health surveillance carried out by Prevention Services, so it is quite viable and without interference with the work.

P.38

0088

CYP2E1 PHENOTYPE AND EVALUATION OF GENETIC DAMAGE IN FOOTWEAR WORKERS EXPOSED TO TOLUENE

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Footwear workers are exposed to organic solvents of which the toluene is a main component. Toluene induces expression of cytochrome P450 E1 (CYP2E1), an enzyme involved in toluene metabolism and that of other toxics including procarcinogens. The aim of this study is to investigate the association between toluene exposure and the CYP2E1 activity, as assessed by mRNA content in blood samples and the possible cytogenetic damage.

Urine and blood samples were collected from 129 footwear-workers and 13 controls. Expression levels of CYP2E1 were determined by mRNA quantification by RT-PCR. As biomarker of exposure we measured the hippuric acid (HA), the main metabolite of toluene in urine. MN frequency in binucleated lymphocytes was analyzed as biomarker of cytogenetic effect.

Results of HA and CYP2E1 activity but not MN frequency showed statistical increased values amongst exposed workers relative to controls ($p<0,05$). A correlation test revealed that age was significantly associated with MN frequency in exposed group ($r=0,352$, $p<0,01$). In this group no correlation was found between CYP2E1 activity and concentration of HA in urine but CYP2E1 activity decreased as the years of occupational exposure increased ($r=-0,190$, $p<0,05$) which is in concordance with results obtained in other studies. The mechanism of this effect remains to be studied.

With further validation, CYP2E1 activity as measured by CP2E1 mRNA content from whole blood samples, which can be easily collected in especial tubes containing and RNA stabilizer, could be a sensitive, rapid and non-invasive biomarker for the monitoring of workers exposed to styrene.

Interpretation of results

P.46

0107

Towards Reference Values Biomarkers of Oxidative Stress in Exhaled Breath Condensate

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Aims: Exhaled breath condensate (EBC) is a fluid collected non-invasively during tidal breathing, proposed to measure several biomarkers of exposure and effect. It has proven useful in the study of airway inflammatory diseases, including asthma, COPD and cystic fibrosis. This study investigated the distribution of biomarkers of oxidative stress associated with aging and tobacco smoking habits in EBC from a reference group of healthy workers.

Methods: We recruited 105 workers (all males, 32 smokers), mean age 44.9+9.06 years, without clinically significant lung diseases and occupationally unexposed to oxidant agents. The following biomarkers of effect were determined: (1) total protein content, marker of dilution; (2) malondialdehyde (MDA) and 4-hydroxy-2-nonenal (HNE), biomarkers of lipid peroxidation; (3) 8-isoprostane, product of free radical-catalyzed peroxidation of arachidonic acid; (4) H_2O_2, biomarker of inflammation and oxidative stress; asymmetric dimethyarginine (ADMA), endogenous inhibitor of nitric oxide (NO) production; 3-nitro-tyrosine ($3NO_2$-Tyr), marker of nitrative stress.

Results: Neither smoking habits (no/yes) nor age did show significant effects. H_2O_2, MDA and HNE correlated with each other ($p<0.026$), as did ADMA and $3NO_2$Tyr ($p<0.0001$).

Conclusions: This study investigated the distributions of a panel of biomarkers in EBC proposed to measure (and monitor) oxidative stress. Our data aims at setting relevant reference values for these markers. The lack of age- and smoking- related effects is a good pre-requisite to assess adverse effects of air pollutants and is very useful to interpret of data obtained from people exposed to oxidizing agents or affected by pathological conditions associated with oxidative stress.

P.02

0004

Evaluation of the current biological exposure index of toluene in Korea

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While the exposure limit of toluene in air was lowered to half of its previous value in 2007 in Korea, the biological exposure index of toluene remained at the level of old ambient monitoring, so the change of this index became necessary. The authors assessed urinary hippuric acid, o-cresol and toluene in blood as a biological marker of toluene for workers using this material.

Ambient monitoring and biological monitoring for 168 workers exposed to toluene and the non-exposure groups of 30 workers who have never been exposed to toluene were selected as the subjects.

TWA of toluene was 0.01 - 114.5 ppm, and 21 workers were exposed to levels over 50 ppm. Urinary hippuric acid in exposure group was in the range of 0.03 - 3.74 g/g creatinine, while that of non-exposure group was 0.02 - 0.47 g/g creatinine. Urinary o-cresol in exposure group was in the range of 0.002 - 3.06 mg/L and that of non-exposure group was 0.002 - 0.24 mg/L. Toluene in blood in exposure group was 0.003 - 1.32 mg/L and that of non-exposure group was 0.003 - 0.08 mg/L. Toluene in air showed good correlation with hippuric acid over 5 ppm, and with o-cresol over 10 ppm. Toluene in blood was the only marker which kept a good correlation with ambient toluene less than 5 ppm.

This result supported the biological exposure index of hippuric acid, o-cresol in urine, toluene in blood as 1.6 g/g creatinine, 0.8 mg/L, and 1.0 mg/L.

P.06

0014

Biomonitoring of Employees Occupationally Exposed to Bisphenol A - A Comparison with Environmental and Occupational Assessment Values

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Because of its irritant and photosensitizing effect and its estrogenic potential the use of Bisphenol A (BPA) is currently under controversial discussion. In order to gain knowledge of the employees' exposure in a BPA processing plant human biomonitoring was carried out i) during a BPA free working interval (background exposure, 58 samples), and ii) during a production campaign where BPA was used (51 samples). Results were compared to a BASF internal control group (66 samples) without occupational exposure to BPA. Free and total BPA were analyzed by a validated GC-MS method (limit of determination: 1 µg/L).

During the production campaign BPA concentrations were clearly increased (up to 2,062 µg/g creatinine post-shift in individual cases) compared to control samples or samples collected during the BPA free working period. The exposure seemed to be mostly influenced by the use of personal protective equipment as well as by the smoking status of the employees. However, in all examination periods BPA concentrations were below the biological guidance value (80 mg/L) of the DFG and also below the HBM-I-Value (2,500 µg/L) of the German Federal Environment Agency, which is based on the TDI value of the EFSA.

Direct handling of BPA resulted in urinary BPA concentrations clearly above the background of the general population in Germany. However, the exposure of the employees was below occupational and environmental assessment values. Thus, according to current knowledge adverse health effects due to BPA exposure in the plant are not to be expected.

P.12

0028

Biomonitoring as an early warning of increased exposure to toxic substances in humans

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Aim

An important part of the National Food Agency's (NFA) work includes the estimation of levels of hazardous substances which consumers are exposed to through the diet. The project focuses on methods for early warning of increased exposure to toxic substances in the Swedish population, as well as on cases of possible threats/crisis.

Methods and Results

We have recently conducted a biomonitoring study of deoxynivalenol exposure in the adult population (collaboration with University of Leeds, UK, and University of Maryland, USA). In collaboration with the Swedish Environmental Protection Agency and Stockholm University, the exposure of Swedish adult consumers to perfluorinated alkyl acids (PFAA) has also been studied in a densely populated region. Drinking water was identified as a major source of PFAA-exposure. The distribution of the contaminated water was discontinued, and expected changes in PFAA-exposure are currently followed up. In collaboration with the Institute of Sciences of Food Production (ISPA) in Italy, a study of multiple mycotoxin biomarkers in human and pig urine samples has been initiated. Furthermore, a study on wild game consumption and its association with blood lead levels in children and adults within hunting families is on-going.

Conclusions

The system for the collection, storage and analysis of human samples for different types of biomarkers might be used to recurrent monitor the hazard exposures as well as to react in case of threat/crisis. Furthermore, the project provides a possibility to strengthen the capacity of the NFA to make informed risk management decisions and to follow up risk-reducing/preventive actions.

P.28

0075

Can Occupational Biological Limit value be recommended for Acrylamide?

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The French Occupational Exposure Limit (OEL) Committee considered acrylamide as a non-threshold carcinogen. In accordance with its operation manual, it therefore indicated airborne concentrations of 4, 0.4, and 0.04 µg/m^3 corresponding respectively to risk levels of 10^{-4}, 10^{-5}, and 10^{-6}. Given additionally that this substance was attributed a skin notation, the Committee also explored the possibility of proposing a biological monitoring strategy for the prevention of the deleterious effects of acrylamide in workers.

Literature review of the metabolic scheme and toxicokinetics of this carcinogen led to the identification of haemoglobin adducts as the best potential candidate biomarkers of exposure integrated over a few months. Among the potential candidates, scientific information was deemed adequate for N-carbamoylethylvaline hemoglobin adducts (AAVal) only. The information between AAVal concentrations and either health effects (cancer and neurotoxicity) or airborne acrylamide was deemed inadequate to recommend a numeric value for this biomarker. Consequently only a reference value for the concentration of AAVal in non-occupationally-exposed populations was provided. This value is only intended to provide guidelines regarding the contribution of occupational acrylamide exposure to its total body burden. This value was taken as the 95th percentile of AAVal in the European population (40-60 years). It corresponds to 85 and250 pmol/g globin in non-smokers and smokers, respectively

P.51

0119

Case Study: Conveying Biomonitoring Results in a Multi-Ethnic Community Study Through Collaborative Educational Protocols

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Conveying individual biomonitoring study results to study participants who request such information needs to be done with full consideration for cultural frameworks, differences in learning styles, available resources, and assessment of need for follow-up counseling or consultation, while respecting individual rights and privacy concerns.

Building trust between community members and scientific researchers can be accomplished by including community participation in the design, implementation and evaluation of results conveyance protocols. Educational activities and materials developed collaboratively can lead to a deeper understanding of factors contributing to individual health and to community engagement in public policy decision-making.

The California Department of Public Health Environmental Health Investigation Branch, the US Centers for Disease Control, Commonweal Biomonitoring Resource Center, and El Comite Civico developed a set of results communication methods by engaging community health workers and community leaders in planning a study that measured concentrations of perchlorate in water, produce and humans in the California Imperial Valley.

The perchlorate biomonitoring team developed a series of community planning meetings, field-tested informational materials, physician consultant informational flow charts, and individual and community meeting frameworks that utilized a variety of teaching techniques.

Subsequent evaluations with participants have indicated a high rate of understanding about the significance and possible use of the study results, and community leaders were interested in further activities that could lead to a decrease in perchlorate exposure.

(Paper in process)

Practicalities

P.10

0023

Quantification of cyclosiloxanes in exhaled air by thermal-desorption gas chromatography mass spectrometry.

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Consumer exposure to personal care products (PCPs) can be studied by analysis of cyclosiloxanes present in exhaled air. A promising non-invasive approach to study consumer exposure in a residential setting.

Aim

Development of a method for the quantitative determination of the cyclosiloxanes octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) in end-exhaled air.

Method

Exhaled air samples were collected using a Bio-VOC breath sampler (Markes). We used stainless steel automatic thermal desorption (ATD) tubes filled with Carbograph (Camsco). For calibration, we prepared 0-10 ng/µL solutions of D4/D5 and 13C-labeled D4/D5 in methanol for use as internal standards. Standards were loaded on ATD tubes, removing the solvent by helium flushing. The analytical instrument consisted of a thermal desorber (Markes) and a gas chromatograph mass spectrometer (Thermo).

Results

Low concentrations of cyclosiloxanes are difficult to determine due to a high and ubiquitous background. The TD-GC-MS itself was not a source of contamination. However, conditioned new tubes contained µg amounts of D4 and D5, presumably originating from the manufacturing process. Tube conditioning takes 4 hours at 350 °C. Reproducibility expressed as coefficient of variation was below 13%. The limit of quantification was below 0.1 ng/tube (< 0.7 ng per liter of exhaled air).

Conclusion

Cyclosiloxanes can be quantified in exhaled air down to sub ng/L levels using a TD-GC-MS approach. The instrument and chemicals are not a critical source of background contamination but ATD tubes are.

P.17

0044

Background Levels of Environmental Chemicals in Blood Collection and Storage Supplies for Alberta Biomonitoring Program Studies

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Aims: The Alberta Biomonitoring Program's current study is examining levels of a large suite of environmental chemicals in pooled serum from pregnant women and umbilical cords. The chemicals included are: cotinine, methylmercury, polychlorinated dioxins and furans, polychlorinated biphenyls, organochlorine pesticides, polybrominated diphenyl ethers (PBDEs), perfluorinated compounds (PFCs), phthalates, parabens, phenols, phytoestrogens, metals and micronutrients. The ubiquity of many of these chemicals in the environment presents a concern for background contamination of the blood collection and storage supplies. To have confidence at low concentrations the levels of these chemicals in the supplies must be known. The objective of this study is to determine concentrations of the most pervasive environmental chemicals in the blood collection and storage supplies.

Methods: Calf serum was used to test for the presence of PFCs, dioxins, furans, PBDEs, phenols, phthalates and metals in needles, vacutainer tubes, butterfly needles, pipettes, alcohol prep pads, and storage bottles. The serum was subjected to conditions similar to those used for actual collection and storage of the maternal and cord blood samples. The serum was analyzed by LC-MSMS and HRGC-HRMS for these compounds.

Results and Conclusions: Preliminary analysis determined concentrations of the PFC, dioxin, furan, and PBDE congeners in blank serum and in serum passed through the needles, vacutainer tubes, pipettes, and storage bottles. These concentrations were compared to limits of detection and 50th percentiles listed in the CDC's Fourth National Report on Human Exposure to Environmental Chemicals. The results highlight the need for the validation of supplies used for biomonitoring studies.

P.23

0063

An inter-laboratory comparison for the analyses of pyrethroid metabolites in urine with respect to the comparability of exposure levels in national population studies

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In the last years the application of human biomonitoring for environmental related population studies has grown worldwide distinctly. Due to the multitude of participating laboratories the question for comparability of the results arises. The aim of the present study was to examine the analytical comparability of two laboratories, which applied their procedures for population studies on pyrethroid exposure in Germany and Japan.

The comparison was performed by simultaneous determination of the pyrethroid metabolites 3-phenoxybenzoic acid (PBA) and 3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane carboxylic acid (Cl2CA) in 25 urine samples of the German Environmental Survey on Children and 22 samples of four Japanese surveys. One laboratory (Lab1) performed the analysis by acidic hydrolysis, extraction by hexane, derivatisation with MTBSTFA and GC-MS. The second laboratory (Lab2) performed the analysis by acidic hydrolysis, extraction by tert-butyl methyl ether, derivatisation with PFBBr and GC-MS.

The urinary levels found by both laboratories ranged between <0.1-40 µg/l for PBA and 0.15-15 µg/l for Cl2CA. The results of the two laboratories were found to be very comparable for PBA as well as for Cl2CA. In the correlation analysis a significant linear association was found for PBA expressed by the function C(Lab2) = 0.934 C(Lab1) + 0.484 (R^2=0.9437). The linear association for Cl2CA was found to be C(Lab2) = 0.897 C(Lab1) + 0.511 (R^2=0.9368).

The results of the study revealed a high comparability of the analyses of pyrethroid metabolites in urine in both laboratories. Inter-laboratory comparison studies to prove the analytical comparability of different national population studies are recommended.

P.36

0086

BIOETHICS OF BIOLOGICAL MONITORING IN THE WORKPLACE: MEDICAL ACTIVITY AND TOXIC RISK PREVENTION

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The aim of this study was to analyze the ethical and legal reasons that justify that biological monitoring should be considered essentially as a medical activity. This study evaluate the role of the doctor in the program of biological monitoring for prevention of the toxic risk, both from a legal perspective, arising from the European directives and their transposition into the laws of different countries, and from an ethical perspective. A biological monitoring program in the workplace is intended to provide the information necessary to assess, individually at an early stage, the toxic risk factors that may have harmful effects on the health of workers. The approach and development requires a multidisciplinary team of industrial hygienists, occupational toxicologists and doctors. This equipment should be coordinated and led by a specialist in Occupational Medicine, given that biological monitoring is an essentially based medical activity, according to its purpose, methodology and the legal and ethical issues that it raises. The legal reasons justifying that biological monitoring should be considered essentially as a medical activity are based on the principle that the doctor is, and will always be responsible for the health of workers. Moreover, from an ethical perspective, the doctor is the guarantor of the ethical principles of autonomy and nonmaleficence in the management and request of biological monitoring and of the principles of justice and charity in the handling and managing of this information.

Public health

P.04

0011

Worrying exposure to trace elements in the population of Kinshasa, Democratic Republic of Congo (DRC)

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Background and objectives: The particularly high rate of urbanization in Kinshasa (Democratic Republic of Congo) is associated with environmental degradation. Outdoor and indoor air pollution, as well as water pollution and waste accumulation, are issues of major concern. However, little documented information exists on the nature and extent of this pollution. A biomonitoring study was conducted to document exposure to trace elements in a representative sample of the population in Kinshasa.

Methods: Fifteen trace elements were measured by ICP-MS, CV-AAS, or HG-AFS in spot urine samples from 220 individuals (50.5% women) aged 6–70 years living in the urban area and from 50 additional subjects from the rural area of Kinshasa. Data were compiled as geometric means and selected percentiles, expressed without (µg/L) or with creatinine adjustment (µg/g cr).

Results: Overall, living in urban Kinshasa was associated with elevated levels of several parameters in urine as compared to the population living in the rural area (Asi, Ba, Cd, Cr, and V) as well as compared to an urban population of the southeast of Congo (Al, As, Cd, Cr, Cu, Pb, Mn, Ni, Se, V, and Zn). Elevated levels were also found by comparison with the reference values in databases involving American, Canadian, French, or German populations.

Conclusions: This study provides the first biomonitoring database in the population of Kinshasa, revealing elevated levels for most urinary TE as compared to other databases. Toxicologically relevant elements such as Al, As, Cd, Pb, and Hg reach levels of public health concern.

P.07

0016

Urinary levels of cadmium and cotinine of general population in Slovenia

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In the framework of biomonitoring programmes funded by Slovenian and EU funds parents (age <45 years) and their children (6-11 years) were recruited through schools from urban and rural area in Slovenia. Several biomarkers were analysed in hair, urine and blood, among them also cadmium in urine/blood and cotinine in urine samples from 155 mother-child pairs and 69 men. All concentrations in urine were adjusted for creatinine. Detailed questionnaires about residential environment and residence, nutrition, smoking behaviour, exposure relevant behaviour, occupation, socio-demography and sampling were also completed.

Concentrations of cadmium were low in general. Urinary levels were for mothers 0.25 ,fathers 0.20 and children 0.08 mg/g creatinine (GM), blood levels were for mothers 0.36, fathers 0.32 and children 0.18 mg/g (GM). But if the results are looked from another perspective i.e. 12 % of mothers and 14 % of fathers exceeded HBM-I values. Concentrations of cadmium and cotinine in samples can be explained by life style information from questionnaire. The most important influential factor on both cadmium and cotinine was as expected smoking behaviour of parents regardless of creatinine level. The second factor was age i.e. concentration of Cd in urine were significantly higher in mothers, fathers had the highest cotinine levels. Passive smoking in children influenced cotinine but not Cd levels. In 26 % of children measurable amount of cotinine was found in urine. Children were mostly exposed to tobacco smoke outside their homes.

P.08

0019

Selected results of human biomonitoring studies in Slovenia - Cd, Pb, As and Se in blood

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Several cross-sectional studies following nearly the same protocol were conducted in recent years to assess the exposure of Slovenian population to environmental chemicals. In addition to current topics of environmental pollutants such as POPs, phthalates, BPA, parabens and triclosan we were also interested in toxic metals/metalloid including Hg, Pb, Cd and As. Additionally, status of essential elements Cu, Zn and Se was also assessed. Sampling in rural and urban sites was performed. Democophes pilot study included sampling of urine/hair/blood from 155 mother-child pairs and 69 men (fathers/partners). Within EU research project PHIME urine/hair/blood were collected from 150 children aged 6-11 and 60 women aged 50-60. In the framework of National Human Biomonitoring programme, 150 pairs (mothers-partners) were sampled in pilot study phase for urine/hair/blood/ mother's milk.

Significant difference between different population groups was observed for Pb and Cd in blood, fathers had the highest exposure to Pb and children lowest. In case of cadmium, the highest exposure was observed in mother's blood and the lowest in children. No significant difference between rural and urban areas was observed for Cd/Pb. Arsenic in blood was found to be higher in urban areas than in rural, mothers having the highest As exposure and children lowest. Selenium was the highest in fathers and the lowest in children. Overall Se level was significantly higher in urban areas. Contrary to Cd and Pb, significant difference between rural and urban areas were observed for As and Se in blood which could be explained by different dietary habits.

P.14

0032

Biomarkers of manganese exposure and neuropsychological deficits in adults environmentally exposed

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Manganese (Mn) is an essential element to humans, but in excess can cause neurotoxic damage. Mn exposure assessment has no ideal biomarker so far. This study aims to evaluate the association between endogenous levels of Mn measured by non-invasive biomarkers of exposure and neuropsychological effects in environmentally exposed adults.

Eighty-nine people living in two communities close to a ferro-manganese alloy plant in Bahia, Brazil were included in this study. Volunteers donated hair, fingernails and saliva specimens for Mn determination by graphite furnace atomic absorption spectrometry. Several neuropsychological battery tests were applied to evaluate the performances in motor, executive and cognitive functions; attention and memory were also evaluated.

Significant correlations were observed between manganese levels in hair (MnH) and IQ, visual working memory and motor function performances after Spearman correlation analysis. Mn levels in fingernail (MnN) correlated significantly with visual working memory, motor function and cognitive flexibility performances. No association was observed between manganese levels in saliva (MnSal) and any neuropsychological function. Multiple linear regression analysis detected an inverse association between log MnH and IQ (β= –4.763 [CI95% –9.171 to –0.355]) and between log MnN and visual working memory (β= –3.333 [CI95% –6.148 to –0.519]). Direct association was observed between log MnN and execution time of the cognitive flexibility task (β= 56.293 [CI95% 2.405 to 110.182]).

These results provide evidences that excessive Mn exposure, when measured by these non-invasive biomarkers, has detrimental effect on several neuropsychological functions of adults environmentally exposed.

P.15

0035

Manganese biological monitoring by non-invasive biomarkers in adults living near an alloy-plant

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Several biomarkers of exposure to manganese (Mn) are currently being used to assess its chronic exposure. Although Mn in hair is the most used biomarker and the better to correlate with neuroeffect endpoints, there is no consensus about it so far. The aim of this study was to assess Mn exposure levels by measuring it in hair (MnH), axillary hair (MnAx), fingernail (MnN) and saliva (MnSal) in environmentally exposed people.

Eighty-nine adults living in two communities close to a ferro-manganese alloy plant in Brazil were evaluated. Manganese levels were quantified by graphite furnace atomic absorption spectrometry. MnH, MnAx, MnN and MnSal levels (median and range) were 8.95 (0.62-44.61) µg/g, 18.49 (3.83-85.62) µg/g, 6.91(0.70-22.21) µg/g and 4.21 (0.36-81.63) µg/L, respectively. Statistically significant differences were observed in MnH, MnAx and MnN levels according to local of residence, unexpectedly in those living in the further community presenting the higher levels. Mild direct correlations were observed between MnH and MnN levels (Spearman rho=0.473, $p<0.001$) and between MnAx and MnSal levels (rho=0.547, $p<0.05$). Strong correlations were observed between MnH and MnAx levels (rho=0.703, $p<0.01$) and between MnAx and MnN levels (rho=0.792, $p<0.001$). MnN levels were significantly associated (rho=0.226, $p=0.047$) with time of residence in the community, a variable that reflects chronic and cumulative exposure.

These results revealed elevated airborne Mn exposure in the studied population and demonstrate that MnH and other biomarkers, especially MnN, may be used as a surrogate of internal dose in environmentally exposed individuals.

P.21

0058

Occupational PCB exposure in Finland: results of biomonitoring in 2002-2012

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Aims

The aim of this study was to evaluate the occupational exposure to polycarbonated biphenyls (PCBs) in Finland between 2002 and 2012. In addition, PCB analytics applied at FIOH and reference limit for non-occupationally exposed persons was reviewed.

Methods

GC-MS was used to analyse PCB congeners in fasting serum. 24 PCB congeners were measured until 2007, when the method was reviewed and the use of 8 main congeners was tested. Concerning the reference data on general population 24 PCB congeners were measured. The results were given as a sum of 24 PCB congeners (=total PCB).

Results

In 2002-2003 the average total PCB concentration was 1.3 ug/l, 95th and 99th percentiles around 3 ug/l and 5 ug/l (n=2360). Since that the average total PCB concentration has decreased to a level of 0.5-0.6 ug/l, where it has remained over 2010-1012. The respective 95th and 99th percentiles were 1.5 ug/l and 2-3 ug/l. Highest concentrations were obtained in joint sealing.

It was found that measuring 8 PCB congeners and converting the results to that of 24 congeners with the aid of a correction factor worked fine.

The results obtained with general population in 2011 were the following: average total PCB 0.9 ug/l and 95th percentile 2 ug/l (n=100). Based on this data, the FIOH reference limit for non-exposed was corrected from 3 ug/l to 2 ug/l.

Conclusions

Both occupational and environmental PCB exposure in Finland has decreased. The occupational results exceeding the reference limit were rarely obtained during the last couple of years.

P.30

0078

REFERENCE VALUES FOR SELECTED ORGANOCHLORINATED COMPOUNDS IN SERUM BY USING TRIPLE QUADRUPOLE GC-MS/MS

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Aims. The objective of this work is the establishment of reference (background) values of some selected organochlorinated compounds for different population groups living in Italy.

Methods. A GC-MS/MS multiple reaction monitoring (MRM) method has been developed and validated on the Agilent 7890A/7000A GC triple quadrupole mass spectrometer system (GC/QQQ). The extraction procedure had been previously validated on single quadrupole GC-MS. Serum samples from general population groups, were collected and analyzed for 15 PCB congeners (#31, 52, 77, 81, 101, 105, 118, 126, 128, 138, 153, 169, 170, 180), selected on the basis of their occurrence and toxicity, and for 10 organochlorinated pesticides (HCB, three HCH isomers, and six DDT isomers).

Results. The method was validated in the range 0-10 µg/L. The limit of quantification was 0.025 µg/L for alpha-, beta-, and gamma-HCH, HCB, p,p'-DDE, o,p'-DDT, o,p'-DDE, PCB 31, 28, 52, 101, 105, 153, 138, 156, 180, 170, and 0.050 µg/L per p,p'- and o,p'-DDD, p,p'-DDT and for congeners #77, 118, 126, 128 and 169. Uncertainty has been also evaluated, and has confirmed the reliability of the results. The productivity of the method has been further implemented so as to avoid false positives or overestimation in real samples.

Conclusions Multiple Reaction Monitoring (MRM) helps producing clear data to help evaluate complex samples at lower levels. The implementation of the procedure, with special regard to an increased sensitivity with the adequate uncertainty on the results, has allowed to provide more realistic reference values for the target analytes in the general population.

P.34

0084

Internal dose of metals in Italian urban adolescents.

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The first Italian human biomonitoring survey (PROBE - PROgramme for Biomonitoring general population Exposure) examined a reference population of adolescents, aged 13-15 years for their exposure to metals. The study included a total 453 adolescents as representative of subjects of the same age living in Italian urban areas. Whole blood specimens were analyzed for metals, namely, As, Be, Cd, Co, Cr, Hg, Ir, Mn, Mo, Ni, Pb, Pd, Pt, Rh, Sb, Sn, Tl, U, V and W, by sector field inductively coupled plasma mass spectrometry. The aim of the campaign was to improve: i), the evaluation of the metals internal dose with regard to specific sites of residence; ii),, the assessment of reference values (RVs) suitable as reference terms for public health prevention and protection.

P.42

0097

Human biomonitoring studies in Slovenia - mercury

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In Slovenia, several cross-sectional studies following the same protocol were conducted to find out to what extent the Slovenian population of women in childbearing age (N=550), women 50-60 years (n=60), men (n=210) and children 6-11 years (n=300) is exposed to environmental chemicals including Hg. Different geographical regions including rural and urban environments, as well as contaminated sites were included.

Combining results of different studies, we found out overall Hg blood level was significantly higher in urban areas (GM=1.13 µg/L) than in rural (GM=0.818 µg/L) ($p<0.001$). Significant difference was observed also between different population groups - fathers/partners having the highest exposure to Hg (GM=1.47 µg/L) and children the lowest (GM=0.708 µg/L) ($p<0.001$). Hg levels were also dependent on age groups, showing elevated levels in older population. Hg levels in blood and hair were dependant on frequency of fish consumed, while the number of amalgam fillings affected levels in urine and human milk. Higher values in urine were also observed in families reporting broken thermometers and energy saving lamps. Also, Hg in urine in contaminated sites showed slightly elevated values. Mercury speciation in blood, hair and human milk was also done in a subset of samples; indicating high percentage of Hg as MeHg in blood and hair, while maternal milk exhibited significantly lower concentrations.

Experimental studies

P.26

0073

Methamidophos volunteer study to define expected urine levels after ingestion of the Acceptable Daily Intake.

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An oral dose of the organophosphate insecticide methamidophos was administered to six volunteers at the acceptable daily intake (ADI, 0.004 mg/kg).

Urine was collected from the volunteers at timed intervals for at least 24 hours post-exposure. Methamidophos itself was quantified in the urine using liquid/liquid extraction and LC-MS-MS analysis (detection limit 7 nmol/L, CV (70 nmol/L) =4%).

Methamidophos exhibited a rapid elimination half-life of 1.1 hours, (range 0.4 - 1.5hrs). Mean methamidophos levels found in 24-hour total urine collections were 1.39 µmol/mol creatinine (range 0.23-2.80). One volunteer was exceptional; excluding this result, the range was 2.07-2.8 µmol/mol creatinine, with a mean of 1.72. Individual urine samples collected over the first 24 hours ranged from below the detection limit up to 237nmol/L.

Two environmental studies have been reported in the literature with the following results: Montesano et al in Italy (N=499), 7.2 - 66 nmol/L, and Olsen et al in the US (N=140) 0 - 16.3 nmol/L, although the number of positive results in both studies was low (~1.5% of total samples analysed).

When compared with our results (up to 237nmol/L for a spot urine sample), the studies suggest general population exposure within that expected from exposure below the Acceptable Daily Intake.

P.45

0102

Urinary excretion of 2-ethoxyacetic acid after exposure to 2-ethoxyethanol in volunteers

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Aims

Biomonitoring of 2-ethoxyethanol (EE) by determination of 2-ethoxyacetic acid (EAA) in urine is preferred to analysis of workplace air if significant dermal absorption of EE occurs. In this study, a new method of EAA determination was developed and kinetics of EAA excretion was characterized with the aim to reappraise the biological exposure limit thereof.

Methods

Five volunteers were exposed to EE at 29.4 mg/m^3 for 4 h. Urinary EAA was converted to ethyl ester and determined using head space - solid phase microextraction combined with gas chromatography - mass spectrometry.

Results

In exposed volunteers, the excretion rate of EAA reached its maximum 24 h post-exposure (12.5 mg/g creatinine) and then declined exponentially with a half-life of 78 h. A mathematical model of the cumulation of urinary EAA during repeated exposure to EE (5 d, 8 h/d) was constructed. For current occupational exposure limit of EE (8 mg/m^3), 8 h/d exposure periods, and pulmonary ventilation of volunteers with no physical activity, EAA level at the end of last shift of working week was assessed to 22 mg/g creatinine.

Conclusions

At occupational exposures with higher pulmonary ventilation, EAA levels will be enhanced proportionately. Thus, the current biological exposure limit for EAA (50 mg/g creatinine at the end of working week) is supported by our study. From the volunteers' urine, freeze-dried reference material for determination of EAA was prepared and made available commercially (http://www.comar.bam.de/en).

Acknowledgement: The study was supported by the grant NS 9644-4/2008 from Internal Grant Agency of the Czech Ministry of Health.

P.48

0111

Time profiles of permethrin metabolites in orally exposed volunteers

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Pesticide exposure is a wide concern. Biomonitoring of pyrethroid [YUN1] insecticides is largely conducted but the toxicokinetics has not been fully documented. Knowledge of the time profile of exposure biomarkers is essential for a proper interpretation of biomonitoring data.

The time courses of key biomarkers of exposure to a largely used pyrethroid, permethrin, were assessed in biological matrices of orally exposed volunteers. Six volunteers ingested 0.1 mg/kg bw of permethrin acutely. Blood samples were taken at fixed time periods over 72 h post exposure and complete urine voids were collected over 84 h post dosing. Analysis of *cis*- and *trans*-2,2-(dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acids (*trans*- and *cis*-DCCA) and 3-phenoxybenzoic acid (3-PBA) metabolites were quantified in these samples using an ultra-high performance liquid chromatography tandem mass-spectrometry time-of-flight system (UHPLC-MS-Q-TOF).

A similar bioexponential plasma-concentration time course was observed for all three metabolites over the 0-48 h period post-dosing. Maximum plasma values were reached ≈2 h post dosing, showing a rapid absorption. Subsequent elimination phase had an average apparent half-life of 10.5 h for *trans*-DCCA, 11 h for *cis*-DCCA and 18 h for 3-PBA. Plasma concentration-time courses and urinary excretion rate profiles evolved quite in parallel as expected. From the urinary rate profiles, peak rate was observed within 8 h post dosing and average apparent elimination half-lives were calculated to be less than 14 h.

Overall, >97% of the permethrin dose was eliminated from the body after 48 h. These data provide valuable kinetic data for this contaminant to assess internal exposure accurately.

P.56

0124

Manganese: A Potential Reprotoxicant or Not?

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Essential nutrient manganese impacts our lives, not only from a health perspective but also from its numerous applications such as objects made of steel, of portable batteries, or of aluminum beverage cans. However, in occupational settings high levels of exposure may occur or low levels over a long period of time may lead to some adverse health effects. Contradictory findings exist on reproductive effects upon such exposures. The aim of this study is to investigate if manganese is a reprotoxicant using manganese chloride ($MnCl_2$).

Four groups of Sprague Dawley rats, 20 per group (10 females and 10 males) were exposed to $MnCl_2$ via the inhalation route (nose only) for 9 weeks at concentrations 0 (control -air only) 5, 10, and 30 ug/L of Mn respectively. At target levels 5 and 10 µg/L (actual 3.79 and 9.92 µg/L), a slight intergroup difference in body weight gains and food consumption was seen but not positively attributed to $MnCl_2$ exposure. Meanwhile, at target levels 30 µg/L (actual 26.26 µg/L) adverse clinical signs on the respiratory tract were seen in 1 male and 2 females resulting in the premature sacrifice of these animals and the cessation of exposure to the test material on the other animals in this group after ca. 3 weeks of treatment (early gestation).

At the end of the study, it was concluded that $MnCl_2$ did not affect mating performance; sperm viability and count; fertility and the duration of gestation in all groups, hence could not be considered a reprotoxicant.

New approaches and new analytical techniques

P.11

0027

Human metabolism and renal elimination of selenium according to the absorbed species

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Aim

The aim of this study was to investigate the toxicokinetics of orally administered sodium selenite, sodium selenate and selenomethionine in human to understand whether and how far absorption, metabolism and elimination diver between these compounds.

Methods

For a defined selenium exposition three different dietary supplements containing either 50µg Se as sodium selenate (group A), 200 µg Se as sodium selenite (group B) and 100 µg Se as selenized yeast (group C) were used. Each supplement was orally administered to six subjects and afterwards their urine for 24h successively collected. In each sample the total selenium content as well as the concentrations of selected Se species were determined.

Results

The amount of selenium eliminated within 24h ranged between 27.3 – 56.9 µg for the selenate administered group, 24.0 – 69.2 µg for the selenite administered group and 23.0 – 60.6 µg for the selenomethionine exposed group. The courses of elimination of total selenium differed between the three groups distinctly. After selenate exposure a fast renal elimination of selenium with a maximum about 2h after intake was observed, whereas the elimination courses were prolonged for the subjects of group B and C. Subjects, who were exposed to selenate, eliminated a huge amount (19.6 – 37.8%) of the administered selenate unmetabolized. In contrast selenosugar1 represented the dominant metabolite after exposure to selenite and selenomethionine, respectively.

Conclusions

The data indicate clearly differences in the toxicokinetics of different selenium compounds. Further investigations shall reveal whether the different toxiokinetics may be relevant for their toxicity.

P.20

0057

Design of Environmental Health Biomonitoring Physical Activity and Nutrition Survey called "Esteban"

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Aims: Esteban addresses the following fields in monitoring: environmental health, nutrition and chronic diseases. The study's objectives are:

- 1) describe levels of impregnation and some of their determinants, establish reference values
- 2) describe food consumption and physical activity
- 3) estimate the prevalence of chronic diseases (diabetes, chronic kidney disease, COPD, asthma) and cardiovascular risk factors (hypertension, dyslipidemia) and the part of undiagnosed diseases
- 4) estimate the prevalence of atopy, asthma and allergic diseases in children

Methods: Over a 1-year period to take into account the seasonality of food and exposure to environmental substances, a sample of 5,000 people residing in continental France and aged 6-74 will be recruited to:

-answer 2 questionnaires submitted by an interviewer at the participants' home and a self-administered questionnaire on occupational and environmental (housing, leisure...) exposures, and food consumption;

-undergo a clinical examination in an health center or at home, including sampling of blood, urine and hair in order to analyze environmental biomarkers belonging to about 16 families of chemicals and to constitute a biobank. Inclusions will begin in 2014.

Results: Protocol and biomarkers selection (based on an expert consensus method, followed by stakeholders consultation) were completed.

Conclusion: This survey will offer a unique opportunity to assess the levels of impregnation of the French population by many chemicals. It will then allow comparison across time, and will be complementary with other national initiatives. The results will be compared with surveys conducted abroad (e.g. in other European biomonitoring programs).

P.43

0099

Specific and sensitive quantification of seven metabolites of synthetic pyrethroids in human urine using GC/MS/MS

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Background: Synthetic pyrethroids are among the most effective insecticides used worldwide with a broad range of applications. The main sources of exposure for the general population are pyrethroid residues in food as well as their use for the conservation of wool carpets or in indoor pest control. Besides their neurotoxicity, some pyrethroids are suspected to be endocrine disruptors, stressing the importance of human biomonitoring.

Aims: Our research was aimed to develop a method for human biomonitoring of environmental exposure to the most common synthetic pyrethroids, including cyhalothrin and/or bifenthrin.

Methods: Based on previous works, we have developed and validated a highly sensitive and specific GC/MS/MS-method to simultaneously quantify the metabolites cis- and trans-Cl2CA, Br2CA, F-PBA, 3-PBA, ClF3CA and bifenthrin-alcohol in human urine. The limit of quantification for these metabolites was 0.01 µg/L urine (bifenthrin-alcohol: 0.2 µg/L). In a pilot study we applied this method to spot urine samples of 38 persons of the general population.

Results: cis-and trans-Cl2CA as well as 3-PBA were quantifiable in every urine sample analysed, while bifenthrin-alcohol could not be detected in any sample. The median levels for cis-Cl2CA, trans-Cl2CA, ClF3CA, Br2CA, F-PBA and 3-PBA were 0.08 µg/L, 0.17 µg/L, 0.04 µg/L, 0.04 µg/L, < 0.01 µg/L and 0.22 µg/L urine. The metabolites showed excellent correlations between cyclopropane carboxylic acids and 3-PBA.

Conclusions: Our method is highly suitable for human biomonitoring of exposures to synthetic pyrethroids in environmental medicine. In future applications, the internal exposure of professional pesticide applicators will be examined.

P.13

0029

The development of a "point of care" test (POCT) for benzene biomonitoring.

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Benzene is an important industrial chemical and common environmental pollutant. Benzene is also a known carcinogen and as a result there is a need to monitor exposure to this volatile solvent. S-PMA is a specific metabolite and sensitive biomarker of benzene exposure allowing the development of benzene biomonitoring programmes.

Traditional methods for the determination of S-PMA are laborious, expensive and require the use of sophisticated analytical equipment. Carefully designed S-PMA protein conjugates and a judicious screening strategy have enabled the development and validation of an S-PMA ELISA. The S-PMA antiserum has also allowed the development of a POCT for benzene exposure monitoring.

Thorough consideration has been given to urine hydration and S-PMA concentration. The target is for a test cut-off of 7.5µg/L which will distinguish between concentrated urines containing background levels of S-PMA and dilute urines containing elevated levels of S-PMA. Analysis of a database of occupationally exposed samples (N=2000) shows that a cut-off of 7.5µg/L would result in 12% of samples screening positive (comparing favourably with drugs of abuse screening).

The POCT will allow cheap and immediate on-site testing. The POCT will eliminate negative results and highlight positive exposures. Positive samples can then be sent to a laboratory for confirmatory evaluation and interpretation. A POCT will significantly reduce the cost of biomonitoring, allowing a greater number of samples to be determined at more regular periods. A POCT will provide "real-time" sample analysis to health professionals and immediate reassurance to workers involved in potentially hazardous tasks.

P.25

0071

Investigation of saliva as an alternative to blood samples for the biological monitoring of inorganic lead

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Aims

This study aims to collect paired samples of blood and saliva from workers occupationally exposed to inorganic lead.

Methodology

Twenty-two workers provided a saliva sample, using a Statsure sampling device, at the same time as a routine blood sample. Samples were hydrolysed for 1 hour at 100^{o}C using 0.5ml concentrated nitric acid. Analysis was by inductively-coupled-plasma mass spectrometry (ICP-MS, Thermo X7 Series 2) in normal mode measuring ^{208}Pb and using ^{195}Pt as an internal standard.

Results

Blood samples from workers showed lead levels ranging from 1 to 25 µg/dl (all below the UK suspension limit of 60 µg/dl). The paired saliva samples showed lead levels between 6 and 398 µg/l. A weak (p=0.065), but positive, correlation was seen between blood and saliva lead measurements. Two outliers in particular were noted where one matrix had an elevated level of lead whereas its pair did not. Excluding these two samples improved the correlation to r=0.68 with a 1:1 relationship between blood and saliva.

Conclusions

The initial data suggest a positive correlation between blood and salivary lead levels with roughly a 1:1 relationship. The data presented here are from workers - depending on their working history these workers may not be at steady-state with regard to lead exposure. The differences in lead absorption and elimination kinetics in blood and saliva would therefore potentially have an influence on the correlation in these samples. These variables are currently being investigated, with further recruitment and analysis also taking place.

P.40

0093

Simultaneous screening of sixteen biomarkers of occupational exposure in urine

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Aims

So far urinary biomarkers of occupational exposure to common industrial chemicals have been determined more or less separately. Here we report a comprehensive approach to rapid simultaneous identification and screening of sixteen acidic metabolites - biomarkers of exposure to benzene, toluene, styrene, xylenes, alkoxyalcohols, carbon disulfide, fural, and N,N-dimethylformamide in human urine.

Methods

The metabolites in urine were subject to a single step derivatization-extraction procedure with ethyl chloroformate - ethanol - pyridine - chloroform medium, followed by GC-MS analysis.

Results

Whereas some metabolites provided solely the expected products, others (e.g., hippuric acid or mercapturic acids) produced also analytical artifacts structure of which was clarified by targeted experiments. Furthermore, a GC/MS method was developed and validated for determination of fourteen most common biomarkers occurring at common levels (low µmol/L to mmol/L) in the urine of exposed persons.

Conclusions

The described method provides a simple and versatile analytical tool for rapid determination of the acidic xenometabolites and opens a way to their comprehensive metabolomic investigations together with endogenous metabolites in persons exposed to harmful industrial chemicals.

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P.47

0108

Automated Preparation of Blood, Urine and Serum Samples for ICPMS Analysis - Offline and/or Inline

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Blood, urine and serum samples need to be diluted prior to analysis by ICPMS due to their high dissolved solid and/or organic content. Sample preparation as well as being the rate determining step in sample analysis throughput, is also one of the key points at which sample contamination can occur. Using the prepFAST™ system, the preparation of blood, urine and serum samples for analysis by ICP and ICPMS can be fully automated, reducing the chances of contamination and improving sample throughput.

The prepFAST can be utilized in both offline mode, where samples can be prepared prior to analysis by the ICP, or inline mode where the undiluted samples are analyzed directly. Utilizing offline mode, allows different types of samples to be prepared for final determination on multiple instruments. While, inline sample preparation minimizes the possibility of sample contamination.

Data for both modes of preparation will be shown with the relevant advantages/disadvantages being discussed.

P.52

0120

Smell test as effect biomarker for the occupational exposure to organic solvents

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Aims

Olfactory capacity is compromised by the exposure to neurotoxic solvents: its evaluation in occupationally exposed workers by smell tests, coupled to personal air monitoring, is investigated as an effect biomarker, to reveal early and still reversible adverse effects.

Methods

Eleven workers of a fiberglass-reinforced plastic plant, exposed to styrene and other solvents, and eleven matched controls, were evaluated using the Sniffin'Sticks (Burghart, Germany), based on a penlike odor-dispensing. The test is divided in Threshold (T), Discrimination (D) and Identification tests (I): the total score is TDI and normal value is > 30. The personal monitoring of styrene and BTEX was performed using Radiello samplers, and quantitative analysis by GC/MS.

Results

The median scores of the smell tests for the workers (34±4,8) are lower than those of controls (38±2,9) for the complete test (TDI). Only one subject (painter) resulted hyposmic (TDI = 27). Exposure data show an average styrene concentration of 107.8±41.1 mg/m^3 for molding workers and a lower level for the painter (4.2±1.0 mg/m^3) who is instead exposed to approximately ten times higher airborne BTEX than molding workers (5.6±1.0 mg/m^3 vs 0.5±0.1 mg/m^3).

Conclusion

The results are encouraging and, despite the small number of workers studied, indicate that the Sniffin'Sticks could be used for the detection of effect biomarkers of exposure to neurotoxic substances. Moreover results suggest that a synergic effect of solvent mixtures is possible and that these indications deserve further investigations.

P.57

0125

Application of a high sensitivity quadrupole ICP-MS for the ultra-trace determination of Be in urine.

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Beryllium is a difficult element to measure in clinical samples as the levels present are usually very low (in the part per trillion range). A highly sensitive analysis technique is therefore required, which necessitates use of ICP-MS instrumentation. Historically, this analysis could only be accurately achieved using high resolution ICP-MS, but recent advances in quadrupole ICP-MS instrumentation have enabled this lower cost technique to be more effectively applied than was previously possible. As beryllium and its compounds are classified as carcinogenic (class 1) to humans (IARC 2007), as well as Be being a known respiratory irritant and sensitising agent, a robust and reliable measurement method is essential for monitoring occupationally exposed workers, to ensure that their protective equipment is effective. Occupational exposure to beryllium can occur during its extraction and uses. Beryllium is most often used as an alloy with copper, aluminum, magnesium, or nickel and the beryllium content of these alloys and its hazards may not always be obvious to workers generating dust and fumes. Recycling of electronics, computers, and scrap alloy to recover copper can also result in beryllium exposure for an unknown number of workers. Biological monitoring of Be generally involves measurement of urine samples, as Be is known to be mainly excreted via this route. This poster describes application of a high sensitivity quadrupole ICP-MS instrument for improved measurement of ultra-trace concentrations of Be in urine samples.

New biomarkers, new and emerging hazard

P.05

0013

French survey of occupational exposure to mycotoxins. Biomarkers and airborne contamination measurements.

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Aims

Ingestion of mycotoxins from contaminated food products is deemed to constitute the main important source of exposure in the general population. There is also a growing interest in the role of mycotoxins as health hazards in the workplace. Mycotoxins have been identified in various occupational environments including poultry productions, agricultural and food processing facilities, livestock feed productions, indicating that inhalation and dermal contact may represent an additional route of exposure. To what extent such exposure results in potential risks for health for these workers remains unclear.

Methods

In order to obtain some data about occupational exposure to mycotoxins, the French Institute of Occupational Health sets up a project to assess external and internal exposure to mycotoxins in various workplaces with a focus on feed processing facilities, livestock and poultry farming. For external exposure, airborne contamination will be determined by personal and ambient air sampling. To investigate the respiratory and dermal intake, human biomonitoring of mycotoxins from a cohort of workers will be implemented. Ochratoxin A, aflatoxins, fumonisin, zearalenone, deoxynivalenol and their metabolites will be determined in urine using a multimycotoxin method by LC-MS/MS. For an interpretation of human biomonitoring data, the results will be compared with those obtained from non-occupationally exposed persons and the relation between airborne contamination and measured biomarkers will be examined.

Results - Conclusions

This survey, which will take place between 2014 and 2016, would allow the mapping of mycotoxins occurrence in occupational settings and further progress in assessing mycotoxins health impact in some typical environments.

P.39

0090

Isotriamine, a Biomarker of Isocyanurate Exposure in Automotive Spray Painters

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Exposure to 1,6-hexamethylene diisocyanate (HDI) monomer and its oligomers is associated with an increased risk for development of contact dermatitis and asthma in automotive repair workers. Isocyanurate derivatives represent the majority of inhalation and skin exposures in automotive spray-painting operations. Therefore, determination of the hydrolysate *N,N,N*-(6-aminohexyl)isocyanurate (isotriamine) as a biomarker of isocyanurate exposure would contribute towards more realistic exposure and risk assessment in this worker population.

Urine (1 mL) from 6 exposed spray-painters (n=24) was treated with acid and heated for 24 h and then extracted using solid-phase extraction. The extract was analyzed with ultra-performance liquid chromatography/tandem-mass spectrometry (UPLC-MS/MS) using a nanoAcquity UPLC system coupled to a TSQ Quantum Ultra triplequadrupole mass spectrometer. Reversed-phase separation was carried out using an Atlantis dC18 analytical column and analytes were ionized by nano-electrospray ionization and detected using selected reaction monitoring. The calibration curve treated with weighted linear regression ($1/x^2$) had a concentration range 0.4-4.0 µg/L (LOQ=0.4; LOD=0.2 µg/L).

Isotriamine was detected in 5 of 6 painters and in 10 of 24 urine samples. The isotriamine concentration in the workers' urine ranged from 0.34-0.72 µg/L. The isotriamine metabolite of isocyanurate in urine of workers exposed to HDI-containing spray paints has not been previously reported.

We have demonstrated that biological monitoring of exposure to isocyanurate can be performed and that the assessment of its exposure-dose relationship is warranted in future studies.

P.01

0001

Biological monitoring of workers exposed to indium compounds in Korea

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Insoluble indium compounds such as indium tin oxide (ITO), indium oxide (In2O3) and indium phosphide (InP) can induce lung disorders. Even though many Korean workers are exposed to indium compounds while they are involved in processes manufacturing and recycling indium compounds, there is no policy or regulation to protect them from occupational disease by exposure to indium compounds. We performed biological monitoring for domestic display industry workers treating indium compounds.

We monitored serum indium by ICP/MS, KL-6 and SP-D by ELISA as biological exposure index for workers of domestic indium oxide and ITO target manufacturers, display manufacturers and indium recyclers.

Among the subjects in 13 companies treating indium, 29 % of the target manufacturing workers, 30.3% of the indium recycling workers exceeded 3 μg/L of indium in serum, the reference value of Japan. KL-6 level, an index of interstitial lung disease, exceeded 500 U/mL, the reference value of Japan, as much as 23.9% and 33.3% for each process.

As there was no previous case of biological monitoring for workers exposed to indium compounds in Korea, the outcomes from this papers could be essential basis to establish biological monitoring measures for workers handling indium compounds, to develop health care guidelines and special medical surveillance.

P.09

0020

Sensitive monitoring of monoterpene metabolites in human urine for biomonitoring studies

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Aims

Monoterpenes are prevalent products of the biosphere**.** Because of their widespread appearance and use, the population is exposed in manifold ways. The most abundant monoterpenes are α-pinene, (R)-limonene, and Δ^3-carene. To study the human body burden and *in vivo* metabolism of these substances, a sensitive analytical procedure has been elaborated for the determination of ten monoterpene metabolites in human urine.

Methods

The method involves enzymatic conjugate cleavage, solid-supported liquid-liquid extraction and two-step silylation of the functional groups. The analysis is performed using gas chromatography coupled with chemical ionisation tandem mass spectrometry. For method assessment, a pilot study was conducted by analysis of urine samples from 36 occupationally non-exposed volunteers.

Results

The method proved to be sensitive and reliable with limits of detection of less than 0.4 µg/L in urine. Therefore, it is sufficiently sensitive for the measurement of α-pinene, (R)-limonene, and Δ^3-carene metabolite background levels. This was confirmed by the results of the pilot study, since the monitored metabolites of α-pinene and (R)-limonene were detected in 89 - 100 % of the samples. Although median levels were low for most of the metabolites, they showed partially broad concentration ranges, which may be explained by different surrounding conditions as well as dietary and life habits.

Conclusion

The present method is the first procedure for the simultaneous and reliable trace level analysis of ten monoterpenoid metabolites in human urine. Thus, it is applicable for the determination of α-pinene and (R)-limonene metabolite background levels in population studies.

Occupational exposures

P.03

0008

Biological monitoring of occupational exposure to di(2-ethylhexyl) phthalate (DEHP) related to the use of vinyl gloves

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Objective

Assess the occupational exposure to DEHP, phthalate classified by the European Union as a product toxic to reproduction, category 1B, in employees wearing vinyl gloves. As gloves are plasticized with DEHP with weak bound, the risk of cutaneous penetration can be envisaged.

Methods

Over 5 days of pre-and post-shift sampling, three urinary metabolites of DEHP, mono (2-ethylhexyl)phthalate (MEHP), mono (5-carboxy-2-ethylpentyl) phthalate (5cx-MEPP) and 2-ethylhexanoic acid (2-EHA) were quantified in 52 workers and 16 controls employees who did not wear vinyl gloves, from three hospitals. Mono(2-ethyl-5-hydroxyhexyl) phthalate (5OHMEHP),mono(2-ethyl-5-oxohexyl) phthalate (5Oxo-MEHP)were measured 2 years later. Analyses were performed by HPLC-MS/MS after on-line extraction. First, an analysis of gloves was carried out to ensure the presence of DEHP. Gloves contained 46% DEHP.

Results

Median concentrations of the pre and post-shift urinary samples in the exposed workers were 6.9 and 9.6 µg/l for MEHP, 20.9 and 29.3 µg/l for 5cx-MEPP and 31,0 and 38.5 µg/l for 2-EHA, respectively. In the controls, the corresponding values were 3.0 and 3.8 µg/l for MEHP,10.2 and 11.5 µg/l for 5cx-MEPP and 17.2 and 30.1 µg/l for 2-EHA, respectively. Statistics analysis performed with a mixed regression model, showed a statistically significant difference for MEHP and 5cx-MEPP between post-shift of controls and post-shift of holders of vinyl gloves. It's not valuable for 2-EHA.

Conclusion

A low exposure to DEHP related to the hold of vinyl gloves might be considered. The results should be confirmed by others studies.

P.18

0046

The relationship between exposure to benzene and the excretion of urinary t,t-muconic acid in petrochemical factory turnaround process workers

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Objective: Using laborers participating in the work of petrochemical factory turnaround process as subjects, this study aims to identify exposure to benzene in the air and examine the relationship between exposure and the excretion of urinary metabolites by measuring concentrations of urinary trans, trans-muconic acid (t,t-MA).

Methods: A passive sampler was used to measure the level of benzene in the air. In order to analyze urinary metabolites, the urine of laborers participating in the turnaround process was collected twice daily, before and after work. In addition, a survey was conducted on work factors and lifestyle habits as factors affecting the concentration of urinary metabolites.

Results: During the survey period, benzene was detected in the samples from all workers, and its average concentration was 0.16±0.22ppm. The average concentration of t,t-MA after work was 1.20±1.86 ㎎/g creatinine, and the results of analyzing urinary metabolites concentration before and after work showed statistically significant differences(p=0.003). There was also a statistically significant correlation (r=0.52, p=0.002) between the benzene in the air and the concentration of after-work urinary t,t-MA.

Conclusions: During the turnaround process, the average benzene concentration in workers was 0.16±0.22ppm, which was below the exposure limit, but their average t,t-MA concentration was 1.20±1.86 ㎎/g creatinine, which exceeded the exposure limit of 1㎎/g creatinine. The characteristics of turnaround process work require considerations such as underestimating the passive sampler being used and the skin absorption of benzene, and there needs to be a simultaneous assessment of working environment measurements and biological monitoring.

P.22

0061

Maintenance workers' multiple exposure to metals in biomass-fired power plants

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The aim of this study was to measure maintenance workers' multiple exposure to metals in order to find an association between exposure and the symptoms reported among workers exposed to ash. Exposure to ash containing aluminium, arsenic, lead, cadmium, and manganese is believed to increase the risk of numerous neurophysiological changes in workers, and may lead to Parkinson's and Alzheimer's diseases.

Maintenance workers' hand exposure was measured by hand washing samples and total exposure was determined by the urinalysis of metals. The maintenance workers washed their hands with sunflower oil before lunch and immediately after the working day. The oil was rubbed into their hands, which were then wiped with cellulose ester towels. The towels were analysed using ICP-MS, and the levels of arsenic, lead, cadmium, and nickel were measured. The urine samples were taken according to the instructions of the biomonitoring laboratory and were also analysed using ICP-MS.

The total amounts of arsenic, lead, cadmium, and nickel on workers' hands were 3.7-17 $ngcm^{-2}$, 2.4-790 $ngcm^{-2}$, 0.6-3.0 $ngcm^{-2}$, and 4.9-450 $ngcm^{-2}$, respectively. Urinary excretions of aluminium, arsenic, lead, and manganese were 0.2-0.7 $\mu mol\ l^{-1}$, 15-30 $nmol\ l^{-1}$, 0.004-0.013 $\mu mol\ l^{-1}$, and 6-28 $nmol\ l^{-1}$, respectively.

Dermal and total exposure measurements revealed that PPE does not fully protect workers against ash, which might expose them to metals and cause the reported health effects. Routine use of powered air respirators with ABEK+P3 cartridges, coveralls and protective gloves was recommended for the workers.

P.24

0064

Biomarkers of sevoflurane exposure in operating room personnel: a still open debate

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Aims: To study the correlations between environmental sevoflurane levels and urinary concentrations of sevoflurane (Sev-U) or its metabolite hexafluoroisopropanol (HFIP), and to discuss the main related issues to establish the best biomarker of sevoflurane exposure.

Methods: On 100 healthcare operators from many hospitals of the north-east Italy, the personal sevoflurane exposure was performed by Radiello and Sev-U and HFIP were dosed in urine collected at the end of operating-session. All analysis were carried out by gas chromatography-mass spectrometry. In addition, environmental pollution of sevoflurane in the operating rooms was performed continuously using an infrared photoacoustic analyzer.

Results: Our results showed very low levels of sevoflurane, generally less than 0.5 ppm with personal exposure in the range of 0.007-0.940 ppm (mean 0.116 ppm). Sev-U and HFIP concentrations were in the range of 0.1-17.28 µg/l and 5-550 µg/l, respectively. Both biomarkers are correlated statistically with the environmental exposure (Sev-U r=0.67; HFIP r=0.65) but with a large scattering of data. Sev-U seems to be influenced by peaks of exposure, especially when they happen at the end of operating-session, while HFIP levels by the exposure of the previous day. These issues could be explained, for both, with their half-life (2.8 and 19 h, respectively).

Conclusions: On the basis of our results, the two biomarkers could be used to assess the sevoflurane exposure, even if both of them, present some aspects that are not completely clarified. More researches are needed to choose the best biomarker and to contribute to the definition of the biological exposure limits.

P.33

0083

Biomonitoring of occupational exposure to PAHs and benzene at vehicle repair shops

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Introduction:

Mechanics and electricians working in vehicle repair shops are exposed to vehicle exhausts containing benzene (gasoline additive) and PAHs (diesel exhaust). The aim of this study was to monitor PAHs and benzene metabolites in vehicle repair shops workers in order to assess health risks.

Methods:

Workers from 8 vehicle repair shops were recruited and a biomonitoring study was implemented, based on the analysis of 1-OHP / 3-OHBaP (pyrene / benzo(a)pyrene metabolites) as well as S-phenylmercapturic acid (S-PMA, benzene metabolite) in urine samples collected at the end of working week. Analyses were performed using HPLC with fluorescence detection for PAHs metabolites and LC-MS-MS for S-PMA. Exposure conditions (polluting activities, LEV used, proportion of diesel engines repaired...) were recorded.

Results:

Low 1-OHP concentrations were measured, rarely exceeding 0.5 µmol/mol creatinine, and significantly higher levels were observed for smokers (geometric mean M_G: 0.25 µmol/mol) than for non-smokers (M_G: 0.08 µmol/mol). 3-OHBaP levels were extremely low, frequently below the limit of quantitation (0.05 ng/L) and never exceeding 0.1 nmol/mol creatinine. S-PMA levels remained low (M_G: 0.35 µg/g creatinine), rarely exceeding 2 µg/g creatinine, with again higher values among smokers.

Conclusion:

Altogether our results showed low exposures to PAHs and benzene for vehicle repair shop workers (mechanics, car body repairers, painters) and pointed out the strong influence of smoking on studied biomarkers levels under these exposure conditions. These results are coherent with the protective equipment used within repair shops (natural or mechanical ventilations associated punctually with vehicle exhaust extractions).

P.41

0094

Feasibility study to centralize French occupational blood lead levels

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The department of occupational health of the French Institute for Public Health Surveillance (Institut de veille sanitaire, InVS) was requested by the Ministries of Health and Work to establish an occupational blood lead level (BLL) surveillance system.

About 130,000 French employees, potentially exposed to lead, are regularly monitored for BLL during occupational health visit. However, no data on workers BLL are currently available at a national level. The objective of the new surveillance system is to centralize these BLL data to provide lead levels among French employees and to formulate workers surveillance recommendations.

In 2012, a feasibility study was initiated for one year in two pilot regions, Ile-de-France and Nord-Pas-de-Calais. For each BLL prescription, occupational health physicians are asked to fill a questionnaire including BLL result as well as information about the employee and his occupational activity and to send it to InVS. All employees monitored for BLL during occupational health consultation should be concerned.

This study will test the feedback of the experimental protocol and explore the feasibility to use individual BLL to monitor lead exposure of French employees and to follow the trend of BLL.

The final goal is to extend this system across the country to allow us to estimate BLL averages among employees according to occupation in France and access adequacy of current recommendations for workers surveillance, especially with regard to certain situations of work, age or gender.

P.44

0100

Bioaccessibility of vanadium, chromium, nickel and titanium present in welding aerosols

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Aims
The main aim was to assess the soluble metal content of welding aerosols and to relate these results to the concentrations in biological fluids.

Methods
137 referents and 137 welders were investigated. Welding aerosol solubility was characterised by use of artificial lung lining fluid simulant (Hatch´s solution). Exposure was assessed by full-shift air sampling on the two days preceding collection of blood/urine samples. Metals were determined by HR-ICP-MS and ICP-OES techniques.

Results
The geometric mean (GM) concentration of vanadium (V), chromium (Cr), nickel (Ni) and titanium (Ti) was statistically significantly higher in the welders´ urine as compared to the referents. There was observed a statistically significant correlation between Hatch soluble V in the welding fume sampled two days before collection of the biological samples and urinary V and serum V. No significant association was observed when Hatch insoluble V was considered. There was observed a statistically significant correlation between Hatch soluble Cr in the welding fume collected two days before and one day before urine sampling and Cr in urine. No association was observed when Hatch insoluble Cr was considered. Results for Ti and Ni will be presented as well.

Conclusions
The study shows that the analytical approach of using a lung fluid simulant like Hatch´s solution to mimic the dissolution of welding fume components in the lungs will improve associations between welding fume exposure and the concentrations of these components in biological fluids.

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P.49

0114

Plasma and urine manganese as short-term biomarkers of exposure

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Background

Despite evidence of adverse health effects resulting from exposure to manganese (Mn), biomarkers of exposure are poorly understood. Mn in whole blood has been the most commonly studied short-term biomarker, but literature presents mixed poor of its validity. Therefore, we consider the less-studied plasma (MnP) and urine (MnU) as short-term biomarkers of Mn, requiring very low limits of detection to obtain meaningful results.

Methods

Ten students enrolled in a welding training program were enrolled at inception, and followed over a 10-week training program. Air, blood and urine samples were collected at the beginning and end of the first and last week of the period, with biological samples collected prior to, and after the work shift. Biological samples were analyzed by the trace metals laboratory at the UK Health and Safety Laboratory, which can achieve a limit of detection at least 3 times lower than our previous analyses, on the order of 0.092 ng/mL for urine. Results are examined in relation to time, and measured exposure during specific time windows prior to sample collection, including the day of sample, previous day, and cumulative exposure over varying time windows.

Conclusion

These analyses overcome many of the limitations of previous studies of Mn biomarkers and will support a more definitive determination of the quantitative validity of Mn in urine and plasma as biomarkers for Mn exposure.

P.50

0115

Hair as a biomarker for welder's exposure to manganese

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Aims: Determine if hair can be used as a biomarker for welders exposed to manganese (Mn). Specifically: Does hair Mn increase with time in welding school program and with cumulative air exposure.

Methods: Welding students are enrolled in the study as they enter a training program and followed for subsequent Mn exposure with air sampling and collection of biomaterials. Individual Mn air exposures (247 samples) were measured with personal sampling pumps on the Monday and Friday of the first and last week of each welding school quarter. Hair samples were collected from 47 welding school students by cutting 1 cm bundles proximal to the scalp and washed. All hair and air samples were acid digested and analyzed with ICP-MS. Individual daily air exposure by welding type was calculated with a random effects model. For each hair sample the student's duration in the welding program at hair sampling time and a 30 day cumulative exposure was calculated.

Results: Preliminary results indicated low hair Mn levels (1.1 ± 1.4 µg/g) in students without prior exposure that increased from baseline to 2.9 (± 4.1) and 4.8 (± 7.3) µg/g after 3 and 6 months welding training. Mn hair samples increased similarly with increasing cumulative exposure.

Conclusions: The ability to detect an increase of hair Mn with time and with increasing cumulative exposure suggests that hair Mn may be a suitable biomarker for inhaled Mn exposure but requires additional quantitative evaluation.

P.53

0121

Validation of analytical method for biological monitoring of benzene exposure

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With strict regulation on benzene exposure, the concern focuses on benzene exposure of chronic low level along with less tendency of high level exposure. To search for the clue for a case requesting compensation for leukemia, urinary S-phenylmercapturic acid (SPMA) and trans,trans-muconic acid (tt-MA) was investigated.

For biological monitoring of workers in an electronic factory, GC/MS method was applied for analysis of SPMA and tt-MA after pre-treatment of samples by derivatization of dried residue with acidic methanol following liquid-liquid extraction of acidified sample with ethyl acetate. The accuracy of analysis was 99 - 104% for SPMA, and 102-106% for tt-MA. The precision of analytical method was 10.7% of coefficient of variance(CV) for SPMA of 12 - 100 ug/L, and 5.1% of CV for tt-MA of 0.5 - 2 mg/L. The detection limit of SPMA and t,t-MA was 3.3 ug/L and 0.13 mg/L, respectively. SPMA and tt-MA corrected by creatinine for 21 workers in an electronic factory and 14 controls were both lower than biological exposure index regulated in Korea, 50 ug/g creatinine for SPMA and 1 mg/g creatinine for tt-MA.

P.54

0122

Occupational exposure to low-doses of styrene and biological monitoring: state of the art and future prospects

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Aims

There is a growing interest in defining new biomarkers for low-doses exposures, which presently characterize workplaces. The paper is intended to summarize the available biomarkers and define future prospects with regard to low levels of exposure to styrene.

Methods

For each possible human metabolic pathway, traditional and newer biomarkers of styrene exposure were examined, taking into account all the accessible biological matrices.

Results

Urinary mandelic acid (MA) and phenylglyoxylic acid (PGA) are still the most reliable and sensitive metabolites for the biological monitoring of styrene, despite there are some confounders for the quantitative relationship between styrene exposure and the urinary concentration of MA+PGA, such as the consumption of ethanol or the co-exposure to ethylbenzene. Biomarkers of styrene exposure also include 4-vinylphenol, but it is also an important constituent of cigarette smoke. The use of urinary mercapturic acids as indicators should be supported by the characterization of the genetic polymorphism of exposed worker. Finally, the study highlights the usefulness of unmetabolized styrene in saliva, already validated for high levels of exposure, also at low-doses: because of its low concentration, it requires appropriate enrichment procedures.

Conclusion

The reduction of exposure doses and the lack of specificity of some biomarkers, that could be affected by voluptuary habits or co-exposures, emphasize the need for new exposure biomarkers, more specific and sensitive, able to discriminate between styrene exposure and confounding factors.

P.55

0123

Handling of mercury containing medical devices and related issues among nurses in a tertiary care paediatric hospital in Sri Lanka.

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Aim

To describe the use of mercury containing medical devices and accidental exposure, management of spillage and disposal of mercury among nurses at Lady Ridgeway hospital, Sri Lanka.

Methodology

A descriptive cross-sectional study was conducted among nurses (n=538) working in Lady Ridgeway Hospital. Information on use of mercury containing medical devices, and accidental exposure, management of spillage and disposal of mercury was gathered using a self-administered questionnaire

Results

Nearly half (47.0%,n=222) of the study population had used only mercury thermometers. Of the 347 who used mercury thermometers, 1.4%(n=05) had experienced more than 50 thermometer breakages in their units during the 3 months period prior to the study. With regards to mercury sphygmomanometers, 85.8%(n=405) had used them and 20.0%(n=81) had been involved in mercury sphygmomanometer breakages in their units. Of the study population, 271(57.4%) had either cleaned a mercury spillage or had supervised a mercury spillage being cleaned. During the last such mercury spillage that they managed, 112 (41.3%) had incorrectly collected mercury and glass pieces together. The collected mercury globules and pieces of glass had incorrectly been disposed to the sharps bin by 67.0% (n=75). A total of 199 (42.2%) have received some training on managing a mercury spillage. Wearing gloves before cleaning a mercury spillage (p=0.196) were not statistically associated with previously having a training on managing a mercury spillage.

Conclusion

Gaps in practices on managing a mercury spillage were evident. Thus effective training activities at the basic nurses' training and in-service training programmes are recommended.